AFRICAN JOURNAL OF MEDICINE
and Medical Sciences

Website: http://www.ajmms.com
 ISSN 1116-4077 EISSN 2659-143X

AFRICAN JOURNAL OF MEDICINE
and Medical Sciences

Aims

The aims of *The African Journal of Medicine and Medical Sciences* are: (1) to provide a medium for wide dissemination of information resulting from biomedical research in Africa and elsewhere; (2) to act as a channel whereby appropriate international medical and health organisations may transmit information to medical scientists throughout Africa; (3) to serve as a medium for publication of proceedings of international conferences on medical sciences in Africa; (4) to serve as a medium for the exchange of information and opinion among medical scientists in medical institutions of Africa and elsewhere; (5) to promote inter-regional cooperation amongst medical scientists in Africa.

Publication details

The Journal is owned and published by the College of Medicine, University of Ibadan, Ibadan and the University College Hospital, Ibadan. The Journal is published quarterly; four issues form one volume and feature in Index Medicus.

All correspondence should be addressed to the Editorial Office, African Journal of Medicine and Medical Sciences, Institute for Advanced Medical Research and Training (IAMRAT), College of Medicine, University College Hospital, Ibadan, Nigeria. Telephone Numbers: 08190563347 and 08023451177. Fax: 234-022411768. E-mail: afrijmed@ comui.edu.ng; afrijmed@yahoo.com. Website: http://www.ajmms.com

The overseas subscription price for Institution is £400.00 (sterling) or $400.00 while personal subscription rate is £200.00 (sterling) or $300.00. The subscription price for local subcribers is available on a special form at the Editorial Office on request.

Orders for subscription (current and back issues), advertisement and all other business correspondence, including orders for offprint should be forwarded to The Business Manager, African Journal of Medicine and Medical Sciences, IAMRAT, College of Medicine, University College Hospital, Ibadan, Nigeria,

Notes for Contributors

All manuscripts should be addressed to the Editorial Office of the African Journal of Medicine and Medical Sciences, Institute for Advanced Medical Research and Training (IMRAT), College of Medicine, University College Hospital, Ibadan, Nigeria. African Journal of Medicine and Medical Sciences is an official journal of the College of Medicine, University of Ibadan, Nigeria and it is published four times a year in March, June, September and December. The journal is an educational and training resource integrating clinical, translational and educational research towards promotion of innovations in medicine and medical sciences. The Journal endorses the Uniform Requirements for Manuscripts (URM) issued by the International Committee of Medical Journal Editors (ICMJE): details of their current recommendations on the conduct, reporting, editing and publication of scholarly works in medical journals can be accessed at: http://www.icmje.org/recommendations.

Manuscripts are accepted on the understanding that no substantial part has been or will be published elsewhere. This does not refer to abstracts of oral communications that are printed in proceedings of societies or symposia.

Manuscripts should be submitted online through the journal submission system, accessible through: http://www.ajmms.com. The corresponding author will be required to register as an author on the submission site prior to submitting the manuscript. The type of manuscript must be specified during the submission process.

Cover Letter: Manuscripts being submitted must be accompanied by a covering letter affirming that the manuscript is being submitted only to this Journal. In the case of a manuscript with more than one author, all authors must sign the covering letter confirming that they participated sufficiently in the work.

Formatting: Manuscripts, in English Language, should be submitted typed double-spaced with margins of at least 2.5cm. Microsoft Word or similar software should be used to prepare the manuscript. The main text (excluding abstract, tables and references) of original research articles, review articles and case reports should not exceed 3,000 words, 5,000 words and 2,000 words respectively. Workshop and conference reports are welcome and should not exceed 3 to 10 double-spaced A4-sized pages. Viewpoints, which could be papers expressing personal or group opinion on political, socio-economic and other matters as they relate to the practice of medicine should be limited to 2,500 words. Letters to the Editor may be comments on articles published in the Journal or clinical observations, replies to comments, or other matters of importance and relevance to medicine and related professions. Such letters should not exceed 500 words with not more than eight references and one or two tables and figures.

Original research articles should include the following sections: title page, abstract, introduction, methods, results, discussion, references, acknowledgements, tables and figures.

The title page is submitted as a separate document and should contain the following: (a) title, (b) author(s)'s names and initials, (c) department(s) in which the work was done, (d) the name and address (including email address and phone number) of the author to whom correspondence should be addressed, (e) author(s)'s present address if different from the department(s) in which the work was done, (f) if the paper was presented at a meeting, the name of organization, city, month and year should be provided.

The title should be short, specific and clear. Omit phrases such as "The use of, "observations on". Authors should provide a short running title and four to six keywords that are arranged in alphabetical order. Manuscripts should include a structured abstract not exceeding 250 words on a separate page. The abstract will be translated into French by the journal office at a cost to the author. The numbers of photographs and illustrations in the manuscript should be kept to a minimum. The legends for figures and tables should be numbered in Arabic numerals and should appear on a separate page after the references. Any footnotes to tables should be indicated by superscript characters and tables must be referred to in the main text in running order. Tables must be simple and not duplicate information given in the text. Authors should not use abbreviations in headings and figure legends.

All figures should be clear and of reproducible quality. All details on charts and graphs must be legible when reduced to the size used in this journal. The author(s) will be required to pay for publication of coloured figures at the time of acceptance.

The onus of preparing a manuscript in a suitable form for publication rests with the author(s). The need for editorial revision for badly prepared typescripts or diagrams may lead either to rejection of the manuscript or delay in publication.

Ethics: **Authors should indicate by a statement in the body of the manuscript that they complied with the standard requirements of the Ethics Committee of the institution in which the work was done. A Letter of Ethics Committee approval must also accompany the manuscript at the time of submission. In addition, the Helsinki Declaration principles as revised should be followed strictly. In all research involving experimental animals, evidence of ethical approval by the appropriate ethics review committee must be provided. The details of anaesthesia, housing and husbandry in experimental animals must be provided in relevant manuscripts. The authors are required to comply with the US National Research Council's "The Guide for the Care and Use of Laboratory Animals" or similar international approved guidelines.**

The authors must declare any conflicts of interest in a sentence after the Acknowledgement section. The authors must comply with ICMJE guidelines on authorship and the

reported to the African Journal of Medicine and Medical Sciences will be investigated.

Plagiarism: The Journal does not tolerate plagiarism of any sort. All listed authors must indicate that the work being submitted is original. Any concerns about plagiarism will be investigated comprehensively and misconducts may lead to rejection, sanctions and/or retraction of article.

References: This Journal will only consider manuscripts with references prepared in accordance with the Vancouver style. Citation of references within the body of the article should be in block form, i.e., [1,2].

References should be numbered in the order in which they are cited in the text. At the end of the manuscript, the references should be listed as numbered in the text. Each reference should give the names and initials of all authors (unless there are more than six, when only the first three should be given, followed by *et al.*). The authors' names should be followed by the title of the article, the journal title (abbreviated according to the style of *Index Medicus)*, the year of publication, the volume number and the first and last page numbers. Titles of books should be followed by the publisher, place of publication, and year. Examples of the format for references are as follows:

Edington GM, Osunkoya BO and Smith JA. Immunopathology of Burkitt's lymphoma. West Afr Med J 1986; 85: 76 – 87.

Brown A. Primary Health Care and the Medical Curriculum Edinburgh: Universities Press. 1977.

Lewis A. Primary liver cell carcinoma. In: Ajose A. and Odeku E.L. (Eds.) Priorities in Health Planning. Ibadan: University Press, 1983; 110 - 117

Reference to tables should be in Arabic numerals, e.g. Table 3, and tables should include titles, which are easily understood without reference to text. Tables should be typed separately from the text.

Processing fees: A non-refundable processing fee of ₦10,000.00 (£100.00, $160.00) per article will be charged authors who do not subscribe to the Journal while subscribers will pay ₦5,000.00 only. Furthermore, a non-refundable acceptance fee of ₦25,000.00 (£100.00, $160) per article is charged author(s) who do not subscribe to the Journal while subscriber will pay ₦15,000.00. In addition, the fee for abstract translation is ₦2,500.00 ($50.00) non-refundable, which shall be paid when manuscript is found acceptable for publication. Payment should be made through electronic transfer or bank deposit on www.remita.net The payment should be in favour of College of Medicine, University of Ibadan while the service type is "grant processing and admin. fee." Generated receipt and bank teller should be presented at the Finance Department where College receipt will be issued. Non-Ibadan resident contributors can forward the remita receipt to afrijmed@yahoo.com. In addition, authors of manuscripts submitted from Nigeria should send ₦500.00 worth of postage stamps for subsequent correspondence.

Peer Review: The African Journal of Medicine and Medical Sciences operates a double-blind peer review system. "Blinded" versions of the manuscript, which do not contain any author details, must accompany the submission and will be reviewed by the Editor in Chief and sectional Editor. Submissions that are considered suitable at this stage will then be sent to a minimum of two independent experts in fields relevant to the subject of the manuscript to evaluate the scientific quality, merit and integrity. The reports of the reviewers will be communicated to the corresponding authors. The decision to accept or reject manuscripts is entirely that of the editorial team of the Journal and such decision is final.

After acceptance of manuscripts, galley proofs are sent to the corresponding author for review. Correction of proofs other than printers' errors should be kept to a minimum. Authors must return proof corrections within three days of receipt. Failure to do this will result in the article being published with the Editor's corrections only. Articles accepted for publication remain the copyright of the Journal.

Offprints, which will be available in the Editorial office of the Journal must be paid for at the time of final acceptance of the paper. Four journal pages will be printed at four hundred and fifty naira (₦450.00). Extra pages will attract page-printing charges at the rate of ₦700.00 (£5, $7) per page (approximately 5 quarto-size pages of manuscript).

This first article in this issue of the Journal will interest most readers who have been longing for alternative therapy for HIV infection bearing in mind the recent deluge of plausible and supposedly potent herbal remedies for the new Coronavirus pandemic (COVID-19). Onifade's review did not pinpoint any specific herbal agent as the one to use but cautioned about efficacy, safety profile, and possible drug interactions. It is gratifying that the common treatment combinations for acute uncomplicated falciparum malaria (artemether-lumifantrine vs. artesunate-amodiaquine} were reported to be free of cardiac toxicity according to the study by Funwei and others. The prescribing pattern of doctors was analysed by Opadeyi and colleagues who posited poor utilization of the Essential Medicines List and that more than 40% of the Doctors used generic names. Another study reported huge expenditure on cardiovascular and anti-infective drugs which would indirectly point at the pressing medical problems in our environment now.

Two articles are featured on infections – one on tinea infections with a prevalence of nearly 50% in a rural community, associated with low socio-economic conditions and prompting a call for better school-based health education services. The second article by Akere and others reported an alarmingly high burden of hepatitis B virus infection among apparently healthy subjects. Such asymptomatic carriers can spread the infection unless adequate immunization programmes are instituted. There are four manuscripts on oral health and dental procedures highlighting poor knowledge of caries prevention, high clinic default after tooth extraction procedure, restoration failure of non-carious cervical lesions particularly on the left side being more common in older males, and exploration of the myth surrounding natal and neonatal teeth in a rural community.

An echocardiographic study of dilated cardiomyopathy provides a revisit of the old problem of heart muscle disease and the findings by Adebiyi et al were structural and functional alterations. Higher socioeconomic status, urban residence, being employed and contraceptive use were reported to be linked with better child spacing and resulting in better maternal and child health. Balogun and others reported that about 50% of women suffer from spousal control, and this could be accompanied by gender-based violence. Low body mass index was common in women with advanced breast cancer and this can be linked with cachexia of malignancy. Diabetes mellitus was strongly associated with the development of Founier's gangrene which is a fatal condition. Kuti and colleagues determined the 10-year risk of cardiovascular disease from lipid measurements and reported positive correlations of some of the parameters with clinical applications. Lastly, Bello and co-workers noted the poor quality of life of caregivers of children with cerebral palsy and this was influenced by their age and educational status. These interesting articles make this issue a good collection of materials covering many specialties in health care and should stimulate further analytical research on some of these observations.

Tribute

Adieu Emeritus Professor Oladipo Olujimi Akinkugbe (1933-2020)

Emeritus Professor O. O. Akinkugbe died on Monday, June 15, 2020 at the ripe age of 86 years, one month short of his 87th birthday. He served the African Journal of Medicine and Medical Sciences as foundation Assistant Editor from April 1971 to December 1980. The pioneer Editor was Professor Olufemi Williams while Professor Benjamin O. Osuntokun was the second Assistant Editor. These trio in conjunction with a powerful Editorial Board established the journal as an important medium for disseminating information about medical sciences in Africa and elsewhere, a tradition of excellence that has endured.

Professor Akinkugbe had a chequered career as a teacher, clinician, researcher, and administrator. He rose to the position of preferment in October 1968 and was the Dean of the Ibadan Medical School between 1970 and 1974. He served as the Chairman, Board of Management of the University College Hospital (2000-2003. He distinguished himself in the field of hypertension and diseases of the kidney, and he was generally acclaimed as an authority on hypertension in blacks. He was passionate about reforms in medicine and tertiary education in Nigeria. He was a recipient of many national and international honours for his scholastic contributions and service to humanity. Notable honours were the Nigerian National Order Merit Award (NNOM) and the

Commander of the Federal Republic of Nigeria (CFR). His legacy was excellence in teaching and clinical practice. He left giant footprints in the various positions he held and his footnotes in the various seminal presentations and documentations.

As the last member of the foundation editorial team to exit, his death marked the end of the beginning of the African Journal of Medicine and medical sciences. May his gentle soul rest in perfect peace.

A. Ogunniyi
Editor-in-Chief

Contents

Afr. J. Med. Med. Sci. Vol. **49**, No. 2 June 2020

Afr. J. Med. Med. Sci. (2020) **49,** 201-206

Evaluation of the clinical utility of lipid metrics using the pooled cohort equation

MA Kuti[1], OA Ogundeji[2] and GO Ayoade[3]

Department of Chemical Pathology[1], College of Medicine, University of Ibadan, Department of Chemical Pathology[2], College of Health and Medical Sciences, Afe Babalola University, Ado-Ekiti and Department of Chemical Pathology[3], University College Hospital, Ibadan, Nigeria

Abstract

Introduction: Several prospective trials have established the relationship between lipids and apolipoproteins in the prediction of atherosclerotic cardiovascular disease. Data from trials have also been used to develop prediction equations that quantify the risk for atherosclerotic cardiovascular disease (ASCVD). We used one of the most recent prediction equations, the pooled cohort equation, to evaluate the clinical utility of a variety of lipid metrics.

Methodology: The pooled cohort equation was used to calculate 10-year risk of cardiovascular disease among a group of apparently healthy Nigerian participants. The score was then compared with their values of fasting plasma total cholesterol (TC), Triglycerides (TG), High density lipoprotein cholesterol (HDL–C), Apolipoprotein B, Apolipoprotein A1 as well as LDL-C/HDL-C and Apo B/Apo A1 ratios. The risk score and the lipid metrics were divided into 2 groups based on association with high risk of CVD.

Results: Out of the 157 participants, 30 (19.1%), participants had an estimated risk score $\geq$ 7.5%. Apo B/Apo A1 ratio, LDL-C/HDL-C and TG had significant positive correlations and ApoA1 and HDL-C had significant negative correlations with ASCVD risk score, all with $p < 0.01$. LDL-C and TC did not show a significant linear relationship with ASCVD risk score. The odds ratios for the Apo B/Apo A1 and LDL-C/HDL-C ratio had the strongest associations with the ASCVD risk category.

Conclusion: Risk prediction equations may be used in the evaluation of the clinical utility of lipid metrics, reaching conclusions similar to those from prospective studies.

Keywords: *Lipids, pooled cohort equation, clinical utility*

Résumé

Introduction : Plusieurs essais prospectifs ont établi la relation entre les lipides et les apolipoprotéines dans la prédiction de maladie cardiovasculaires athérosclérotique. Les données des essais ont également été utilisées pour développer des équations de prédiction qui quantifient le risque de maladie cardiovasculaire athérosclérotique (MCVAS). Nous avons utilisé l'une des équations de prédiction les plus récentes, l'équation de cohorte regroupée, pour évaluer l'utilité clinique d'une variété de paramètres lipidiques.

Méthodologie : L'équation de cohorte regroupée a été utilisée pour calculer le risque de maladie cardiovasculaire sur 10 ans parmi un groupe de participants nigérians apparemment en bonne santé. Le score a ensuite été comparé à leurs valeurs de cholestérol total à jeun (CT), Triglycérides (TG), cholestérol à lipoprotéines de haute densité (HDL – C), Apolipoprotéine B, Apolipoprotéine A1 ainsi que les ratios LDL-C / HDL-C et Apo B / Apo A1. Le score de risque et les métriques lipidiques ont été divisés en 2 groupes en fonction de l'association avec un risque élevé de MCV.

Résultats : Sur les 157 participants, 30 (19,1%) participants avaient un score de risque estimé $\geq$ 7,5%. Le ratio Apo B / Apo A1, LDL-C / HDL-C et TG avait des corrélations positives significatives et Apo A1 et HDL-C avaient des corrélations négatives significatives avec le score de risque MCVAS, tous avec $p < 0,01$. LDL-C et CT n'ont pas montré de relation linéaire significative avec le score de risque MCVAS. Les rapports de cotes pour les ratios Apo B / Apo A1 et LDL-C / HDL-C étaient les plus fortement associés à la catégorie de risque MCVAS.

Conclusion : Les équations de prédiction du risque peuvent être utilisées dans l'évaluation de l'utilité clinique des métriques lipidiques, aboutissant à des conclusions similaires à celles d'études prospectives.

Correspondence: Dr. M.A. Kuti, Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: modupekuti@yahoo.com

Mots - clés : *Lipides, équation de cohorte regroupée, utilité clinique*

Introduction

Observations from the 30 year follow-up of participants of the United States-based Framingham Heart study noted a significant relationship between total cholesterol (TC) and coronary heart disease. The study also noted the increased risk prediction of CVD achievable by considerations of the concentrations of low density lipoprotein cholesterol (LDL-C) [1]. The Scandinavian Apolipoprotein Mortality Risk study (AMORIS), a 10-year prospective study, further demonstrated the enhanced predictive abilities of the structural proteins of lipoproteins, specifically apolipoproteins B, A1 and their ratio (Apo B/Apo A1), compared with LDL-C amongst individuals free of coronary heart disease at baseline [2]. These, and other large scale prospective studies [3, 4] have provided evidence on the important clinical utility of lipid and lipoprotein markers in both primary and secondary preventive measures aimed at reducing the burden of cardiovascular disease (CVD).

Another major outcome of the Framingham study [1] was the development of a prediction equation that incorporated the risk factors identified by the study into a multivariable risk factor algorithm. The product of this equation, the Framingham risk score has subsequently been used to quantify CVD risk and guide preventive care [5]. In the recent review towards the development of a joint guideline, the American College of Cardiology (ACC) and American Heart Association (AHA) prescribed the use of a new equation based on observed weaknesses in the Framingham risk score [6].

These weaknesses included the fact that the data used for its development was obtained from a largely Caucasian population with only limited representation from other ethnic groups. Another equation, the pooled cohort equation, was therefore developed based on a data from several lengthy population-based cohort studies, including those with substantial inclusion of data from African American individuals [7]. The equation demonstrated good calibration for predicting atherosclerotic cardiovascular disease (stroke and coronary heart disease) in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, which had a population consisting over 40% black [8].

The present study used the 10-year estimate of risk derived from the pooled cohort equation as a surrogate for major adverse cardiac event. The parameters included in the pooled cohort equation are age, gender, race, systolic blood pressure, history of treatment for high blood pressure, diabetes mellitus and smoking as well as the plasma levels of total cholesterol and high-density lipoprotein cholesterol. The possible relationship between various lipid metrics (plasma levels of Apolipoprotein B, Apolipoprotein A1 and the Apo B/Apo A1 ratio) and estimated risk was determined among an apparently healthy Nigerian population.

Methodology

Study population

Participants were consenting hospital workers who were at least 40 years old and were without any previous or current history of atherosclerotic cardiovascular disease (myocardial infarction, stroke) or drugs for dyslipidemia.

Laboratory measurements

The lipid metrics: fasting plasma total cholesterol (TC), Triglycerides (TG), High density lipoprotein cholesterol (HDL–C), Apolipoprotein B, Apolipoprotein A1 and fasting plasma glucose concentration were determined on the Landwind C100 plus automated analyzer (Landwind Medicals, Shenzhen, China). Low density lipoprotein cholesterol (LDL – C) was calculated using the Friedewald formula (LDL-C = TC minus [HDL-C + TG/2.2]).[9]

Estimation of cardiovascular risk

Ten year cardiovascular risk was determined using an ASCVD risk estimator plus application developed and validated by the American College of Cardiology.[10] Participants were grouped into 2 groups: risk estimate <7.5% or $\geq$ 7.5%. Persons with ASCVD risk estimate score $\geq$ 7.5% should receive statin therapy, according to the ACC/AHA guideline.

Classification of lipid metrics

We grouped all the lipid metrics into two groups, using criteria published by Millan et al and in Tietz textbook of clinical chemistry and molecular diagnosis .[11, 12] Total Cholesterol: $\geq$ 6.22 mmol/L; Triglyceride: $\geq$2.25 mmol/L ; LDL-Cholesterol: $\geq$ 4.14mmol/L; Apo B: $\geq$127mg/dL. Males - HDL-Cholesterol: >1.04 mmo;l/L ; Apo A1: <109mg/dL; LDL/HDL ratio: >3.5; Apo B/Apo ratio A1: >0.9. Females – HDL-Cholesterol: >1.29 mmol/L; Apo A1: <123mg/dL; LDL/HDL ratio: >3.0; Apo B/Apo A1 ratio: >0.8.

Statistical analysis

Statistical Analysis was performed using Statistical Package for Social Sciences (SPSS) version 21. Statistical significance was set at $p< 0.05$. Quantitative and qualitative variables are presented as mean (standard deviation) and number (percentage), respectively. Medians of all the lipid metrics were compared using the Mann-Whitney U test. Correlations were done using Spearman's correlation co-efficient while binary logistic regression was used to evaluate the relationship between the lipid metrics and the ASCVD risk score categories.

Ethical approval was obtained from the University of Ibadan/University College Hospital, Ibadan Ethics Committee.

Results

One hundred and fifty seven (157) participants were enrolled into this study. Their clinical and biochemical characteristics, grouped by gender, are shown in Table 1. The median (IQR) HDL-C and Apolipoprotein A1 levels were significantly lower among the female participants compared with the male participants. Within the entire age range of the participants (40 – 66 years), there was no significant relationship between the age and any of the lipid metrics studied. The proportion of participants who had lipid values associated with increased risk of cardiovascular risk, TC >5.18 mmol/L, TG > 1.70mmol/L, LDL-C >3.37mmol/L and HDL-C < 1.04mmol/L were 38.9%, 1.9%, 52.9% and 54.1% respectively.

The estimated ASCVD risk for the participants ranged from 0.2% to 20.3%. Fifty one (32.5%), 30 (19.1%), and 15 (9.6%) participants had an estimated risk score exceeding 5%, 7.5% and 10%, respectively. Age, systolic blood pressure and diastolic blood pressure had strong positive linear relationships with ASCVD risk ($r = 0.665$, p value =0.000, $r = 0.581$, p value = 0.000 and $r = 0.504$, p value = 0.000, respectively). Table 2 shows the correlations of lipid metrics with ASCVD risk score. Triglycerides, LDL/HDL and ApoB/ApoA1 were significantly positively related with ASCVD risk score while HDL-C and Apo A1 were negatively related.

Table 3 compares the median concentrations of the lipids and apolipoprotein as well as the mean values of the derived ratios in persons with ASCVD risk estimate of <7.5% and $\geq$ 7.5%. The difference between the parameters (median or mean) across the 2 risk categories was most profound with the calculated ratios. Table 4 shows the odds ratio and confidence interval of having an estimated ASCVD risk of greater

Table 1: Characteristics of Study Participants

	Total	Female	Male	p- value
n (%)	157	115 (73.2)	42 (26.8)	
Age, yrs.				
mean (SD)	51.0 (8.2)	51.9 (8.3)	48.5 (7.6)	0.018
BMI, kg/m^2				
mean (SD)	25.7 (3.5)	25.8 (3.7)	25.7 (2.7)	0.910
<25.0; n (%)	72 (45.9)	16 (38.1)	56 (48.7)	0.238
Blood pressure (mmHg)				
Systolic; mean (SD)	123.9 (1.2)	123.0 (14.3)	126.3 (17.4)	0.236
Diastolic; mean (SD)	78.7 (0.8)	77.8 (10.5)	81.0 (10.5)	0.103
Lipid Profile (mmol/L)				
Total Cholesterol; median (IQR)	4.90 (1.22)	4.97(1.17)	4.71(1.33)	0.189
Triglycerides; median (IQR	0.77 (0.33)	0.78 (0.40)	0.80 (0.35)	0.768
HDL-Cholesterol; median (IQR	1.04 (0.25)	1.06 (0.26)	0.98 (0.22)	0.012
LDL-Cholesterol; median (IQR	3.39 (0.97)	3.42 (0.91)	3.38 (1.10)	0.352
Apolipoproteins (mg/dL)				
B; median (IQR)	97.0 (31.5)	98.0 (30.0)	95.5 (34.5)	0.36
A1; median (IQR)	139.0 (33.5)	145.0 (34.0)	132.0 (37.0)	0.025
Ratios				
LDL-C/HDL-C	3.4 (1.0)	3.4 (0.9)	3.5 (1.1)	0.435
Apo B/Apo A1	0.7 (0.2)	0.7 (0.2)	0.73 (0.2)	0.733

than 7.5% for the lipid metrics not included in the pooled cohort equation. The odds ratio was highest with the Apo B/Apo A1 ratio.

Table 2: Correlations of Lipid Metrics with ASCVD risk

Lipid Metric	Spearman's rho	p value
Total Cholesterol	0.093	0.246
Triglyceride	0.235	0.003
HDL- Cholesterol	-0.249	0.002
LDL – Cholesterol	0.125	0.120
Apolipoprotein B	0.118	0.142
Apolipoprotein A1	-0.220	0.006
LDL-C/HDL-C	0.221	0.005
Apo B/Apo A1	0.231	0.004

Table 3: Lipid metrics by estimated ASCVD risk category

	<7.5%	≥ 7.5%	p value
n (%)	127 (81.9)	30 (19.1)	
Total Cholesterol (mmo/L)$^{+}$	4.82 (1.17)	5.36 (1.20)	0.042
Triglycerides (mmo/L)$^{+}$	0.77 (0.32)	0.85 (0.49)	0.064
HDL-Cholesterol (mmo/L)$^{+}$	1.06 (0.29)	0.98 (0.19)	0.101
LDL-Cholesterol (mmo/L)$^{+}$	3.32 (0.98)	3.81 (0.82)	0.02
Apo B (mg/dL)*	94 (29)	108 (29.5)	0.019
Apo A1 (mg/dL)*	145 (35)	131.5 (22.8)	0.048
LDL-C/HDL-C*	3.3 (1.0)	3.9 (1.0)	0.005
Apo B/Apo A1*	0.7 (0.2)	0.8 (0.2)	0.002

*Values are $^{+}$median (interquartile range); * mean (SD)*

Table 4: Logistic regression of Lipid Metrics and ASCVD risk category

Lipid Metric	Odds Ratio	Confidence Interval	p value
Triglyceride	1.013	0.999 – 1.026	0.062
LDL – Cholesterol	1.014	1.002 – 1.027	0.026
Apolipoprotein B	1.018	1.003 – 1.033	0.020
Apolipoprotein A1	0.984	0.961 – 1.001	0.069
LDL-C/HDL-C	1.595	1.096 – 2.323	0.015
Apo B/Apo A1	13.549	2.351 – 78.079	0.004

A chi square test was performed to examine the relationship between the ASCVD grouping and the grouping of the lipid metrics according to risk stratification. The Spearman's chi-square score (p values) for TC, LDL-C, HDL-C, Apo B, Apo A1, LDL-C/HDL-C ratio and Apo B/Apo A1 ratio were 2.171 (0.141); 1.521 (0.217); 1.661 (0.197); 3.174 (0.075); 0.23 (0.879); 3.257 (0.071); and 6.931 (0.008), respectively.

Discussion

Among the lipid metrics measured as part of this study, the Apo B/Apo A1 ratio demonstrated consistent strong associations with the calculated ASCVD risk scores. Although the concentration of several lipid metrics demonstrated expectedly strongly linear relationships with risk scores, regression analysis showed that a unit

increase in Apo B/Apo A1 ratio alone was associated with an almost 14 times more likelihood of having a risk estimate score of ≥7.5% and requirement of statin therapy. An examination of the associations between lipid metrics and the risk of coronary heart disease using the Framingham Risk Score in healthy Korean men also observed much higher odds ratio for Apo B/ Apo A1 ratio compared with Apo B1, LDL-C and Triglycerides (43.18 vs. 1.99, 1.02, and 1.01, respectively) in identifying persons with FRS ≥ 10%.[13] This is consistent with the findings of prospective trials.[14-16] The results of the present study indicate that the evaluation of the predictive ability of lipid/lipoprotein metrics as done in the latter prospective multicentre follow up study may also be inferred by use of risk estimating equations.

In a demonstration of its real life and practical applicability, Apo B/Apo A1 ratio greater than or equal to 0.9 in the males and 0.8 in the females, showed significant identity with persons who had ASCVD risk scores greater than 7.5%. None of the other metrics displayed a similar significant association. This would imply that the inclusion of the Apo B /Apo A1 ratio, and its risk categories, on the laboratory report may provide information that may contribute to the identification of persons at increased risk of adverse cardiovascular outcomes. This is the practice where the operational costs of measuring the apolipoproteins B and A1 have been considerably reduced [17]. The utility of the Apo B/Apo A1 ratio may be related to its indication of both the number of potentially atherogenic lipoprotein particles, Apo B, and the antiatherogenic HDL particles reflected by Apo A1. The lipid accumulation, an essential part of the evolution of the atheromatous plaque, ensues if the amount of lipid entering the artery wall as a consequence of endogenous lipid transport (effected by Apo B containing lipoproteins) exceeds that removed by the reverse cholesterol transport (effected by the Apo A1 containing lipoproteins) [18].

An interesting observation from our results is the lack of significant linear relationship between total cholesterol, LDL-C and Apolipoprotein B and the calculated ASCVD risk score as determined by the pooled cohort equation. This contrasts with the findings of Ryoo et al[13], comparing these indices with the Framingham Risk Score where strong linear relationships were demonstrated. The possibility of finding associations of the pooled cohort equation with specific lipid metrics that are contrary to general trends was also suggested in a computer based simulation analysis performed across the whole range of boundary limits for the continuous variables in the pooled cohort 10 year risk equations by Schiros et al.[19] They found that, in African American females, increasing HDL-C level may result in higher 10 year risk for women older than 69 years. They concluded that this may be explained by the complexity of the interactions accounted for in the development of the equation and the use of natural logarithm of certain variables which render the relationships between variables parabolic, rather than linear.

In conclusion, we have demonstrated the potential ability of risk prediction equations in evaluating the clinical utility of various lipid metrics. Our evaluation supports the primacy Apo B/Apo A1 ratio in defining an individual's risk of atherosclerotic cardiovascular disease.

References

1. Castelli WP, Anderson K, Wilson PW and Levy D. Lipids and risk of coronary heart disease. The Framingham Study. Annals of epidemiology. 1992; 2 (1-2):23-28.
2. Holme I, Aastveit AH, Jungner I and Walldius G. Relationships between lipoprotein components and risk of myocardial infarction: age, gender and short versus longer follow-up periods in the Apolipoprotein MOrtality RISk study (AMORIS). Journal of internal medicine. 2008;264(1):30-38.
3. Kozarevic D, McGee D, Vojvodic N, *et al.* Serum cholesterol and mortality: the Yugoslavia Cardiovascular Disease Study. American journal of epidemiology. 1981;114(1):21-28.
4. Szatrowski TP, Peterson AV, Jr., Shimizu Y, *et al.* Serum cholesterol, other risk factors, and cardiovascular disease in a Japanese cohort. Journal of chronic diseases. 1984;37(7):569-584.
5. D'Agostino RB, Sr., Vasan RS, Pencina MJ, *et al.* General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743-753.
6. Goff DC, Jr., Lloyd-Jones DM, Bennett G, *et al.* 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129(25 Suppl 2):S49-73.

7. Preiss D and Kristensen SL. The new pooled cohort equations risk calculator. The Canadian journal of cardiology. 2015;31(5):613-619.
8. Muntner P, Colantonio LD, Cushman M, *et al.* Validation of the atherosclerotic cardiovascular disease pooled cohort risk equations. JAMA. 2014;311(14):1406-1415.
9. Friedewald WT, Levy RI and Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clinical chemistry. 1972;18(6):499-502.
10. American College of Cardiology. ASCVD risk estimator plus 2017 [updated August 2017; cited 2017]. Available from: http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/.
11. Millan J, Pinto X, Munoz A, *et al.* Lipoprotein ratios: Physiological significance and clinical usefulness in cardiovascular prevention. Vascular health and risk management. 2009;5:757-65.
12. Burtis CA, Ashwood ER, Bruns DE, Tietz NW. Tietz textbook of clinical chemistry and molecular diagnostics. 5th ed. St. Louis, Mo.: Saunders; 2013. xviii, 2,238 p. p.
13. Ryoo JH, Ha EH, Kim SG, Ryu S and Lee DW. Apolipoprotein B is highly associated with the risk of coronary heart disease as estimated by the Framingham risk score in healthy Korean men. Journal of Korean medical science. 2011;26(5):631-636.
14. Meisinger C, Loewel H, Mraz W and Koenig W. Prognostic value of apolipoprotein B and A-I in the prediction of myocardial infarction in middle-aged men and women: results from the MONICA/KORA Augsburg cohort study. European heart journal. 2005;26(3):271-8.
15. Lind L, Vessby B and Sundstrom J. The apolipoprotein B/AI ratio and the metabolic syndrome independently predict risk for myocardial infarction in middle-aged men. Arteriosclerosis, thrombosis, and vascular biology. 2006;26(2):406-10.
16. McQueen MJ, Hawken S, Wang X, *et al*. Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. Lancet. 2008;372(9634):224-233.
17. Lima LM, Carvalho MdG and Sousa MO. Apo B/apo AI ratio and cardiovascular risk prediction. Arquivos brasileiros de cardiologia. 2007;88(6):e187-e90.
18. Kasper D, Fauci A, Hauser S, Longo D and Jameson J. Harrison's Principles of Internal Medicine. New York: McGraw-Hill Education; 2015.
19. Schiros CG, Denney TS, Jr. and Gupta H. Interaction analysis of the new pooled cohort equations for 10-year atherosclerotic cardiovascular disease risk estimation: a simulation analysis. BMJ open. 2015;5(4):e006468.

Assessment of cardiac safety following artemether-lumefantrine (AL) or artesunate- amodiaquine (ASAQ) treatment of acute uncomplicated falciparum malaria in children from Ibadan Southwest Nigeria

RI Funwei[1,2], OS Micheal[1], OO Abiodun[1], SO Ogundele[3], OO Ogunkunle[4] and CO Falade[1,5]

Department of Pharmacology and Therapeutics[1], University of Ibadan, Ibadan, Department of Pharmacy Technician Studies[2], Bayelsa State College of Health Technology, Yenagoa, Department of Pharmacology, Therapeutics and Toxicology[3], Lagos State University, College of Medicine, Lagos. Departments of Pediatrics[4] and Institute for Advanced Medical Research and Training[5], University of Ibadan, Ibadan, Nigeria

Abstract

*Background***:** Artemisinin-based combination therapies (ACTs) have become first line antimalarial drugs globally and are available over-the-counter (OTC). This allows for unsupervised malaria treatment with ACTs. Some antimalarial drugs have been associated with cardiotoxicity. There is thus a need to evaluate the cardiac safety of artemether-lumefantrine (AL) and artesunate-amodiaquine (ASAQ), the ACTs of choice for the treatment of malaria in Nigeria.

Method: As part of a larger study that evaluated the comparative safety and efficacy of AL and ASAQ, a of 32 participants were enrolled into an electrocardiographic (ECG) study. Participants were randomly allocated to receive either AL or ASAQ under supervision at standard dosage for three days. A standard 12-lead ECG was done to compare baseline (day 0) ECG readings with post treatment values daily on days 1 - 3 and then on days 7, 14, 21 and 28.

Results: Sinus tachycardia was the commonest ECG changed at enrollment. A remarkable reduction of sinus tachycardia was observed after fever resolution ($p = 0.008$) for AL and ($p = 0.001$) for ASAQ respectively. Changes in ECG intervals were not significantly different during the follow up period following AL or ASAQ treatment ($p > 0.05$). There was no record of cardiac arrhythmia on ECG and no clinical evidence of cardiac disturbance through-out the study.

Conclusion: AL and ASAQ have no clinically significant prolongation of cardiac parameters or rhythm disturbance at the therapeutic doses used during the study.

Keywords: *Electrocardiogram, cardiotoxicity, sinus-tachycardia, malaria, ACTs, Nigeria*

Résumé

Contexte **:** Les thérapies combinées à base d'artémisinine (ACT) sont devenues des médicaments antipaludiques de première ligne dans le monde et sont disponibles en vente libre (OTC). Cela permet un traitement non supervisé du paludisme avec ACT. Certains médicaments antipaludiques ont été associés à une cardiotoxicité. Il y a donc un besoin d'évaluer la sécurité cardiaque d'artéméther-luméfantrine (AL) et d'artésunate-amodiaquine (ASAQ), les ACT de choix pour le traitement du paludisme au Nigéria.

Méthode : Dans le cadre d'une étude plus vaste qui a évalué l'innocuité et l'efficacité comparatives d'AL et d'ASAQ, un sous-segment de 32 participants a été inscrit à une étude électrocardiographique (ECG). Les participants ont été répartis au hasard pour recevoir soit AL ou ASAQ sous surveillance à la dose standard pendant trois jours. Un ECG standard à 12-indices a été effectué pour comparer les lectures ECG de référence (jour 0) avec les valeurs post-traitement quotidiennement les jours 1 à 3, puis les jours 7, 14, 21 et 28.

Résultats : La tachycardie sinusale était la modification ECG la plus courante à l'inscription. Une réduction remarquable de la tachycardie sinusale a été observée après la résolution de la fièvre ($p = 0,008$) pour AL et ($p = 0,001$) pour ASAQ respectivement. Les changements dans les intervalles ECG n'étaient pas

Correspondence: Prof. Catherine O Falade, Department of Pharmacology and Therapeutics, College of Medicine, University of Ibadan, Ibadan, Nigeria, Email: lillyfunke@yahoo.com

significativement différents au cours de la période de suivi suivant un traitement AL ou ASAQ (p> 0,05). Il n'y avait aucun enregistrement d'arythmie cardiaque à l'ECG et aucune preuve clinique de troubles cardiaques tout au long de l'étude.
Conclusion : AL et ASAQ n'ont pas d'allongement cliniquement significatif des paramètres cardiaques ou de perturbation du rythme aux doses thérapeutiques utilisées pendant l'étude.

Mots - clés : *électrocardiogramme, cardiotoxicité, tachycardie sinusale, paludisme, ACT, Nigeria*

Background

Despite global reduction in the prevalence of malaria, this parasitic infection remains a public health concern globally, especially in sub-Saharan Africa where the burden of the disease is still high [1]. Following the emergence of widespread resistance to previously efficacious monotherapies, artemisinin-based combination therapies (ACTs) have become the standard treatment for acute uncomplicated f*alciparum* malaria [2]. The safety of ACTs poses a major concern especially in endemic areas where under five-year-old children may have repeated attacks in a year [3]. Several antimalarial drugs have been reported to affect the cardiac conduction pathways with significant prolongation of P-R interval and of A-V block following treatment with notable antimalarial drugs [4-6].

The discovery of the cardio-toxic effect of halofantrine within a few years of its approval for marketing and subsequent reports of its fatal adverse cardiovascular effects [7] underscore the need for thorough investigation of the cardiac safety of antimalarial drugs. Significant delays in ventricular repolarisation resulting in prolonged Q-T interval have also been associated with quinine and quinidine in an earlier report [8].

The Nigerian National Malaria Elimination Programme (NMEP) in consonance with the WHO recommendation, adopted ACTs as the drug of choice for the treatment of acute uncomplicated malaria in 2005 [2,9]. Artemether-lumefantrine (AL) and artesunate-amodiaquine (ASAQ) are the preferred options in Nigeria in that order [9]. The widespread use and availability of ACTs are also actively promoted by national and international agencies such as the Affordable Medicine Facility-malaria. ACTs are now available as over-the-counter drugs in Nigeria and almost all malaria endemic areas of the world [10], resulting in extensive, largely unsupervised use of ACTs in malaria endemic areas.

The chemical similarities between halofantrine and lumefantrine; the partner drug with artemether have raised concerns of possible cardiotoxicity of artemether-lumefantrine. The cardiac safety of lumefantrine has been investigated by previous workers both during and after development of artemether-lumefantrine [11-13].

Amodiaquine and chloroquine belong to the same class of antimalarial drugs (4-aminoquinoline) with structural similarities. Amodiaquine has been reported to cause minor cardiac effect, such as bradycardia while chloroquine has significant cardiac effects, including lethal cardiovascular toxicity in over-dose [14]. The biologically active metabolite of artesunate and artemether (dihydroartemisinin) is well tolerated. However, a high dose of the artemisinin derivatives have been associated with Q-T prolongation in dogs, raising the possibility of a class effect with the artemisinin derivatives [15].

Despite the widespread use of AL and ASAQ in Nigeria, data on the cardiac safety of these most commonly prescribed and used ACTs on the cardiac P-wave, Q-T interval, P-R intervals, QRS complex and corrected Q-Tc in Nigerian children are relatively limited. The findings reported in this paper evaluated the electrocardiographic changes following artemether-lumefantrine (AL) or artesunate-amodiaquine (ASAQ) treatment of acute uncomplicated *Plasmodium falciparum* malaria in Nigeria children.

Methods

Study site and patients

This study was part of a larger study evaluating the comparative efficacy and safety of AL and ASAQ in children aged 6 months to 10 years in southwest Nigeria [16]. The study was conducted at the General Out-patient Department of the University College Hospital (UCH), Ibadan, Nigeria between September 2004 and March 2005. The open label, randomized controlled clinical trial enrolled thirty two children who met the following inclusion criteria: signs and symptoms compatible with acute uncomplicated malaria, axillary temperature $\geq 37.5^{o}C$ or history of fever within 48hrs of presentation, microscopically confirmed asexual forms of *P. falciparum* with parasite density between 1,000 and 200,000 parasite D μL, willingness to comply with study protocol and provision of additional written informed consent for the ECG study by parent/ guardian. Children with severe malnutrition, presence of mixed infection, signs of severe and complicated

malaria or other febrile illnesses and history of hypersensitivity to any of the study drugs were excluded from the study.

Ethical Issues

Ethical approval was obtained from the University of Ibadan/University College Hospital ethics Committee. A written Informed Consent was obtained from the parents or guardians of each child for the drug efficacy study before any study-related procedure was carried out. A second informed consent was obtained for the ECG study from the parents/guardian of each enrollee.

Study procedures

At enrolment, a thorough history and clinical examination was carried out on each prospective enrollee. Capillary blood samples were obtained for the preparation of blood smears and hematocrit value at baseline. Thick blood smears were prepared on microscope slide, air-dried and stained with 10% freshly prepared Giemsa stain at pH 7.2 using standard procedures [17]. Thick smears were examined under oil immersion (x1000) by two independent microscopists. Asexual parasitaemia at a parasite density of 1000/μL was the minimum parasite density for enrolment. Blood smears were considered negative if no parasites were observed after the examination of 100 high power microscope fields.

Drug treatment and follow-up

Children in group 1 (n = 16) received ASAQ as Artesunate (Asumax™ 50mg Sanofi- Synthelabo) and amodiaquine (Camoquine™ 200mg, Pfizer Pharmaceuticals Nigeria Limited). Artesunate was administered at a dose of 4 mg/kg body weight once daily for 3 days (rounded to the next quarter tablet) and amodiaquine at a dose of 10 mg amodiaquine base/kg body weight at the same time as artesunate once daily for 3 days (rounded to the next quarter tablet).

Patients randomized to group 2 (n = 16) received AL (Coartem™ Novartis Pharma) twice daily for 3days. Each tablet of AL contained 20 mg artemether and 120 mg lumefantrine. AL was given according to the weight of the enrolled child. Children weighing 5- < 15kg received one tablet, those weighing 15- < 25 kg received two tablets while those weighing 25- < 35 mg received three tablets twice daily for 3 days.

All doses of the study drugs were administered under the supervision of a nurse or doctor, AL was administered with milk while ASAQ was administered with water. Participants were observed for 30 min after drug administration for vomiting. Full dose of the study drug was re-administered if the participant vomited within the 30-minute period. Participants were withdrawn if they vomited the same dose at least twice, withdrew consent, violated the study protocol or were lost to follow up. Participants were followed up daily on days 0, 1, 2 and 3, then on days 7, 14, 21 and 28.

At every follow up visit, history of symptoms was obtained from each parents/guardians and thorough medical examination was carried out including axillary temperature. In addition, capillary blood was obtained by finger prick for thick blood smears and haematocrit. Parents/guardians were also encouraged to bring their children/wards to the clinic any time the children were unwell, or they have any concern about the children's health.

Treatment outcome classification

Treatment outcome was classified as early treatment failure (ETF), late clinical failure (LCF), late parasitological failure (LPF) or adequate clinical and parasitological response (ACPR) according to WHO treatment guideline [18].

Parasite clearance time (PCT) was the time interval between the initiation of AL or ASAQ treatment until blood film was free of parasitaemia while fever clearance time (FCT) was defined as the time between initiations of therapy among participants with axillary temperature $\geq$ 37.5^{o}C until it dropped below 37.4 ^{o}C and remained so for at least 48 hrs.

Electrocardiogram (ECG) recordings

At the scheduled time points (8 am – 10 am) participants were made to rest for 10 minutes in supine position before a baseline (pre-treatment) 12-lead electrocardiogram at the ECG room of the University College Hospital. All ECG investigations were carried out using Universal ECG Ref Z-7000-0300 Office Medic 5.2.1 at 25mm/sec paper speed and 10mm/mV sensitivity. The ECGs were evaluated with respect to heart rate, P-wave, P-R interval, QT interval, QRS interval, QT interval, corrected-QTc, R-R segment and T-wave. The same reference ECG lead (lead II), was used for measurement of P-R interval was the same in all patients. QT interval was measured in the lead showing the longest interval and was corrected for heart rate (QTc) according to Bazzet's formula (QTc = QT/RR) [19]. The QT interval was measured from the beginning of the Q wave to the end of the T wave; the

Table 1: Clinical and demographic characteristics of study participants

Characteristic	AL (n=16)	AS/AQ (n =16)	p –value
Age (years)			
Mean ± s.d	5.27 ± 2.670.	4.77 ± 2.970.	0.618
Range	0.5 – 10 yrs.	0.5 – 10 yrs.	
Sex (M : F)	11:5	6:10	0.077
Weight (kg)			
Mean ± s.d	16.75 ± 5.01	13.56 ± 5.42	0.094
Range	11.0 – 25.0	7.0 – 25.0	
Axillary Temperature (°C)			
Mean ± s.d	38.29 ±1.33	38.29 ± 1.0	1.000
Range	36.60 – 40.1	36.4 – 39.9	
Parasite density (/µL)			
GEOM	20,463	10,705	0.405
Range	(1,646 – 120,426)	(1480 – 150,879)	
PCV (%)			
Mean ± s.d	30.17 ± 3.81	30.25 ± 4.28	0.958
Range	24 – 37	24 – 37	
Heart rate (/min)			
Mean ± s.d	129.08 ± 27.44	130.07 ± 24.07	0.829
Fever Clearance Time (days)			
Mean ± SD	2.40 ± 0.99	2.00 ± 0.96	0.279
Range	1 – 2	1 – 2	
	5 (31.25%)	2 (12.5%)	0.231
No. febrile patients after day 2			
Parasite Clearance Time (days)			
Mean ± s.d	1.15 ± 0.90	1.57 ± 0.64	0.630
Range	1 – 4	1 – 3	
Day 28 Cure Rate (%)	100.00%	100.00%	

GEOM (Geometric Mean)
SD (Standard Deviation)

latter was defined as the return of T-P to baseline. The U-waves were not included in the QT measurement. A QTc interval was considered significantly prolonged if it was greater than 125% of the baseline pre-treatment measurement or if it was greater than 0.44s [4].

Electrocardiographic tracings were also monitored and recorded on follow up days with the same procedure. The ECG printouts were evaluated by an independent pediatric cardiologist (OOO) for interpretation of the tracings for rhythm, intervals and variations. The ECG intervals were re-measured manually, whenever they were found to be incorrect by the computer evaluation.

Statistical analysis

Data was entered into SPSS IBM version 20 and Graph Pad Prism version 5. ECG intervals are expressed as mean ± S.D. Comparison of ECG values at specified time points and intervals after dosing with the baseline values was assessed using the paired student's t-test. Values of $\rho < 0.05$ was considered statistically significant.

Results

Characteristics of the participants at enrolment

Baseline clinical and demographic evaluation of the participants showed 17 (53.1%) males while pyrexia (axillary temperature ≥ 37.5) was present in 22 (68.8%) at baseline. There were no significant differences in respect of age and body weight among the treatment groups. The geometric means parasite density among the participants were 20,463 parasites/µL for AL and 10,705 parasites/µL for ASAQ ($\rho = 0.405$). Further details are shown on Table 1.

Table 2: ECG parameters in children with uncomplicated *falciparum* malaria following treatment with AL

ECG Parameters (Unit = seconds)	Days 0	1	2	3	7	14	21	28
P-wave	53 ± 14 (n = 16)	[a]50 ±14 (n=14)	[a]47 ± 14 (n= 12)	[a]54 ± 13 (n= 13)	[a]53 ± 12 (n=12)	[a]41 ± 14 (n=7)	[a]50 ± 16 (n=6)	[a]47 ± 19 (n=6)
P-R interval	132 ± 16 (n = 16)	[a]129 ± 15 (n = 14)	[a]131 ± 19 (n = 12)	[a]141 ± 22 (n = 13)	[a]135 ± 17 (n = 13)	[a]135 ± 21 (n = 7)	[a]135 ± 18 (n = 6)	[a]137 ± 15 (n = 6)
Corrected-QTc	412 ± 39 (n = 16)	[a]401 ± 19 (n = 13)	[a]401 ± 17 (n = 12)	[a]406 ± 19 (n = 13)	[a]394 ± 26 (n = 12)	[a]389 ± 21 (n = 6)	[a]398 ± 13 (n = 6)	[a]383 ± 22 (n = 6)
QRS interval	70 ± 10 (n = 16)	[a]68 ± 8 (n = 14)	[a]68 ± 10 (n = 12)	[a]73 ± 10 (n = 14)	[a]72 ± 8 (n = 13)	[a]73 ± 11 (n = 7)	[a]75 ± 10 (n = 6)	[a]77 ± 7 (n = 6)
QT interval	291 ± 36 (n = 16)	[a]306 ± 31 (n = 14)	*307 ±30 (n = 12)	*327 ±34 (n = 14)	*319 ±36 (n = 13)	[a]310 ± 33 (n = 7)	*325 ±47 (n = 6)	*327 ±34 (n = 14)
R-R segment	48 ± 20 (n = 16)	[a]46 ± 22 (n = 14)	[a]45 ± 19 (n = 12)	[a]45 ± 18 (n = 14)	[a]50 ± 22 (n = 13)	[a]50 ± 17 (n = 7)	[a]52 ± 18 (n = 6)	[a]52 ± 16 (n = 6)
T-wave	38 ± 12 (n = 16)	[a]37 ± 11 (n = 14)	[a]37 ± 11 (n = 12)	[a]42 ± 13 (n = 14)	[a]44 ± 7 (n = 13)	[a]42 ± 9 (n = 7)	[a]45 ± 8 (n = 6)	[a]49 ± 8 (n = 6)

Values presented as mean ± standard deviation
( ) Number of participants
Values with superscript [(a)] indicate no significant difference ($p > 0.05$) while superscript with [(*)] indicate significant difference ($p < 0.05$).

Table 3. ECG parameters in children with uncomplicated *falciparum* malaria following treatment with ASAQ

ECG Parameters (seconds)	Days 0	1	2	3	7	14	21	28
P-wave	55 ± 10 (n = 16)	[a]54 ± 10 (n=15)	[a] 52 ± 10 (n= 9)	[a]51 ± 10 (n= 12)	[a]54 ± 9 (n =11)	[a]56 ± 8 (n=11)	[a]50 ± 9 (n=5)	[a]46 ± 11 (n=9)
P-R interval	123 ± 15 (n = 16)	[a]128 ±15 (n = 15)	[a]129 ± 12 (n = 9)	[a]128 ± 16 (n = 12)	[a]129 ± 19 (n = 15)	[a]122 ± 11 (n = 11)	[a]130 ± 18 (n = 5)	[a]125 ± 14 (n = 8)
Corrected-QTc	405 ± 20 (n = 16)	[a]406 ± 21 (n = 15)	[a]401 ±16 (n = 9)	[a]407 ± 17 (n = 12)	[a]404± 17 (n = 15)	[a]411 ± 13 (n = 11)	[a]414 ± 17 (n = 5)	[a]413 ± 16 (n = 8)
QRS interval	65 ± 8 (n = 16)	*67 ± 8 (n = 15)	*70 ± 10 (n = 9)	*69 ± 7 (n = 12)	*68 ± 8 (n = 15)	[a]68 ± 6 (n = 11)	[a]68 ± 4 (n = 5)	[a]68 ± 7 (n = 8)
QT interval	281 ± 32 (n = 16)	*306 ±38 (n = 15)	*331 ±29 (n = 9)	*319 ±31 (n = 12)	*305 ±44 (n = 15)	*304 ±47 (n = 11)	[a]275 ± 28 (n = 5)	*309 ±28 (n = 8)
R-R segment	54 ± 15 (n = 16)	[a]52 ± 23 (n = 15)	[a]60 ± 13 (n = 9)	[a]56 ± 15 (n = 12)	*60 ± 16 (n = 14)	[a]60 ± 21 (n = 11)	[a]60 ± 21 (n = 5)	[a]52 ± 23 (n = 8)
T-wave	39 ± 14 (n = 16)	[a]40 ± 15 (n = 15)	[a]35 ± 12 (n = 9)	[a]33 ± 15 (n = 12)	[a]42 ± 16 (n = 15)	[a]46 ± 17 (n = 10)	[a]37 ± 13 (n = 5)	[a]37 ± 21 (n = 8)

Values presented as mean ± standard deviation
(n) = Number of participants
Values with superscript [(a)] indicate no significant difference ($p > 0.05$) while superscript with [(*)] indicate significant difference ($p < 0.05$).

Malaria treatment outcome

Participants enrolled into the ECG study that completed at least five of eight follow up evaluation days were included in the analysis. Response to AL and ASAQ for the treatment of malaria infection was prompt. The mean fever clearance time (AL = 2.40 ± 0.99 and ASAQ = 2.00 ± 0.96; ρ = 0.279) and parasite clearance time (AL = 1.15 ± 0.90 and ASAQ = 1.57 ± 0.64; ρ = 0.630)

were short and comparable in both treatment groups respectively. Both drugs were well tolerated as earlier reported in the main study. The cure rates for both treatments were 100% at day 28 (Table 1). At no point in time did any of the participants present cardiovascular symptoms.

ECG findings

Sinus tachycardia, (heart rate >130 bpm) was the most common ECG finding at baseline which occurred in 90.6% (29/32); this was observed for both treatment groups and normalized as the fever settled and children recovered. A sustained decrease in heart rate was observed as fever resolved following treatment but no case of bradycardia was recorded at any time point. There was also no rhythm disturbance at enrolment and throughout the follow up period.

Comparison of the paired differences of the evaluated ECG parameters with day 0 readings following AL treatment only showed significant difference on the QT interval on days 2, 3, 7, 21 and 28 respectively (Table 2) while ASAQ showed a significant difference on the QRS interval from day 1 to 7, QT interval on days 1, 2, 3, 7, 21 and 28 respectively. Similar findings was observed for the R-R interval on day 7 (Table 3). Comparison of P-wave with baseline value were also within normal limits for both treatment groups on day 0 and on follow up days ($\rho > 0.05$). Similarly, the Bazzet's corrected QTc values for both drugs did not show any significant difference when compared with pre-treatment values. However, ASAQ demonstrated a sustained shortening rather than prolongation of the QTc on days 2 and 3. This was however not statistically significant. In the same manner, the P-R interval showed no significant difference between baseline and post-treatment values for both AL and ASAQ ($\rho > 0.05$). There was no evidence of deleterious cardiac effect from both AL and ASAQ on the QRS complex, the R-R segment and the T wave (ventricular repolarization) when compared with baseline values.

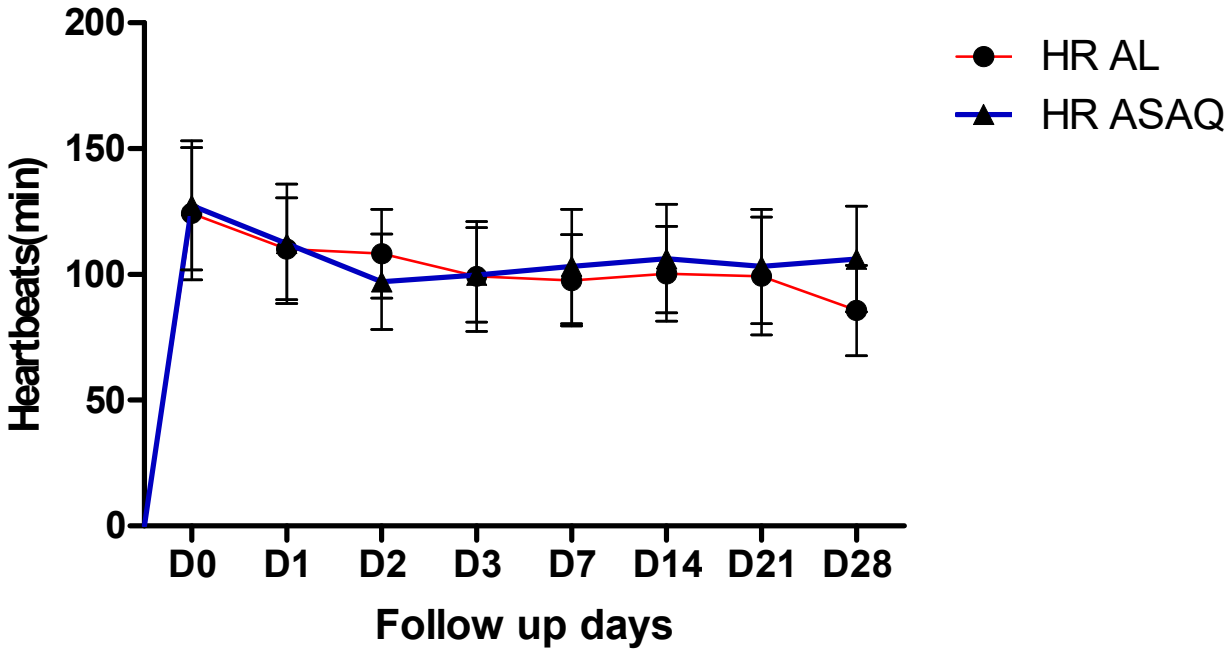


Fig.1: Trend of heat rates of children from southwest Nigeria who received artemether-lumefantrine or Artesunate-amodiaquine for acute uncomplicated malaria

Discussion

This study evaluated the cardiac safety of the first line artemisinin-based combination drugs (AL and ASAQ) in Nigerian children with acute uncomplicated *falciparum* malaria. AL and ASAQ were found to be efficacious and well tolerated during the study. The

efficacy and safety of the larger study have been reported elsewhere [16]

The findings of sinus tachycardia as the most prevalent ECG changes at enrolment is consistence with pyrexia which is a hallmark symptom of malaria infection. Tachycardia subsided as the fever resolved among the study participants following successful treatment of the infection with AL or ASAQ. Previous research findings have reported the association between fever and heart rate in children [20, 21]. Sinus tachycardia was also reported to be the most common ECG finding among the cohort of children treated for malaria by Sowunmi *et al* [5]. In those previous reports, tachycardia resolved as following fever resolution [5, 20, & 21]. There was a significant decrease observed in the heart rate, but such significant differences were not observed in the P- wave, P-R interval and QTc interval. In our opinion, the significant drop in heart rate is as a result of fever resolution [22]. Unlike the study reported by Adjei *et al* [23], bradycardia was not seen in any of the participants (Figure 1). Although, a mild decrease in the corrected QTc was observed in the ASAQ arm on days 2 and 3, the difference was not statistically significant. However, a significant difference was observed in the QT interval post AL treatment while ASAQ also demonstrated a significant difference on QT, QRS intervals and R-R segment. This implies that an intake of AL or ASAQ at doses above the recommended dosage may induce cardiac disturbance especially with ASAQ.

Furthermore, in no patient was rhythm disturbance detected on ECG and there were no clinical features of cardiac disturbance throughout the follow up period. This is in keeping with previous studies evaluating cardiac safety of AL and ASAQ as well as artemisinin monotherapy which have not reported major cardiac toxicity at standard doses [14, 24]. A study that evaluated the cardiac safety indices of lumefantrine and its active metabolite desbutyl-lumefantrine, suggested that both lumefantrine and desbutyl-lumefantrine had weaker pro-arrhythmic potential than halofantrine [13].

A possible limitation of our study is not evaluating the drug plasma levels during treatment and follow up. However, this may not be important as the response of the malaria infection (adequate and parasitological cure rate of 100%) among the participants in the ECG study suggesting that the drug blood level was adequate. In addition, cardiac tolerance as well as overall tolerance among the children were quite good.

Conclusion

The results from this study support previous reports that artemether-lumefantrine and artesunate-amodiaquine have no significant cardiovascular effect in Nigerian children with acute uncomplicated *falciparum* malaria when used at standard dosage.

Acknowledgements

We thank the children and their parents for participating in this study. Our appreciation also goes to the nurses and staff of the General Outpatients' Department, University College Hospital and the staff of ECG room, University College Hospital, Ibadan, for their valuable assistance. We specifically thank Mrs. Iyabo Abdusalam, Mrs Bolatito Akinyele and Miss Grace Egunyomi for their technical and clinical support. Coartem™ was provided by Novartis Pharma, Nigeria; Sanofi-Sycitilabo Nigeria provided artesunate (Arsumax™) while Pfizer Pharmaceuticals Limited Nigeria provided Amodiaquine (Camoquine™).

References

1. World Health Organization. World Malaria Report. World Health Organization. 2016.
2. World Health Organization. Monitoring Antimalarial Drug Resistance, World Health Organization. Geneva, Switzerland; 2002.
3. Fenando SD, Gunawardena DM, Bandara MRSS, *et al.* The impact of repeated malaria attacks on the school performance of children. Am J Trop Med Hyg. 2003; 69(6): 582-588
4. Bouchaud O, Imbert P, Touze JE, *et al*. Fatal cardiotoxicity related to halofantrine: a review based on a worldwide safety data base. Malar J. 2009 ;8:289.
5. Ogunkunle OO, Fehintola FA, Ogungbamigbe T and Falade CO. Comparative Cardiac Effects of Chlorproguanil/Dapsone and Chloroquine during Treatment of Acute Uncomplicated Falciparum Malaria Infection in Nigerian Children. Afr J Biomed Res. 2011; 14(3):161–167.
6. Sowunmi A, Falade CO, Oduola AM, *et al.* Cardiac effects of halofantrine in children suffering from acute uncomplicated falciparum malaria. Trans R Soc Trop Med Hyg. 1998; 92(4):446–448.
7. Nosten F, ter Kuile FO, Luxemburger C, *et al.* Cardiac effects of antimalarial treatment with

halofantrine. Lancet Lond Engl. 1993 ;341(8852):1054–1056.
8. Supanaranond W, Davis TM, Pukrittayakamee S, *et al.* Disposition of oral quinine in acute falciparum malaria. Eur J Clin Pharmacol. 1991;40(1):49–52.
9. Federal Ministry of Health (FMoH). Federal Republic OF Nigeria National Antimalaria Treatment Policy. 2005.
10. Ajayi IO, Browne EN, Garshong B, *et al.* Feasibility and acceptability of artemisinin-based combination therapy for the home management of malaria in four African sites. Malar J. 2008;7:6.
11. van Vugt M, Ezzet F, Nosten F, *et al.* No evidence of cardiotoxicity during antimalarial treatment with artemether-lumefantrine. Am J Trop Med Hyg. 1999 Dec;61(6):964–967.
12. Falade CO, Ogundele AO, Yusuf BO, Ademowo OG and Ladipo SM. High efficacy of two artemisinin-based combinations (artemether-lumefantrine and artesunate plus amodiaquine) for acute uncomplicated malaria in Ibadan, Nigeria. Trop Med Int Health TM IH. 2008 May;13(5):635–643.
13. Traebert M, Dumotier B, Meister L, *et al.* Inhibition of hERG K+ currents by antimalarial drugs in stably transfected HEK293 cells. Eur J Pharmacol. 2004 Jan;484(1):41–48.
14. White NJ. Cardiotoxicity of antimalarial drugs. Lancet Infect Dis. 2007 Aug;7(8):549–558.
15. Maude RJ, Plewes K, Faiz MA, *et al*. Does artesunate prolong the electrocardiograph QT interval in patients with severe malaria? Am J Trop Med Hyg. 2009 Jan;80(1):126–132.
16. Falade CO, Ogunkunle OO, Dada-Adegbola HO, *et al.* Evaluation of the efficacy and safety of artemether-lumefantrine in the treatment of acute uncomplicated Plasmodium falciparum malaria in Nigerian infants and children. Malar J. 2008 Nov;7:246.
17 Trape, J.F. 1985. Rapid evaluation of malaria parasite density and standardization of thick smear examination for epidemiological investigations. *Trans. R. Soc. Trop. Med. Hyg.* 1985 79: 181–184.
18 WHO. Guidelines for the treatment of malaria: Second edition: Geneva, World Health Organization 2010. 19. Bazzet H 1920. An analysis of time relation of electrocardiograms. Heart. 7:353–370.
20. Assi S-B, Aba YT, Yavo JC, *et al.* Safety of a fixed-dose combination of artesunate and amodiaquine for the treatment of uncomplicated Plasmodium falciparum malaria in real-life conditions of use in Côte d'Ivoire. Malar J. 2017 Jan;16.
21. Davies P and Maconochie I. The relationship between body temperature, heart rate and respiratory rate in children. Emerg Med J EMJ. 2009 Sep;26(9):641–643.
22. Karjalainen J and Viitasalo M. Fever and cardiac rhythm. Arch Intern Med. 1986 Jun;146(6):1169–1171.
23. Adjei GO, Oduro-Boatey C, Rodrigues OP, *et al.* Electrocardiographic study in Ghanaian children with uncomplicated malaria, treated with artesunate-amodiaquine or artemether-lumefantrine. Malar J. 2012 Dec;11:420.
24. Touze JE, Heno P, Fourcade L, Deharo JC, Thomas G, Bohan S, et al. The effects of antimalarial drugs on ventricular repolarization. Am J Trop Med Hyg. 2002 Jul; 67 (1):54–60.

Afr. J. Med. Med. Sci. (2020) **49,** 207-213

Serological markers of HBV infection: A community-based study of urban dwellers in Southwest Nigeria

A Akere[1], EC Omoruyi[2], MO Adewumi[3], TOC Faleye[4], IM Ifeorah[5], AS Bakarey[6] , AO Ogunwale[7], IN Dafikpaku[4], OE Oni[4], OV Tomo[4], AO Akinola[4], AG Onyenucheya[4] and JA Adeniji[3]

Departments of Medicine[1], Institute of Child Health[2] and Virology[3], College of Medicine, University of Ibadan, Ibadan, Department of Microbiology[4], Faculty of Science, Ekiti State University, Ado-Ekiti, Ekiti, Department of Medical Laboratory Sciences[5], College of Medicine, University of Nigeria, Nsukka, Institute for Advanced Medical Research and Training[6], College of Medicine, University of Ibadan, Ibadan, and Oyo State College of Agriculture and Technology[7], Igboora, Oyo State, Nigeria.

Abstract

*Background and Aim***:** Globally, hepatitis B virus (HBV) infection has been a major public health issue. In sub-Saharan Africa, about 10-20% of the general population are chronic carriers of HBV infection thus, making it a high endemic region. This study was designed to evaluate the pattern of distribution of markers of HBV among asymptomatic subjects in an urban community in southwest Nigeria.

Methodology: The study was carried out among apparently healthy subjects without prior knowledge of their HBV status. A structured questionnaire was used to collect demographic and relevant information while ELISA kits were used to detect HBsAg/Ab, HBeAg/Ab, Total antiHBc and antiHBc IgM using the participants' sera.

Results: The results of 438 subjects comprising, 133 (30.4%) males and 305 (69.6%) females were analysed, age ranged 1.5-70 years (35.7±15.7 years). Overall, 31 (7.1%) of the participants had detectable HBsAg, 2 (6.5%) and 7 (1.6%) subjects had detectable HBeAg and anti-HBc IgM respectively. Anti-HBs was detected in 83(18.9%) subjects, while 39 (8.9%) had anti-HBe. Of the HBsAg positive participants, 1 (3.2%) of them was also positive for both anti-HBc IgM and HBeAg, 25 (80.6%) had antiHBe while 3 (9.7%) had only anti-HBc IgM. None of them had antiHBs. Among those who were HBsAg negative, 83 (20.4%) had anti-HBs as the only serological marker, while 313 (76.9%) had no serological markers of HBV infection. Only 145 of the total population were tested for anti-HBc Total, of whom 65(44.8%) were positive.

Conclusion: This study has highlighted the burden of HBV infection in the population studied. There is therefore, the need for more awareness through information programmes to the public and for preventive measures through vaccination programmes.

Keywords: *HBV infection, Serological markers, Urban, Southwest Nigeria*

Correspondence: Dr. S.B. Bakarey, Institute for Advanced Medical Reseach and Traing, College of Medicine, University of Ibadan, Ibadan, Nigeria. Email:drbakarey@yahoo,com.

Résumé

Contexte et objectif **:** À l'échelle mondiale, l'infection par le virus de l'hépatite B (VHB) a été un problème majeur de santé publique. En Afrique subsaharienne, environ 10 à 20% de la population générale sont donc porteurs chroniques de l'infection par le VHB, ce qui en fait une région fortement endémique. Cette étude a été conçue pour évaluer le modèle de distribution des marqueurs du VHB chez les sujets asymptomatiques dans une communauté urbaine du sud-ouest du Nigéria.

Méthodologie : L'étude a été menée auprès de sujets apparemment sains sans connaissance préalable de leur statut VHB. Un questionnaire structuré a été utilisé pour collecter des informations démographiques et pertinentes tandis que des kits ELISA ont été utilisés pour détecter HBsAg / Ab, HBeAg / Ab, Total antiHBc et antiHBc IgM en utilisant le sérum des participants.

Résultats : Les résultats de 438 sujets comprenant 133 (30,4%) sujets masculins et 305 (69,6%) sujets féminins ont été analysés, l'âge variait de 1,5 à 70 ans (35,7 ± 15,7 ans). Dans l'ensemble, 31 (7,1%) des participants avaient un HBsAg détectable, 2 (6,5%) et 7 (1,6%) sujets avaient respectivement un HBeAg détectable et un IgM anti- HBc. Anti-HBs a été détecté chez 83 (18,9%) sujets, tandis que 39 (8,9%) avaient anti- HBe. Parmi les participants positifs pour HBsAg, 1 (3,2%) d'entre eux était également positif pour IgM anti- HBc et HBeAg, 25

(80,6%) avaient antiHBe tandis que 3 (9,7%) n'avaient que IgM anti- HBc. Aucun d'eux n'avait d'antiHB. Parmi ceux qui étaient négatifs pour AgHBs, 83 (20,4%) avaient des anti-HBs comme seul marqueur sérologique, tandis que 313 (76,9%) n'avaient aucun marqueur sérologique d'infection par le VHB. Seulement 145 de la population totale ont été testés pour le total anti-HBc, dont 65 (44,8%) étaient positifs.

Conclusion : Cette étude a mis en évidence la charge de l'infection par le VHB dans la population étudiée. Il est donc nécessaire de sensibiliser davantage le public par des programmes d'information et de prendre des mesures préventives par le biais de programmes de vaccination.

Mots-clés : *infection par le VHB, marqueurs sérologiques, urbain, sud-ouest du Nigéria*

Introduction

Globally, Hepatitis B Virus (HBV) infection has been a major public health concern. Over 2 billion of the world's population are infected, among whom, about 257 million are chronic carriers of the virus [1,2]. Majority of these carriers are resident in sub-Saharan Africa and South East Asia [3]. About 25% of chronic carriers of the infection die from its sequelae such as liver cirrhosis, liver failure and hepatocellular carcinoma [4].

Infection at a very young age is more likely to progress to chronicity. Specifically, it has been observed that, about 90% of infected newborns eventually turn out to be chronic carriers [5]. On the other hand, 90-95% of infected adults get rid of the virus with no sequelae, while 5-10% become chronic carriers [6]. However, there are many HBV infected individuals who are asymptomatic carriers living within and cohabiting with other members of the same community especially in endemic areas [2].

In sub-Saharan Africa, about 10-20% of the general population are chronic carriers of HBV infection, thus, making it a high endemic region [1]. It has been observed that at least one marker of HBV infection is found in about 70-95% of adults in this region [7]. HBV has markers of infection found in the blood at different stages which include, hepatitis B surface antigen (HBsAg); antibody to HBsAg (anti-HBs); hepatitis B 'e' antigen (HBeAg); antibody to HBeAg (anti-HBe) and antibody to hepatitis B core antigen (anti-HBc). The presence of any of the markers of infection may signify either infectivity or immune status of such individual [8].

In Nigeria, the prevalence of HBV infection ranges between 9-39% [9-13]. In most studies, HBsAg is the only serological marker used to assess infection, prevalence and endemicity of HBV infection [8,14]. However, the natural history and serology of HBV are complex with multiple laboratory markers. In view of this, this study was designed to evaluate the pattern of distribution of HBV markers of infection among asymptomatic subjects in an urban community in Ibadan, southwestern Nigeria.

Methodology

*Study Area***:** The study was carried out in Ibadan, an urban city in southwest Nigeria. According to the National Population Commission Census of 2006, Ibadan has a population of over 2.5 million people. Majority of the inhabitants of the city are low income earners.

Study Population: The study was carried out among consenting apparently healthy subjects who did not have prior knowledge of their HBV status. Parental accents were sought and obtained for the under aged participants before their enrolment into the study. Participants were educated on HBV infection, risk factors for its transmission, early symptoms of diseases that can result from the infection, as well as ways of preventing the infection.

Data Collection:

A structured questionnaire was used to collect demographic and other relevant information from the participants.

Sample collection and analysis

About 5mLs of venous blood was collected from each participant under aseptic condition. Serum was recovered from each blood specimen by centrifugation for 15 minutes at 1,500 rpm. Recovered sera were transferred into appropriately labelled tubes and then stored at -20^{o}C until analyzed. All samples were tested for HBV markers including HBsAg, antiHBs, HBeAg, anti-HBe, and anti-HBc IgM, using Enzyme Linked Immunosorbent Assay (ELISA) test kits (Diagnostic Automation/Cortez Diagnostic, California, USA). Only 145 samples were screened for anti-HBc-Total using similar kit. Assays were performed in accordance with the manufacturer's instructions. Optical density (OD) was read using the Emax endpoint ELISA microplate reader (Molecular Devices, California, USA) and

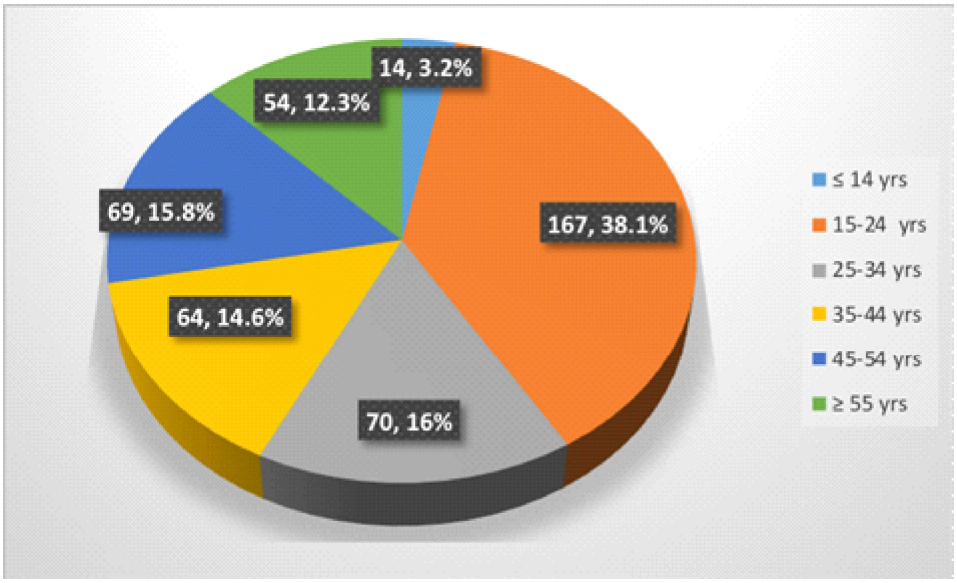


Fig. 1: Frequency and age category of the study participants

subsequently interpreted in line with the manufacturer's instructions.

Data analysis

Data were analyzed using SPSS version 21. Means, charts and tables were used to describe the results with $p<0.05$ considered statistically significant.

Ethical approval

Ethical approvals for the study were granted by the UI/UCH Institutional Review Board (UI/EC/11/0058) and Ministry of Health (AD3/479/349).

mean of 35.7±15.7 years. The analysis showed that, 167 (38.1%) of the subjects were in the age category of 15-24 years, 70 (16%) were in 25-34 age bracket, while 14 (3.2%) were ≤ 14 years (Figure 1).

The frequency of the serological markers of HBV infection is as follows; HBsAg was detected in 31 (7.1%), 19 (61.3%) of whom were in the age range 15-34 years (Table 1). Analysis by gender of those positive for HBsAg showed that 17 (54.8%) were males, while 14 (45.2%) were females and there was significant difference (p= 0.035) between the two

Table 1: Overall age distribution of HBV Markers in the subjects

Age Range (yrs)	No Tested n (%)	HBsAg	HBeAg n (%)	AntiHBe n (%)	AntiHBcIg n(%)	Anti-HBs M n(%)
≤14	14	0(0.0)	0(0.0)	0(0.0)	0(0.0)	5(35.7)
15-24	167	10(6.0)	1(10.0)	12(7.2)	2(1.2)	27(16.2)
25-34	70	9(12.9)	1(11.1)	11(15.7)	2(2.9)	9(12.9)
35-44	64	4(6.3)	0(0.0)	7(10.9)	2(3.1)	11(17.2)
45-54	69	6(8.7)	0(0.0)	6(8.7)	1(1.4)	15(21.7)
≥ 55	54	2(3.7)	0(0.0)	3(5.6)	0(0.0)	16(29.6)
Total	438	31(7.1)	2(6.5)	39(8.9)	7(1.6)	83(18.9)

Results

The results of 438 subjects comprising, 133 (30.4%) males and 305 (69.6%) females were analyzed. Respondents' ages ranged from 1.5–70 years with a

groups. Anti-HBs was found in 83 (18.9%) subjects. Two (6.5%) subjects were HBeAg positive, while anti-HBe was detected in 39 (8.9%) subjects. HBV DNA was detected in 27 (6.2%) subjects, among whom 3

(11.1%) were HBsAg negative. Of the HBsAg positive participants, 1 (3.2%) of them was also positive for both anti-HBc IgM and HBeAg, 25(80.6%) had antiHBe while 3 (9.7%) had only anti-HBc IgM. None of them had anti-HBs (Table 2).

Table 2: Serological profile of HBsAg positive subjects (n=31)

Profile	Additional Marker	n (%)	Interpretation
A1	Anti-HBcIgM, HBeAg	1 (3.2)	Probably acute infection with active viral replication
A2	AntiHBe	25 (80.6)	Probably chronic infection with low viral replication
A3	AntiHBcIgM	3 (9.7)	Probably recent infection
A4	AntiHBs (negative)	0 (0)	No immunity
A5	No other markers	4 (12.9)	Early infection/post vaccination

Among those who were HBsAg negative, 83 (20.4%) had anti-HBs as the only serological marker, anti-HBc IgM and anti-HBe were present in 4 (1.0%) and 14 (3.4%) subjects respectively, while 313 (76.9%) of them had none of the serological markers of HBV infection (Table 3)

Table 3: Serological profiles of HBsAg-negative subjects (n=407)

Profile	Marker	n(%)	Interpretation
B1	HBeAg negative	407(100)	Low replication
B2	AntiHBe	14 (3.4)	Resolved/Low replication
B3	AntiHBcIgM	4 (1.0)	Recent infection
B4	AntiHBs only	83 (20.4)	Post vaccination immunity
B5	No marker	313 (76.9)	Susceptible to infection

Only 145 of the total population sampled were tested for anti-HBc Total. Sixty-five (44.8%) of them were positive. They included 17(11.7%) male and 48(33.1%) female participants in age brackets 20-65 and 18-70 years respectively. Of this subgroup, 15 (10.3%) had HBsAg while twelve (80.0%) out of this number had both anti-HBc and anti-HBe.

Discussion

In this study, an overall prevalence of 7.1% detected for HBV infection is higher than the 4.1-7.0% range reported by Omeje *et al* [15], in Abakaliki in the southeast, Adoga *et al.*[16] in a study among urban dwellers in the North Central and Okonko *et al* 17], among attendees of an STI clinic in Ibadan southwest of Nigeria. This rate is however much lower than 12.6% and 21.3% respectively reported by Jumbo *et al*. [18] in a rural setting and Otegbayo *et al* 19] among blood donors in the same southwest region of the country. The difference in the prevalence rates might be due to the differences in the sample sizes, ethnicity as well as the composition of the study population [15-19]. The rural setting of their study might explain the higher prevalence observed. It is believed that poor awareness and harmful socio-cultural practices in the rural areas might encourage transmission of HBV infection [16]. This was also the observation of Bwogi *et al* [20] in Uganda, in which significantly higher prevalence of HBV infection was found in rural areas. This study also showed a significantly higher prevalence of HBV infection among males compared to females ($p<0.0035$}. This is consistent with the findings of similar studies conducted in Nigeria [21-23], as well as other parts of the world [24].

In this study we found a rate of 6.5% (2/31) for HBeAg (Table 1) and this falls within the range of 6.4- 8.9% reported among blood donors in Nigeria [25-28]. This rate is however lower than the reported 48.4% and 19% HBeAg sero-positivity found among HBsAg-positive patients by Ojo *et al [*29] in Ile-Ife and Ola *et al [*30], in Ibadan respectively in southwest Nigeria and 19.2% HBeAg prevalence found among HBsAg-positive individuals in north-central Nigeria [31]. The lower rate for HBeAg found in this study when

compared with previous findings in southern and Northern regions of Nigeria could be due to the asymptomatic population sampled in our study. It has been documented that active viral replication in liver cells is an indication of the presence of HBeAg found in the serum of individuals infected with HBV which also reflects the presence of HBV DNA as a surrogate marker.[32] Furthermore, studies have also demonstrated that the detection of HBeAg in the serum can serve as a high risk indicator for development of hepatocellular carcinoma [33].

Furthermore, HBeAg virus has been reportedly found in circulation among the general population which serves as a prelude to the endemicity of HBV in Nigeria, and an indicator of active viral replication irrespective of clinical presentation [31]. It also indicates that high infectivity of the virus is widespread among Nigerians with HBV infection [30]. It is therefore advisable to implement routine HBeAg testing for HBV positive patients to ascertain their status of infection for adequate management. In addition, our study detected anti-HBe rate of 8.9% among the study participants. Although this rate may be low, it is however an indication of immune response against the infection and to control its spread. According to earlier report, the presence of anti-HBe may indicate good prognosis and could be suggestive of controlled viral replication in these individuals, since persons with anti-HBe tend to have lower viraemia [34].

In this study, 65(48.8%) of those tested for anti-HBcTotal were positive and by extrapolation, it can be inferred that about half of the study population may have been previously exposed or infected with HBV at one time in their life time. This rate is lower than the 54% reported by Oyero and Omoruyi [35] in a similar study conducted in two urban cities, which also included Ibadan. A rate of 1.6% for anti-HBc IgM found in this study is much lower than 18.4% reported by Jeremiah *et al* [36] among blood donors. The difference in the study population could have explained the difference in the prevalence observed.

Presence of antiHBc in the absence of HBsAg is of great importance in the setting of blood transfusion and organ transplantation because, screening for HBV infection is done mainly with HBsAg, and absence of this does not totally preclude transmission of the infection through blood transfusion or organ transplantation [37]. The same is true for subjects who have HBV DNA but negative for HBsAg. The detection of HBV DNA in serum as the only serological marker suggests occult HBV infection, because individuals with such status are believed to have high viral replication and are highly infectious [26]. Taking cognizance of this scenario will be vital for blood transfusion safety in Nigeria to prevent transmissible blood borne diseases such as HBV.

It was observed that 20.4% of the HBsAg negative subjects had antiHBs as the only serological marker and this could have come from vaccination against HBV infection. This figure is higher than the 6.7% reported by Oyero and Omoruyi [35] in a similar study. It however, showed that vaccine uptake is still very low in our environment and there is need for more awareness. Also observed is that, 76.9% of the subjects had no markers of HBV infection or immunization. This group of subjects is at risk of contracting the infection considering the high prevalence of the infection in the study population. This signifies presence of large number of susceptible members of the study population who are at risk of HBV infection with attendant public health implication. It is therefore pertinent to identify such individuals and vaccinate them so as to control the spread of HBV in the study community [38].

Conclusion

This study has highlighted the pattern of serological markers of HBV infection, as well as the burden of the infection in the study population. It showed that a large number of susceptible individuals of the study population before our intervention were at risk of HBV infection with attendant public health implication. Therefore, there is the need for more awareness to the public about the mode of transmission of HBV and how it can be prevented.

Acknowledgments

The authors wish to thank the all the participants for their cooperation and express our gratitude to Prof O. G. Ademowo of the Institute for Advanced Medical Research & Training, College of Medicine, University of Ibadan, Nigeria for providing us the laboratory space for analysis.

References

1. World Health Organization. Hepatitis B Fact Sheet No. 204. 2009. Available at http://www.who.int/csr/disease/hepatitis

2. World Health Organisation. Epidemiological Update:Increasing Mortality Calls For Action. Global Hepatitis Report 2017 pp 8. ISBN 978-92-4-156545-5
3. Hudson CP. How AIDS forces reappraisal of hepatitis B virus control in sub-Saharan Africa. Lancet 1990;336:1364-1369
4. Beasley RP and Hwang LY. Epidemiology of hepatocellular carcinoma. In Vijas GN, Dienstag JL, Hoofnagle JH (eds): viral hepatitis and liver disease. Grune and Stratton, Orlando, Florida 1984;2009-14
5. McMahon BJ, Alward WL, Hall DB, *et al*. Acute hepatitis B virus infection: relation of age to clinical expression of disease and subsequent development of the carrier state. J Infect Dis 1985;151:599-603
6. Clement CJ, Kane M, Hu DJ, Kim-farley R *et al.* Hepatitis B vaccine joins fight against pandemic disease. World Health Forum 1990;11:165-168
7. Kire CF. The epidemiology and control of hepatitis B in sub-Saharan Africa. Prog Med Virology 1993;40:143-156
8. Gerlich, W.H. Medical Virology of Hepatitis B: How it began and where we are now. Virol J. 2013;10:239.DOI: 10.1186/1743-422X-10-239.
9. Yakubu AM, Okuonghae HO and Angyo IA. Prevalence of hepatitis B surface antigen in children with sickle cell anaemia. J Trop Paed 1998;13:376-377
10. Fakunle YM, Abdulrahman MB and Whittle AC. Hepatitis B virus infection in children and adults in Northern Nigeria, a preliminary survey. Trans R Soc Trop Med Hyg. 1981;75:626-629
11. Ukaeje CJ, Ogbu O, Inyama PU, Anyanwu GI and Njoku MO. Prevalence of hepatitis B surface antigen among blood donors and human immunodeficiency virus infected patients in Jos, Nigeria. Mom do inst Oswaldo Cruz 2005;100:13-16
12. Abiodun PO, Flach KH and Omoike IU. Hepatitis and sickle cell anaemia. Nig J Paed. 1986;13:95
13. Ezegbudo CN, Agba MI, Agbonlahor DE, *et al.* The seroprevalence of hepatitis B surface antigen and human immunodeficiency virus among pregnant women in Anambra State, Nigeria. Shir E- Med J. 2004;5:20-22
14. Shepard CW, Simard EP, Finelli L, Fiore AE and Bell BP. Hepattis B virus infection: epidemiology and vaccination. Epidemiol Rev. 2006;28:112-125
15. Omeje KN, Ibekwe RC, Ojukwu JO, Una AF and Ibe BC: Risk factors for hepatitis B surface antigenaemia among secondary school students in Abakaliki, South Eastern Nigeria. Niger J Paediatr 2017; 44 (1): 14 –21
16. Adoga MP, Gyar SD, Pechulano S, *et al*. Hepatitis B virus infection in apparently healthy urban Nigerians: data from pre-vaccination tests. J Infect Dev Ctries 2010;4(6):397-400
17. Okonko IO, Okerentugba PO and Akinpelu AO. Prevalence of HBsAg among attendees of ARFH centre in Ibadan, southwestern Nigeria. Am-Euras J Sci Res. 2012;7(3):100-105
18. Jombo GT, Egah DZ and Banwat EB. Hepatitis B virus infection in a rural settlement of Northern Nigeria. Nig J Med 2005;14(4):425-428
19. Otegbayo JA, Fasola FA and Abja A. Prevalence of hepatitis B surface and e antigens, risk factors for viral acquisition and serum transaminase among blood donors in Ibadan, Nigeria. Trop Gastroenterol 2003;24(4):196-197
20. Bwogi J, Braka F, Makumbi I, *et al*. Hepatitis B infection is highly endemic in Uganda: findings from a national serosurvey. African Health Sci 2009;9(2):98-108
21. Balogun TM, Durojaiye IO, Sagoe A and Emmanuel S. Seroepidemiology of Hepatitis B Surface Antigenaemia in HIV Positive Patients. West African J Medicine 2010;29(3):169-173
22. Uneke CJ, Ogbu O, Inyama PU, *et al*. Prevalence of Hepatitis B Surface Antigen among Blood Donors and Human Immunodeficiency Virus Infected Patients in Jos, Nigeria. Mem Inst Oswaldo Cruz, Rio de Janeiro 2005;100(1):12-16
23. Sule WF, Okonko IO, Yunusa IP, Odu NN and Frank-Peterside N. Detection of Hepatitis B surface antigen (HBsAg) and risk factors of transmission among patients attending Universal Hospital, Ankpa, Kogi state, Nigeria. Nature and Sci 2011;9(10):37-44
24. Mehmet D, Meliksah E, Serif Y, *et al*. Prevalence of Hepatitis B infection in the south-eastern region of Turkey: Comparison of risk factors for HBV infection in rural and urban areas. J Infectious Dis 2005;58:15-19
25. Japhet MO, Adesina OA, Donbraye E and Adewumi MO. Hepatitis B Core IgM Antibody (Anti-HbcIgM) among Hepatitis B Surface Antigen (HBsAg) Negative Blood Donors in Nigeria. Virol J. 2011;10:8:513. doi: 10.1186/1743-422X-8-513.

26. Oluyinka, OO, Tong HV, Bui Tien S, *et al*. Occult Hepatitis B Virus Infection in Nigerian Blood Donors and Hepatitis B Virus Transmission Risks. PLoS One. 2015;10(7), e0131912.DOI: 10.1371
27. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. Journal of Viral Hepatitis 2004; 11(2): 97–107
28. Aba HO and Aminu M. Seroprevalence of Hepatitis B Virus Serological Markers among Pregnant Nigerian Women. Ann. Afr. Med. 2016; 15(1): 20–27.
29. Ojo OS, Thursz M, Thomas HC, *et al*. Hepatitis B virus markers, hepatitis D virus antigen and hepatitis C virus antibodies in Nigerian patients with chronic liver disease. East Afr Med J 1995;72:719-721.
30. Ola SO, Otegbayo JA, Yakubu A, *et al*. Pitfalls in diagnosis of hepatitis B virus infection among adults Nigerians. Niger J Clin Pract 2009;12:350-354.
31. Forbi JC, Iperepolu OH, Zungwe T and Agwale SM. Prevalence of Hepatitis B e Antigen in Chronic HBV Carriers in North-Central Nigeria. J Health Popul. Nutr. 2012; 30(4): 377–382.
32. Yang H-I, Lu S-N, Liaw Y-F, *et al.*; Taiwan Community-Based Cancer Screening Project Group. Hepatitis B e antigen and the risk of hepatocellular carcinoma. N Engl J Med 2002;347:168-174
33. You S-L, Yang H-I and Chen C-J. Sero-positivity of hepatitis B e antigen and hepatocellular carcinoma. Ann Med 2004;36:215-224.
34. Milich D and Jake LT. Exploring the Biologic Basis of Hepatitis B e Antigen in Hepatitis B Virus Infection. Hepatology 2003;38:1075–1086. DOI:10.1053/ jhep.2003.50453.
35. Oyero OG and Omoruyi EC. High Prevalence of Isolated Hepatitis B Core Antibody among Adults in Oyo State, Nigeria: The Need for Review of Diagnostic and Vaccination Guidelines. IJTDH 2016;13(1):1-10
36. Jeremiah ZA, Idris H, Ajayi BB, *et al*. Isolated antiHBc IgM antibody among blood donors in the semi-arid region of Nigeria. Human Antibodies 2011;20(3-4):77-82
37. Conjeevaram HS and Lok AS. Occult hepatitis B virus infection: a hidden menace? Hepatology 2001;34:204-206
38. Levy M and Koren G. Hepatitis B vaccine in pregnancy: maternal and fetal safety. Am J. Perinatol. 1991;8(3):227–232

Afr. J. Med. Med. Sci. (2020) **49,** 225-231

Natal and neonatal teeth myths in a rural Nigerian community

OO Bankole[1] and FB Lawal[2]
Departments of Child Oral Health[1] and Periodontology and Community Dentistry[2], College of Medicine, University of Ibadan, Ibadan, Nigeria

Abstract
Introduction: The presence of natal/neonatal teeth in infants is sometimes associated with negative societal attitudes. Literature regarding attitudes and beliefs of residents of Igbo Ora, Nigeria, regarding natal teeth is non-existent. It is therefore important to obtain baseline data to highlight knowledge gaps regarding natal/ neonatal teeth in infants.
Aim: To determine the attitudes and beliefs of residents of Igbo Ora to natal/neonatal teeth in infants.
Methods: A cross sectional study was conducted among 339 women attending dental outreach programmes in Igbo Ora using a pretested 17-item semi structured questionnaire.
Results: Over two fifths (48.7%) believed that a natal tooth is seen in an evil child. A third (36.0%) mentioned that the affected child is an embarrassment to the family. Over half (61.9%) were of the opinion that a natal tooth can affect a child negatively. Of these, 104 (49.5%) and 58 (27.6%) stated that the child "would suffer stigmatization" and "engage in strange things" respectively. Mothers of children with natal teeth were usually advised to extract the teeth, 74 (21.8%), hide the child, 74 (21.8%) and perform sacrifices to appease the gods, 69 (20.4%). The belief that a natal tooth is not associated with spiritual consequences increased with higher educational qualification ($p < 0.001$).
Conclusion: This study reveals that knowledge gaps regarding natal/neonatal teeth are present among inhabitants of Igbo Ora. Appropriate health education is needed for the community members particularly targeted at women and the less educated.

Keywords: *Child, Natal teeth, Neonatal teeth, Myths, Misconceptions*

Résumé
Introduction : La présence de dents natales / néonatales chez les nourrissons est parfois associée à des attitudes sociétales négatives. La littérature concernant les attitudes et les croyances des résidents d'Igbo Ora, au Nigeria, concernant les dents natales est inexistante. Il est donc important d'obtenir des données de référence pour mettre en évidence les lacunes dans les connaissances concernant les dents natales / néonatales chez les nourrissons.
Objectif : Pour déterminer les attitudes et les croyances des résidents d'Igbo Ora vis- à-vis des dents natales / néonatales chez les nourrissons.
Méthodes : Une étude transversale a été menée auprès de 339 femmes participant à des programmes de sensibilisation dentaire à Igbo Ora à l'aide d'un questionnaire semi-structuré prétesté en 17 points.
Résultats : Plus de deux cinquièmes (48,7%) croyaient qu'une dent natale était vue chez un enfant maléfique. Un tiers (36,0%) mentionnait que l'enfant touché est un embarras pour la famille. Plus de la moitié (61,9%) était d'avis qu'une dent natale pouvait affecter négativement un enfant. Parmi ceux-ci, 104 (49,5%) et 58 (27,6%) ont déclaré que l'enfant 'souffrirait de stigmatisation' et 's'engagerait dans des choses étranges' respectivement. Il était généralement conseillé, aux mères des enfants à dents natales, d'extraire les dents 74 (21,8%), de cacher l'enfant 74 (21,8%) et de faire des sacrifices pour apaiser les dieux 69 (20,4%). La croyance selon laquelle une dent natale n'est pas associée à des conséquences spirituelles a augmenté avec une qualification éducative plus élevée ($p < 0,001$).
Conclusion : Cette étude révèle que des lacunes dans les connaissances concernant les dents natales / néonatales sont présentes chez les habitants d'Igbo Ora. Une éducation à la santé appropriée est nécessaire pour les membres de la communauté, particulièrement destinés aux femmes et aux moins instruits.

Mots-clés: *Enfant , Dents natales, Dents néonatales, Mythes, Fausses idées*

Introduction

Natal and neonatal teeth erupt prematurely in infants; while natal teeth erupt at birth, neonatal teeth erupt within the first month of life [1]. Premature eruption of teeth has been a subject of interest since it was first documented by Titus Livinus in 59 BC [2], and has been associated with various beliefs in different cultures. It has been viewed positively in some societies, particularly in developed countries. In

Correpondence: Dr. Folake B. Lawal, Department of Periodontology and Community Dentistry, College of Medicine, University of Ibadan, Ibadan, Nigeria. Email: folakemilawal@yahoo.com.

England, it was believed that children with natal/neonatal teeth will become famous soldiers, while in France and Italy the condition was thought to guarantee conquest of the world [3]. On the other hand, negative opinions have existed among the Chinese as natal teeth were believed to bring ill luck, particularly for girls [4]. Among the Ural/Altaic tribes, affected babies were believed to become witches and sorcerers [5]. In Poland, Africa and India, superstitions regarding natal/neonatal teeth have existed over years [6] and among some African tribes, children born with teeth were murdered soon after birth as it was thought that they would bring misfortune [6].

In Nigeria, 53.7% of residents in a rural community in Ibadan felt the condition was indicative of an evil child [7]. The authors, in their practice, have observed untold anxiety among parents of children with natal/neonatal teeth. This is, possibly, because of its link with negative cultural and societal beliefs.

Literature documenting attitudes and beliefs of residents in Igbo Ora, a remotely located Nigerian town with a primary oral health care outpost, to natal/neonatal teeth is scarce. It is therefore important to obtain baseline data regarding this, to reveal any misconceptions or knowledge gaps about natal teeth. This will serve as a basis in a larger study for the design of appropriate educational materials such as culturally appropriate videotapes to improve knowledge and correct negative attitudes regarding natal/neonatal teeth. The outcome of that approach could then be utilized elsewhere with similar socio-demographic constitution.

The aim of this study was to determine the attitudes and beliefs of residents of Igbo Ora, a rural Nigeria community, to natal/neonatal teeth in children.

Materials and methods

This research used a cross sectional study design and was conducted over a period of four weeks in Igbo Ora. Igbo Ora is a rural town in Oyo State, south-western Nigeria, situated 80 kilometers north of Lagos. It is the headquarters of Ibarapa Central Local Government and has a population of approximately 60,000 people [8]. The characteristics of the town is typical of rural communities in Nigeria of which many of the inhabitants are farmers, artisans and traders.

The study population comprised of women attending dental outreach programmes in Igbo Ora. A minimum sample size of 266 was calculated for the study using a sample size calculation formula for cross sectional study [9] at a power of 90%, a degree of error of 5% and prevalence rate of 22.2% obtained from a previous study [7].

Ethical approval for the study was obtained from Ethical Review Committee of the Ministry of Health, Oyo State. In addition to this, approval and permission was also obtained from the heads of the health centers and the head nurses in charge of the antenatal clinics.

Data Collection

Data for the study was collected by two trained research assistants using a 17-item semi structured interviewer administered questionnaires. The questionnaire was developed by the authors with guidance from relevant literature in English language. It comprised of questions on biodata of the respondents such as the age, gender, tribe and educational qualification of respondents. Included also were questions that assessed beliefs about natal teeth, implication of natal teeth and its effect on the family and society, how to prevent its occurrence and the fate of such children in the community. Advice for mothers of these children was also sought.

The English version of the questionnaire was translated into Yoruba, the local language of this community and back translated into English by independent dentists well versed in both Yoruba and English Language, and who were not aware of the aims and objectives of the study. Minimal difference was found between the original English version and the back translated version of the questionnaire. The questionnaire was pretested among twenty women in the community who were not part of the study. The questions were further modified based on the interaction with the women to suit the study population as much as possible, before its final administration to the study participants. Before the participants were interviewed, the purpose of the study was explained to them. After this, consent was obtained individually from each participant and only those who consented to participate, understood the Yoruba language and had been resident within the community for at least six months were included in the study. Those below the age of 18 years were excluded from the study.

Data management

Data obtained was processed with SPSS version 21 and analyzed. Frequencies and proportions were generated for qualitative variables. Means and standard deviations were used to summarize numeric variables. Chi square statistics was used to determine associations between categorical variables and the level of significance set at $p < 0.05$.

Results

Three hundred and thirty-nine adult females participated in the study. The mean age of the study participants was 32.0 (± 11.7) years. Table 1 illustrates the demography of the study participants. Responses to eruption date of the first tooth varied among the study participants with 130 (38.3%) mentioning that eruption of teeth into a child's mouth should begin around 6 to 8 months of life (Figure 1).

About a third (33.9%) of the respondents had seen a child born with a tooth or one that erupted a tooth in the first few weeks of life.

A natal tooth is believed to be seen in an evil child (165; 48.7%) and children whose mothers had contravened cultural taboos (12; 3.5%). Less than half of the respondents (131; 38.6%), believed it was a natural occurrence (Figure 2). The effects of having a child with a natal tooth in a family is as shown in

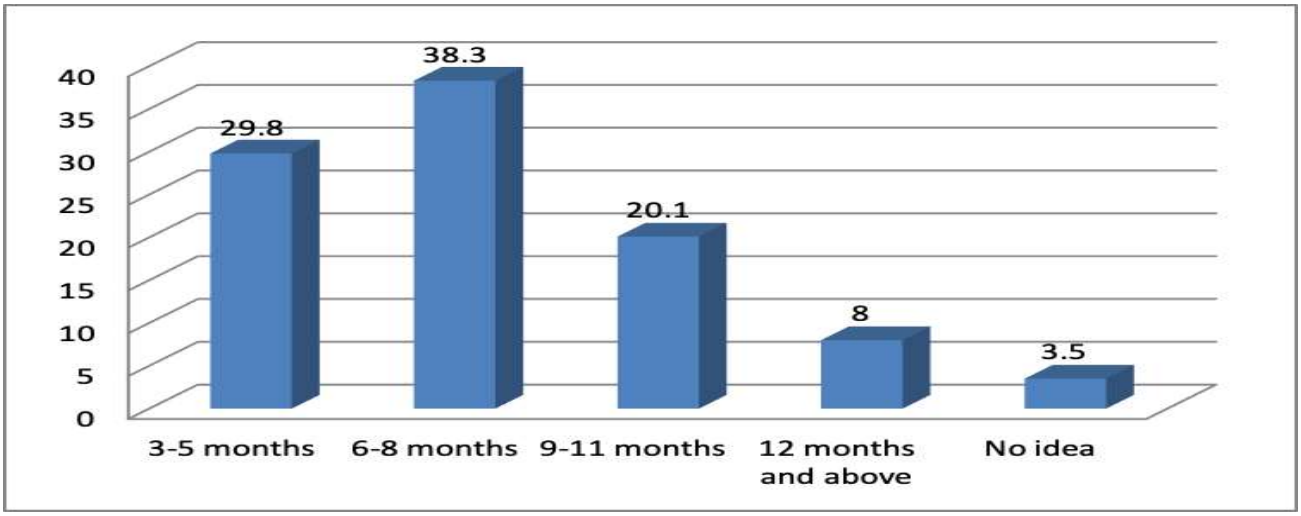


Fig.1: Respondents knowledge about date of eruption of first primary tooth in a child

Table 1: Demography of study participants

Variable	Frequency	%
Age (years) n = 339		
<25	92	27.1
25 – 34	133	39.2
35 – 44	65	19.2
>45	49	14.5
Educational qualification n = 339		
None	52	15.4
Primary	95	28.0
Secondary	131	38.6
Post-secondary	61	18.0
Religion n = 324		
Islam	228	70.4
Christianity	95	29.3
Traditional	1	0.3
Tribe n = 339		
Yoruba	327	96.4
Igbo	4	1.2
Hausa	8	2.4

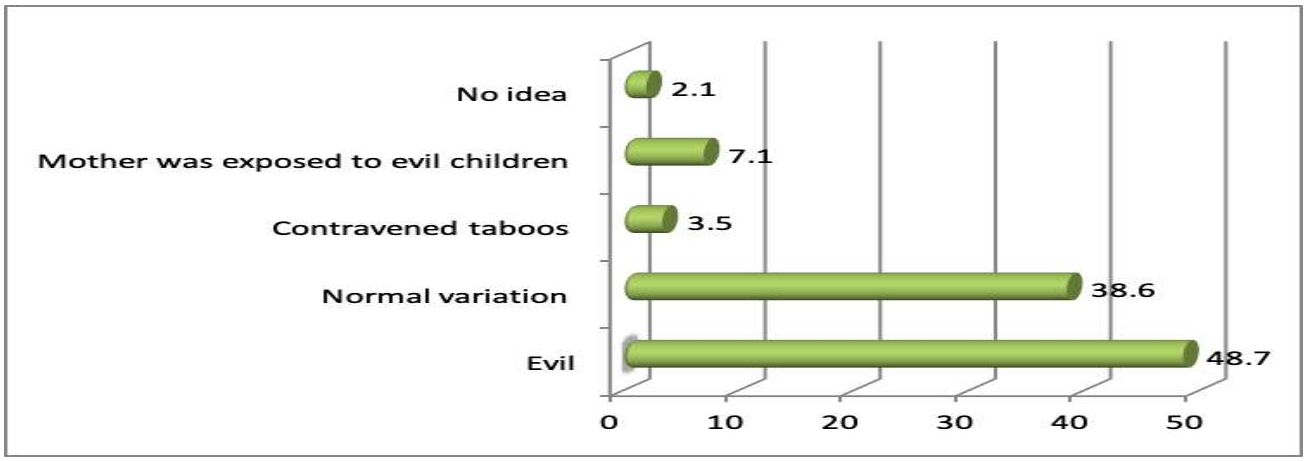


Fig. 2: Perception of respondents about a child with natal tooth

Table 2: Beliefs about the effects of natal tooth on the family and advice to mothers of children with natal tooth

Variables	Frequency	%
Effects of natal tooth on the family (n = 339)		
Source of embarrassment	122	36.0
Family becomes an abomination to the society	122	36.0
A source of fear to the family	52	15.3
A curse to the family	36	10.6
No idea	7	2.1
Perceived effects of natal tooth on the child (n = 339)		
Negative effect	210	61.9
No effect	129	38.1
Perceived negative effects of natal tooth on the child (n = 210)*		
Stigmatization (Curses placed by the child with a natal tooth comes to pass and is permanent).	104	49.5
Child does strange extraordinary things	58	27.6
Child always does his/her things abnormally	27	12.9
Not sure	17	8.1
Child is dangerous	7	3.3
Child is dull	2	1.0
Usual advice to mothers of children with natal tooth (n = 339)*		
Leave the child alone	105	31.0
Extraction the tooth	74	21.8
Hide the child	74	21.8
Perform sacrifices to appease gods	69	20.4
Get rid of the child	8	2.3
Consult a doctor	2	0.6
Spiritual prayer	1	0.3
Consult oracle	1	0.3
No idea	9	1.6
Prevention strategies against occurrence of natal tooth in pregnancy (n = 339)*		
None - just a normal variation	99	29.2
Herbal concoction	96	28.3
Avoid contravening taboos	83	24.8
Engage in cultural rites for pregnant women	48	14.2
Regular attendance at antenatal clinics	6	1.8
Not walking at night	1	0.3
No idea	7	2.1

*Multiple responses

Table 2. Almost half of the respondents (122; 36.0%) stated that such a child is usually a source of embarrassment, and 122 (36.0%) believed the family of the child with natal tooth becomes formidable and is an abomination to the community.

More than half (210; 61.9%) believed that natal tooth affects the child negatively. Of the 210 respondents, 49.5% (104) believed stigmatization is one of the ways natal tooth could affect a child negatively, because the presence of the tooth brings a certainty – "if the child curses someone the curse comes to pass and it is permanent". Also, 58 (27.6%) believed that such child engages in strange things or extraordinary activities (Table 2). A major consideration was that the tooth will exfoliate earlier compared to other teeth.

Mothers of children with natal teeth were usually advised to; extract the tooth (74; 21.8%), "hide the child" (74; 21.8%) or "get rid of the child" (8; 2.3%). Other responses in addition to these were "performing sacrifices to appease gods" (69; 20.4%) (Table 2).

A significant association existed between educational qualification and beliefs about the natal tooth as the tendency of believing that the natal tooth is not associated with spiritual consequences increases with higher educational qualification ($p < 0.001$) (Table 3). No other association was found between demography and beliefs.

Discussion

This study has revealed that myths regarding natal/neonatal teeth abound among residents of Igbo Ora, a rural community in southwest Nigeria. This gives a huge cause for concern as these misconceptions have detrimental effects on the affected children and their families.

Timing of eruption of the primary dentition is considered important among Nigerian parents and they become worried when children erupt their teeth prematurely [7]. Eruption dates of primary teeth vary among various tribes [10]. Almost thirty percent of the respondents stated that babies cut their first teeth between three to five months while about two fifths felt they erupted between six to eight months. Their knowledge on timing of eruption of primary teeth was poorer than observed in a Saudi study where more than four-fifths of mothers knew that the first primary teeth erupt at six to seven months of age [11]. Their poor knowledge could be due to the fact that Igbo Ora is a rural community composed of inhabitants with relatively low literacy levels and probably very little has been done on combating erroneous beliefs about natal teeth in the community.

Regarding their perceptions of children born with teeth, a large proportion of the participants (48.7%) believed this was due to the fact that the baby is evil while others believed it was as a result of close proximity of mothers to other evil children while pregnant. An evil child in the traditional Yoruba culture

Table 3: Demography and beliefs about natal tooth

Demography variable	Beliefs about natal tooth n (%)			
	Normal variation	Other reasons	X^2	p value
Age (years)				
< 25	36 (39.1)	56 (60.9)	2.479	0.479
25-34	49 (36.8)	84 (63.2)		
35-44	30 (46.2)	35 (53.8)		
> 45	16 (32.7)	33 (67.3)		
Total	131 (38.6)	208 (61.4)		
Educational qualification				
None	12 (23.5)	39 (76.5)	41.602	< 0.001*
Primary	27 (28.4)	68 (71.6)		
Secondary	46 (35.1)	85 (64.9)		
Post-secondary	45 (73.8)	16 (26.2)		
Total	130 (38.5)	208 (61.5)		

*statistically significant

is viewed as "demon possessed". It is traditionally believed that when pregnant women are in close contact with evil children, transference of spirits to their unborn babies occurs, leading to anomalies such as a natal tooth. Some of the respondents were also of the opinion that a natal tooth was the consequence of child's mother contravening the cultural taboos. This reveals a high level of ignorance, which may be due to their remote location and strong beliefs in traditional information handed down by their ancestors. The etiology of natal teeth is unknown [12] but has been linked to maternal nutritional deficiency and fever during pregnancy [13], infection eruption accelerated by hormonal stimulation [13], hereditary transmission of a dominant autosomal gene [6] and osteoblastic activity in the area of the tooth germ [14]. Natal teeth are associated with certain syndromes such as Ellis Van Creveld [15], Craniofacial dysostosis and Sotos syndrome [16] and are more frequently associated with cleft lip and palate [17]. Polychlorinated biphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and dibenzofurans (PCDFs) are environmental pollutants that have been known to increase the incidence of natal teeth [18]. However, the superficial position of the tooth germ associated with a hereditary factor seems to be the most accepted possibility [19].

The effect on the child's family is dreadful, as respondents believed that the child would be a source of embarrassment, an abomination and the tooth becomes a source of fear to the family. Thus, the family becomes emotionally disturbed and this is hinged on the fact that these children are believed to be endowed with spiritual powers and authority. Such parents have occasionally resorted to extreme actions such as infanticide or abandonment of the child. Oyapero and Oyapero [20] reported the case of a three-day old Nigerian baby with a natal tooth abandoned on a refuse dump site. In some African communities, such babies are left in forests to die or murdered [21].

The children with natal teeth in the African culture are stigmatized, avoided and called all manner of names [20]. Over a third of the respondents were of the opinion that the natal tooth is an epitome of fear and affected children possess the powers to place permanent and irrevocable curses on people. For this reason, affected children are stigmatized. Effects of stigmatization are terrible as the child is taunted, mocked and avoided by the whole community thus leading to emotional problems. Interestingly, some participants were of the opinion that affected children, as they grow older, engage in dangerous and strange activities even in their pastimes. For this reason, parents of such children at times will seek spiritual protection to forestall these activities. Traditionally, in South Western Nigeria, these children are often referred to as "*abami omo"* meaning strange children. These are wrong views about natal/neonatal teeth still predominant in this community.

Extraction of these teeth was believed to be the solution to this "abomination" by 21.8% of the respondents. Traditional "dentists" and quacks sometimes perform this. Teeth forcibly removed by quacks endanger as well as expose children to infections such as Human Immunodeficiency Virus, tetanus, hepatitis, and bacterial infections due to use of inappropriate and unsterilized instruments. About a fifth of the respondents would advice mothers of affected children to hide them and infanticide was suggested by a few. This is quite worrisome and requires appropriate intervention to disabuse the minds of residents of this community regarding children with natal/ neonatal teeth. "Consultation with the oracle, having spiritual prayers done and offering sacrifices to appease the gods" believed to be solutions to the evil associated with natal/neonatal teeth are reflections of the respondents' strong association of this condition to cultural myths and legend. Similar situations have been experienced in Kenya where parents of the children with natal teeth may have to go to their rural homes for cleansing ceremonies of traditional healers who scrub away the unwanted teeth because it is associated with witch craft [22]. Importantly and worthy of note is that only two participants will advise mothers to seek medical consultation, revealing that only a minority are knowledgeable about this condition.

Preventive strategies to forestall natal teeth as suggested by the respondents are basically related to the cultural beliefs and include intake of herbal concoctions during pregnancy (28.3%). Avoidance of contravening taboos of the land and engagement of pregnant women in cultural rites were also deemed important. These rites include avoiding certain food types, which varies depending on each family's traditional beliefs, and performing required traditional rites. Pregnant women in the Yoruba community are forbidden to walk around the street on sunny afternoons. If there is a need to go out, a stone or pin is fixed to their wrappers or dresses, which allegedly helps to wade away evil spirits believed to be present in the atmosphere on hot sunny afternoons. These evil spirits

are believed to chase away good babies from pregnant women and then "inhabit their wombs". The stone or pin is to drive away "an evil child" from coming near them [23]. All these demonstrate a high level of ignorance regarding natal teeth in this community.

The study revealed that the less educated significantly believed more that natal teeth had spiritual consequences in comparison to the better educated.

Conclusion

The study reveals gross misconception about natal teeth among the inhabitants of Igbo Ora. Thus, improvement of oral health education through health education intervention such as health talks and culturally appropriate videos should be targeted at the mothers and the community in general, particularly the less educated ones.

A limitation of this study is that data were collected from females attending dental outreach programmes, excluding males. A larger and more representative sample would have been gotten if we went from house to house and involved male participants as it is not known if their views differ from of females.

References

1. Massler M and Savara BS. Natal and neonatal teeth: a review of twenty-four cases reported in the literature. J Pediatr 1950;36(3):349-359.
2. Allwright WC. Natal and neonatal teeth. Br Dent J 1958;105:163-172.
3. To EW. A study of natal teeth in Hong Kong Chinese. Int J Paed Dent 1991;1(2):73-76.
4. Zhu J and King D. Natal and neonatal teeth. ASDC J Dent Child 1995;62(2):123-128.
5. Gardiner JH. Erupted teeth in the newborn. Proc R Soc Med 1961;54:504-506.
6. Bodenhoff J and Gorlin RJ. Natal and neonatal teeth: folklore and fact. Pediatrics 1963;32(6):1087-1093.
7. Oyejide CO and Aderinokun GA. Beliefs about prematurely erupted teeth in rural yoruba communities, Nigeria. Public Health 1992;106(6):465-471.
8. Igbo Ora. Available from www.wikipedia.org/wiki/Igbo-Ora Last accessed 5/10/2018.
9. Kish L. Survey Sampling. New York: Wiley Interscience Publications;1965.
10. Oziegbe EO, Adekoya-Sofowora C, Esan TA and Owotade FJ. Eruption chronology of primary teeth in Nigerian children. J Clin Pediatr Dent 2008;32(4):341-345.
11. Kumar S, Tadakamadla J, Idris A, Busaily IAA and AlIbrahim AYI. Knowledge of teething and prevalence of teething myths in mothers of Saudi Arabia. J Clin Pediatr Dent 2016;40(1):44-48.
12. Bigeard L, Hemmerle J and Sommermater JI. Clinical and ultrastructural study of the natal tooth: enamel and dentin assessments. ASDC J Dent Child 1996;63(1):23-31.
13. Goncalves FA, Birmani EG, Sugayai NN and Melo AM. Natal teeth: review of the literature and report of an unusual case. Braz Dent J 1998;9(1):53-56.
14. Jasmin JR, Clergeau-Guerithault S. A scanning electron microscopic study of the enamel of neonatal teeth. J Biol Buccale 1991;19(4):309-314.
15. Weiss H and Crosett AD, Jr. Chondroectodermal dysplasia; report of a case and review of the literature. J Pediatr 1955;46(3):268-275.
16. Hebling J, Zuanon ACC and Vianna DR. Dente Natal—a case of natal teeth. Odontol Clin 1997;7:37-40.
17. Kadam M, Kadam D, Bhandary S and Hukkeri RY. Natal and neonatal teeth among cleft lip and palate infants. Natl J Maxillofac Surg 2013;4(1):73-76.
18. Štamfelj I, Jan J, Cvetko E and Gašperšič D. Size, ultrastructure, and microhardness of natal teeth with agenesis of permanent successors. Ann Anat 2010;192(4):220-226.
19. Hals E. Natal and neonatal teeth; histologic investigations in two brothers. Oral Surg Oral Med Oral Pathol 1957;10(5):509-521.
20. Oyapero A and Oyapero O. Abandonment Of A Neonate With Natal Tooth. Nigerian Journal of Clinical Medicine. 2014;6(1):55-60.
21. Olatosi OO, Oredugba FA, Sote EO, Salami AS and Nzomiwu CL. Nig Dent J 2012;20(1):46-51.
22. It is alright for your baby to be born with teeth, it's not a curse Available from www.standardmedia.co.ke/health/article Last accessed 5/10/2018
23. Adebileje A. Socio-cultural and attitudinal study of selected Yoruba taboos in South West Nigeria. Studies in Literature and Language 2012;4(1):94-100.

Hemi-facial hyperplasia with gingival hyperplasia in a child with occult Teisser1 cleft: Report of a case.

OM Olanloye[1], MT Oyetade[2], OI Opeodu[2], AA Olusanya[3], BO Popoola[1], EB Dosumu[2] and MO Arowojolu[2]

Department of Child Oral Health[1], University College Hospital , Depatments of Periodontology and Community Dentistry[2] and Oral and Maxillofacial Surgery[3], College of Medicine, University of Ibadan, Ibadan, Nigeria.

Abstract

Background: Hemi-facial hyperplasia (HFH) is a rare developmental anomaly that results in facial asymmetry due to an exaggerated growth of the affected side. This condition can be partial or total. Due to its rarity, very few reports can be found in literature. Craniofacial clefts are also rare congenital anomalies with soft tissue and or skeletal components which are commonly categorised by the Teisser classification. No report was found in the literature of a combination of these two rare entities in the same individual thus the reason for this report.

Case description: We report a case of partial HFH (PHFH) with occult Teissier1 cleft in a 15year old girl who presented in our clinic on account of painful left maxillary gingival swelling of 6months duration. Examination revealed a left facial asymmetry with proptosis on the affected side. Oral hygiene (OH) was fair with severe hyperplasia of the gingivae involving the upper left canine tooth to upper left second molar tooth (23 to 27). Gingival hyperplasia was not commensurate with the fairly good oral hygiene. Plain radiograph revealed Teisser1 cleft and angular bone loss around the associated teeth. An assessment of Idiopathic facial asymmetry with severe gingival hyperplasia in a patient with Teisser 1 cleft was made. Full mouth scaling and root planing with stringent oral hygiene instructions were instituted. Gingivectomy with gingivoplasty to restore physiologic gingival contour was done and the patient placed on antibiotics. Histology revealed a reactionary lesion. The gingival condition has remained satisfactory 6months following treatment

Clinical Significance: Clinicians should have a high index of suspicion of Teisser cleft when patients present with idiopathic facial asymmetry.

Keywords: *Craniofacial cleft, Facial asymmetry, Gingival hyperplasia, Hemi-facial hyperplasia*

Correspondence: Dr. O.I. Opeodu, Department of Periodontology and Community Dentistry, College of Medicine, Universiy of Ibadan, Ibadan, Nigeria. Email: opeodulanre@yahoo.com

Résumé

Contexte : L'hyperplasie hémifaciale (HHF) est une anomalie rare du développement qui se traduit par une asymétrie faciale due à une croissance exagérée du côté affecté. Cette condition peut être partielle ou totale. En raison de sa rareté, très peu de rapports peuvent être trouvés dans la littérature. Les fentes crâniofaciales sont également de rares anomalies congénitales avec des tissus mous et / ou des composants squelettiques qui sont généralement classés par la classification de Teisser. Aucun rapport n'a été trouvé d'une combinaison de ces deux entités rares chez le même individu, dans la littérature, d'où la raison de ce rapport.

Description du cas : Nous rapportons un cas d'HHF partielle (HHFP) avec fente occulte de Teissier 1 chez une fille de 15 ans qui s'est présentée dans notre clinique en raison d'un gonflement gingival maxillaire gauche douloureux d'une durée de 6 mois. L'examen a révélé une asymétrie faciale gauche avec proptose du côté affecté. L'hygiène buccale (HB) était passable avec une hyperplasie sévère des gencives impliquant la dent canine supérieure gauche à la deuxième dent molaire supérieure gauche (23 à 27). L'hyperplasie gingivale n'était pas proportionnée à une assez bonne hygiène buccale. Une radiographie simple a révélé une fente de Teisser 1 et une perte osseuse angulaire autour des dents associées. Une évaluation de l'asymétrie faciale idiopathique avec hyperplasie gingivale sévère chez un patient atteint d'une fente de Teisser 1 a été réalisée. Un détartrage complet de la bouche et plantation de racine avec des instructions strictes en matière d'hygiène buccale ont été établis. Une gingivectomie avec gingivoplastie pour restaurer le contour gingival physiologique a été effectuée et le patient a été mis sous antibiotiques. L'histologie a révélé une lésion réactionnelle. L'état gingival est resté satisfaisant 6 mois après le traitement

Signification clinique : Les cliniciens devraient avoir un indice élevé de suspicion de fente de Teisser lorsque les patients présentent une asymétrie faciale idiopathique.

Mots-clés : *fente crâniofaciale, asymétrie faciale, hyperplasie gingivale, hyperplasie hémifaciale*

Introduction

Facial asymmetry can be defined as dissimilarity in the configuration of one side of the face to the other when viewed in relation to a projected mid-sagittal line [1]. It is a specific measure of body asymmetry which is related to a person's health and physical attractiveness [1]. However, an impeccably symmetrical face is a theoretical concept that hardly exists as most individuals have a slight facial asymmetry but are still considered normal [1,2]. The aetiology of facial asymmetry though generally unknown has been classified based on time of onset and progression of the condition, into congenital, developmental or acquired [1,2]. Congenital facial asymmetry occurs during prenatal period and usually seen at birth. Some of the congenital causes of facial asymmetry include cleft lip and palate, Tessier craniofacial cleft, hemifacial macrosomia, neurofibromatosis, torticollis, craniosynostosis and vascular disorders [2]. Congenital hemifacial hyperplasia (CHFH) also known as facial hemihypertrophy, hemimacrosomia, partial gigantism, unilateral gigantism is a rare developmental condition [3]. It was first described by Meckel in 1822 and Rowe in 1962 classified CHFH into three types. Complex Hemifacial Hyperplasia; involving the entire half of the body, Simple Hemifacial Hyperplasia; affecting one or both limbs and Hemifacial hyperplasia. Rowe further classified HFH based on the tissues affected into true and partial. In true HFH, there is unilateral enlargement of all tissues (soft and hard; teeth and bones) with characteristic viscerocranial enlargement, bounded by the frontal bone superiorly (excluding the eye), the lower border of the mandible inferiorly, the midline medially and ear laterally. Partial HFH may involve many structures or may be limited to only one structure [2,3]. It is however important to note that as the individual with CHFH grows older, the features associated with the condition become more apparent and the features are completely expressed by puberty.

Teisser classification utilizes a numbering system to identify the anatomical pathways of soft and or skeletal clefts patterns. The numbering system spans from 0-14 with an isolated 30. Skeletal Tessier 1 cleft is described as a paramedian cleft that occurs in the maxilla and extends posteriorly to form a complete cleft of the hard and soft palate [3,4]. Here, the maxilla is hypoplastic in all three dimensions and the alveolus is keel shaped. The separation between the nasal cavity and the hypoplastic maxillary antrum affected is normal. However, there is distortion of the nasal skeleton resulting in pronounced flattening of the nasal dorsum. There is asymmetry of the pterygoid plates greater and lesser wings of the sphenoid and floor of the anterior cranial fossa with distorted cranial base causing mild plagiocephaly [4].

Case Report

We report a case of a 15-year-old girl who was diagnosed to have "Hemi-facial Hyperplasia with gingival hyperplasia and occult Teisser1 cleft. Informed consent and assent were obtained from the patient's mother and patient respectively before treatment of the patient and report of the case.

Patient was referred from the Oral Diagnosis Clinic of the University College Hospital Ibadan to the Pediatric Dentistry unit on account of gingival enlargement of three years duration. Gingival enlargement had progressively worsened and was associated with indolent mastication on the left side of the mouth and fair oral hygiene. General physical examination was not contributory.

Extra-oral examination revealed a facial asymmetry evidenced by hypertrophy of the left side of the face and proptosis of the left eye which was said to have been noted at birth. The color of the overlying skin of the affected side was similar to that of the surrounding skin. There was deviation of the chin to the unaffected side. (Figure 1)

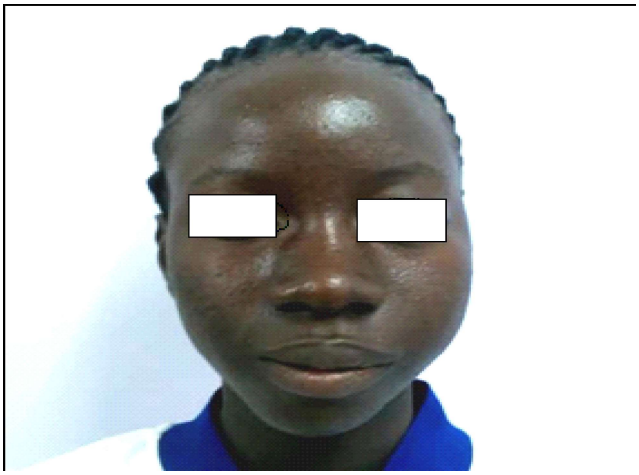


Fig. 1: Hypertrophy of the left side of the face with deviation of the chin to the unaffected side

Intraoral examination revealed gross gingival hyperplasia extending from the 23 to the 27 on the buccal and palatal aspect of the affected side. The gingival lesion was edematous and erythematous covering a major part of the involved teeth with indentation of the lower teeth visible on the gingival surface. There was significant bleeding on gentle probing. However, the buccal mucosae, tongue, palate or floor of the mouth appeared clinically normal. A lingual cross-bite was also noticed. (Figure 2)

Fig. 2: Gingival hyperplasia covering major aspects of the involved teeth

Plain radiograph (Occipitomental) was requested. Occipitomental view revealed normal skull and vault, orbits and paranasal sinuses. However, an oblique bony discontinuity was seen lateral to the midline extending from the medial aspect of the upper left central incisor through the maxilla to floor of the left side of the nose. The mandible was intact. (Figure 3).

Fig.3: Bony discontinuity defect (arrow) lateral to the midline extending from the medial aspect of the upper left central through the maxilla through the floor of the nostril.

Fig.4: Gingival condition following surgical intervention.

Based on the clinical and radiographic findings; a diagnosis of Partial Hemi-facial Hyperplasia

with gingival hyperplasia and occult Teisser1 cleft was made. Treatment of the case was based on the complaint made by the patient and symptomatic management was instituted. Initial scaling and root planing with stringent oral hygiene measure was instituted following which a considerable resolution of the gingival inflammation was noticed, however, the gingival lesion became more fibrotic and was still large enough to impair mastication and aesthetics necessitating surgical intervention. A gingivectomy procedure was performed under local anaesthesia and a course of antibiotics given. Patient was quite satisfied with the results achieved following surgical intervention. (Figure 4)

Discussion

This is a case report of a 15-year-old girl who presented with a left unilateral gingival swelling extending from the upper left canine to the upper left second molar and was found to have idiopathic left Partial Hemi-facial Hyperplasia with an occult Teisser1 cleft. Hemifacial hypertrophy affects either gender and the possibility of sex predilection has been suggested by some reports with varying conclusions. [5-8] Most authors reported that the right side of the face is more affected than the left side but no specific reason has been given for side predilection. [6-9] In this case report, the left side was affected.

The facial asymmetries associated with HFH are often noted at birth but it may be noted much later by the patient or their family. The condition is usually accentuated with age, especially around puberty because of hormonal influence on the facial tissues. At puberty, there is a surge in the level of sex hormones; estradiol in females and testosterone in males. These hormones are responsible for excessive proliferation, differentiation and growth and thus the pubertal growth spurts seen. [12] Due to this growth spurt, there is an exaggerated growth on the affected side which makes the asymmetry more pronounced.

There seems to be no consensus on the gender predilection among cases of hemifacial hyperplasia reported. Some authors have reported this condition to be commoner in males [6,10] while others have reported it to be commoner in females. [7, 11] Hemifacial hyperplasia is more commonly reported among Caucasians than Africans and this may be due to the fact that occurrence amongst Africans is under reported. [4] Hemifacial hypertrophy may be associated with other conditions, such as acromegaly and pituitary gigantism due to the possible effect of growth hormone on the susceptible facial tissue. [4] However in this case, no associated conditions were found

Numerous clinical findings may be seen, of which the more common include gross asymmetry of the facial structures and the presence of edematous hypertrophied areas. [5-8] Radiographically, the mandibular canal may be increased in size. Some of the cases may exhibit larger crowns of teeth on the affected side. The teeth usually involved are the permanent cuspids, premolars, and first molars. [5-8] In addition, precocious eruption and premature development of these involved teeth is not unusual. Larger root sizes, and in some cases root resorption with open bite, malocclusion, and trismus with or without unilateral or bilateral ankylosis may be observed. [5-8] In this case, compared to the unaffected side, the teeth on the affected side appeared clinically and radiographically normal but there was lingual cross-bite on the affected side.

Soft tissues like the lips, uvula, and tonsils may be involved, and frequently the tongue exhibits enlarged lingual papillae with unilateral enlargement and displacement, this was not noticed in our patient. The buccal mucosa may also be hyperplastic, with a velvety and smooth texture hanging in soft pendulous folds. [3-8] However, majority of the soft tissues on the affected side appeared clinically normal except for the hyperplastic gingivae that bled on gentle probing.

Generally, treatment is not indicated for HFH unless cosmetic considerations are involved. Procedures usually are planned when physiological growth ceases. These treatments may include reconstructive procedures like osteotomies, ostectomies, orthognathic surgical procedure in conjunction with orthodontic therapy. [13-15] Other therapies include liposuction, soft tissue debulking and face lifts. [14-15] Cosmetic reconstruction has frequently been performed with limited to moderate gains. [13-15].Typically, no bony regrowth has been reported postoperatively other than some cases of fatty deposits recurring in the cheeks. [13-15]. In this case, there was no significant cosmetic disturbance apart from that presented by the gingival hyperplasia thus no reconstructive procedure was carried out. However, due to the attendant morbidity and functional problems associated with the gingival hyperplasia on the affected side in our patient, periodontal treatment which included oral hygiene instruction and motivation as well as gingivectomy and gingivoplasty were done to reduce the bulk of the hyperplastic gingivae.

Conclusion

Hemifacial hyperplasia, a rare condition with an unknown aetiology may be associated with functional and psychosocial problems as a result of the deformity associated with it. However, due to its rarity and the fact that it is underreported, many clinicians may find its diagnosis and management quite challenging. It was therefore important to document this case thereby increasing the level of awareness about this disease entity, its attendant problems and the various treatment options available.

Declaration of patient's assent and parent's consent

The authors certify that they obtained written informed assent and consent from the patient and parent respectively. In these forms the patient and parent gave assent and consent for images and other clinical information of the patient to be reported in the journal.

References

1. Rogers GF, Greene AK, Oh AK, Robson C, Mulliken JB. Zygomaticotemporal synostosis: a rare cause of progressive facial asymmetry. Cleft Palate Craniofacial Journal. 2007;44:106-111
2. Cheong YW and Lo LJ. Facial asymmetry: etiology, evaluation and management. Chang Gung. Med J. 2011;34:341-351
3. Deshingkar SA, Barpande SR and Bhavthankar JO. Congenital hemifacial hyperplasia. Contemp Clin Dent. 2011; 2:261-264.
4. Islam MN, Bhattacharrya I, Ojha J, *et al*. Comparison between true and partial hypertrophy. Oral Surgery Oral Medicine Oral Pathol Oral Radiol Endod. 2007; 104:501-595.
5. Lawoyin JO, Daramola JO and Lawoyin DO. Congenital hemifacial hypertrophy; Report of two cases. Oral Surg,Oral Med, Oral Pathol. 1989; 68:27-30.
6. Bhuta NH, Yadav A, Desai RS, *et al*. Clinical and imaging findings of True hemifacial hyperplasia. Case Report Dent. 2013;2013: 152528
7. Shanmugasundaram K, Vedan VKV, Ganapathy S,Sathish S and Satti P. Congenital hemifacial hyperplasia; clinical presentation and literature review. Case Report Dent. 2016; 2016:5260645.
8. Neville B, Damm D, Allen C and Bouquot J. Developmental defects of oral and maxillofacial region. In Neville *et al* oral and maxillofacial pathology. 2nd Edition. Philadelphia, 2002. P.37-38.
9. Yoshimoto H, Yano H, Kobayashi K, *et al*. Increased proliferative activity of osteoblasts in congenital hemifacial hypertrophy. Plast Reconstr Surg. 1998; 102:1605-1610.
10. Austin RD, Srivastava KC, Pranavadhyani G and Shrivastava D. A rare clinical case of true hemifacial hyperplasia. Singapore Med J. 2013; 54:e160-e163.
11. Verma P, Gupta K, Rishi S and Triwedi A. Hemifacial hypertrophy; a rare case report. J. Indian. Aca. Oral Med Radiol. 2012; 24: 338-341.
12. Caufriez A. The pubertal growth spurt; effect of sex hormones on growth hormone and insulin-like growth factor I. European Journal of Obstetrics and Gynaecology and Reproductive Biology. 1997; 71: 215-217 .
13. Hall HD. An improved method for treatment of facial asymmetry secondary to jaw deformity. J Oral Maxillofac Surg 1984; 42:673-679.
14. Padwa BL, Evans CA and Pillemer FC. Psychosocial adjustment in children with hemifacial microsomia and other craniofacial deformities. Cleft Palate Craniofac J. 1991; 28:354-360.
15. Nandimath SA, Raikumar GC, Nayak T, *et al*. Hemifacial hypertrophy; exploring new avenues of treatment modalities. Natl.J. Maxillofac. Surg.2016; 7:100-104.

Afr. J. Med. Med. Sci. (2020) **49,** 241-252

Survival analysis of time interval between first and second childbirth among women in Nigeria

AF Fagbamigbe, AE Ojo, NO Onyeike, IP Okafor, SO Atilola, RA Olabuyi, and RF Afolabi

Department of Epidemiology and Medical Statistics, Faculty of Public Health, College of Medicine, University of Ibadan, Ibadan, Nigeria

Abstract

Background: Birth spacing, especially between first and second births, could impact on fertility, and on maternal and child health. While the interval between marriage and first-birth has been widely studied, information on intervals between first and second births (SBI) and its determinants is scarce. We investigated the timing of second childbirth and its determinants among women in Nigeria.

Methods: Using the 2013 Nigeria Demographic and Health Survey, we analysed data on 27451 women of reproductive age who had reported at least one childbirth as of the survey date. We used Kaplan-Meier survival analysis and Cox proportional-hazard regression with 95% confidence interval (CI) computed.

Results: The median SBI among women in Nigeria was 34 months (CI: 33.7–34.3). The hazard of second-birth was higher among women from rural (HR=1.161; CI: 1.13-1.19) compared to those from the urban areas. While women living in other regions had tendencies to shorten SBI compared with the North Central, those from South West were 9% (aHR=0.91; CI: 0.86–0.96) less likely to delay it. For every one year age-at-first-birth delayed among women, the hazard of second-birth increased by 1.9%. Wealth status, contraceptive use, being employed, higher education among women and spouses, and first-child survival are protective of SBI.

Conclusions: Contraceptive use, being employed, living in an urban area, belonging to higher wealth quintile and higher educational attainment could lead to longer second birth interval which could lead to a healthier child, safer motherhood, and reduced fertility. Women should be encouraged to delay SBI as a fertility-control-strategy.

Keywords: *Hazard ratio, Second birth interval, Kaplan Meier, Cox-regression, Median survival time.*

Correspondence: Dr. A.F. Fagbamigbe, Department of Epidemiology and Medical Statistics, Faculty of Public Health, College of Medicine, University of Ibadan, Ibadan,Nigeria. E-mail: fadeniyi@cartafrica.org.

Résumé

Contexte : L'espacement des naissances, en particulier entre la première et la deuxième naissance, pourrait avoir un impact sur la fertilité et sur la santé maternelle et infantile. Bien que l'intervalle entre le mariage et la première naissance ait été largement étudié, les informations sur les intervalles entre la première et la deuxième naissance (DN) et ses déterminants sont rares. Nous avons étudié le moment du deuxième accouchement et ses déterminants chez les femmes au Nigéria.

Méthodes : En utilisant l'Enquête Démographique et de Santé au Nigéria de 2013, nous avons analysé les données sur 27451 femmes en âge de procréer qui avaient déclaré au moins un accouchement à la date de l'enquête. Nous avons utilisé l'analyse de survie de Kaplan-Meier et la régression à risque proportionnel de Cox avec un intervalle de confiance (IC) à 95% calculé.

Résultats : La DN médiane chez les femmes au Nigeria était de 34 mois (IC : 33,7–34,3). Le risque de deuxième naissance était plus élevé chez les femmes des zones rurales (HR = 1,161; IC : 1,13-1,19) par rapport à celles des zones urbaines. Alors que les femmes vivant dans d'autres régions avaient tendance à raccourcir la DN par rapport à celles du centre-nord, celles du sud-ouest étaient 9% fois (aHR = 0,91 ; IC : 0,86-0,96) moins susceptibles de la retarder. Pour chaque âge d'un an à la première naissance retardé chez les femmes, le risque de deuxième naissance a augmenté de 1,9%. Le statut de richesse, l'utilisation de contraceptifs, le fait d'être employé, l'enseignement supérieur chez les femmes et les conjoints et la survie du premier enfant sont protectives à la DN.

Conclusions : L'utilisation de contraceptifs, le fait d'être employé, de vivre dans une zone urbaine, appartenant à un quintile de richesse plus élevé et à un niveau de scolarité plus élevé pourraient conduire à un deuxième intervalle de naissance plus long, ce qui pourrait conduire à un enfant en meilleure santé, à une maternité plus sûre et à une fertilité réduite. Les femmes devraient être encouragées à retarder la DN en tant que stratégie de contrôle de la fertilité.

Mots - clés : *Hazard ratio, Second intervalle de naissance, Kaplan Meier, Cox-régression, Durée médiane de survie.*

Introduction

Nigerian population remains the highest in Africa, and it is among the first ten most populated countries in the world. Despite current significant fertility decline in Africa countries, only slight changes have been observed in Nigeria from the 1970 of 6.5 to 5.7 in 2013 [2,3]. For, instance the current total fertility rate (TFR) in Africa and the 1970 estimate were 3.9 vs 8.1 in Kenya, 4.2 vs 8.2 in Rwanda, and 2.5 vs 7.9 in Morocco [1].

According to Simeon et al, Nigeria population is relatively high taking cognizance of the current estimate of over 170 million people and the current TFR of 5.7 births per woman of Nigeria compared to the overall TFR of 5.2 births in Africa [1]. The situation is worsened by the unmet need of contraceptive which affects birth spacing, and a short interval between births which poses risk not only to the mothers but the demographic structure of any nation [4,5]. The unprecedented transition in China's fertility rate initiated by a government-sponsored birth control has had positive social, economic and demographic implications for China. Unarguably, the inability of the Nigeria government to control TFR may pose a serious obstacle to its developmental efforts.

The time interval between first and second childbirth (SBI), otherwise called the second birth interval, among women plays important role in any nation's fertility rate or parity [6]. A short First Birth Interval (FBI) after the marriage of a woman leads to a rapid transition to higher parity and consequently to high fertility, particularly when the first birth is a female child [7,8]. Besides FBI, SBI like any other birth intervals could impact on the health of the mother and second birth in that sufficient SBI help to avoid preterm and low birth weight and also to reduce fertility in the long run [9–12].

Literature is replete with the fact that SBI is highly influenced by several socio-economic and demographic factors including education level [13–15]; wealth status [16,17]; residence [13]; religion[18,19], and working status. Cohen et al. reported that a low level of education is associated with high fertility[20]. Furthermore, Kim et al. emphasized that both the demand for children and the cost of fertility control are major forces in fertility decline, the time interval when a woman is exposed to the risk of pregnancy after the first birth is closely related to the duration of breastfeeding due to postpartum amenorrhea [21]. Higher female education has been found to be associated with longer SBIs [6].

Health consequences of short SBI include but are not limited to neonatal and infant mortality, low birth weight and maternal anaemia due to postpartum haemorrhage [22,23]. According to Campbell et al, women who give birth again within 18 months of having a baby, especially within a year, are more likely to have a very premature child and are also running a higher risk of having a child with a birth defect or childhood behavioural problems [24]. It has been noted in an earlier study that at least a year and a half between children is "optimal birth spacing" [25]. It is generally recommended that a woman should wait at least 12 months in between pregnancies. More so, low birth weight and preterm have been linked to both short and long interval between pregnancies [26]. However, other factors and individual circumstances must be taken into accounts, such as maternal age or pre-existing health conditions. These confounding factors may determine whether a woman chooses to conceive slightly earlier than recommended [25]. Often, couples without any natural delay consider an economic advantage, opportunity cost and income in choosing SBI.

The level of contraceptive uptake in Nigeria, estimated at 16% is one of the lowest among several countries [27]. The low uptake leads to an increase in the number of unwanted pregnancies, which are usually characterized by short birth intervals [28,29], SBI inclusive. A reduced fertility rate is connected to a longer birth interval [5]. In other words, a decrease in the birth interval increases fertility and demographic odds [30].

While the interval between marriage and first birth has been studied, there is a paucity of information on SBIs. Understanding the intervals and its determinants is important to fertility and demographic dividends. The information on the timing of second births and its determinants will provide evidence-based information to population programmers and policymakers. The goal of this study is to assess the SBI among women in Nigeria and identify the factors influencing the intervals.

Methods

Study design and setting

The nationally representative and cross-sectional 2013 NDHS data was used for this study [27]. The data comprised of self-reported information on the sexual and reproductive health history of the sampled women in Nigeria. The survey used multistage cluster sampling

techniques using the 2006 Population Census of the Federal Republic of Nigeria, provided by the National Population Commission as the sampling frame. The Enumeration Areas, referred to as clusters, were the primary sampling units; 904 (372 in urban; 532 in rural) clusters were sampled for the survey.

Study variables

The outcome of interest is the SBI among women in Nigeria. Women without any birth as at the time of the survey were excluded from the analysis. Women who have not had a second birth were right-censored as of the survey date. The explanatory variables included in the study are region of residence, religion, wife education, husband education, wealth index, type of residence, age at first birth, employment status, contraceptive use, marital status at first birth and survival of the first child.

Data analysis

Descriptive statistics and survival analysis methods were used for the analysis. The use of survival analysis approach in studies involving censored data is replete in the literature[28,31–35]. The "failure time" for participants who had already had second births was the SBI. However, for the women without second births yet, their censored time was the time since first birth and interview date. We estimated the survival and hazard functions using equations (1) and (2) respectively.

$$S(t_i) = \prod_{i=1}^{j} P(T > t_i | T \geq t_i) \quad \text{.....(1)}$$

$$h(t) = \lim_{\Delta t \to 0} \frac{P(t \leq T < t + \Delta t | T \geq t)}{\Delta t} \quad (2)$$

The estimates of survival probabilities at specific times and the median survival time (MST) are point estimates and should be interpreted as such with the corresponding confident interval. The standard error and 100(1-á)% confidence interval for S(t) was estimated using equations (3) and (4) respectively.

$$S.E\{S(t)\} = \left\{S(t)\sqrt{\sum_{j=1}^{k} \frac{d_i}{n_i(n_i - d_i)}}\right\} \quad \text{..... (3)}$$

$$S(t) \pm Z_{1-\alpha/2} . S.E\{S(t)\} \quad \text{..... (4)}$$

We carried out Cox proportional hazards regression analysis to identify the effects of participant's characteristics on SBI. The Cox regression modeled the hazard function as the dependent variable to determine which combination of explanatory variables significantly affects the hazard. We thus expressed the Cox regression model with the predictors as:

$$h(t_i) = h_0(t)exp(\beta_1 X_{1i} + \beta_2 X_{2i} + \cdots + \beta_p X_{pi})$$
$$= h_0(t)exp(\sum_{j=1}^{p} \beta_j X_{ji})$$
$$\xrightarrow{yields} \ln \frac{h(t)}{h_0(t)} = \beta_1 X_{1i} + \beta_2 X_{2i} + \cdots + \beta_p X_{pi}$$
$$\cdots\cdots (5)$$

Where β_j is a vector of the coefficients of the explanatory variables,

$h_0(t)$ the baseline hazard function and

$\frac{h(t)}{h_0(t)}$ the hazard ratio (HR).

Three assumptions were made in the model: (1) Independence of survival times between distinct individuals in the women sampled, (2) There exists, a multiplicative relationship between the predictors and the HR and (3) A constant HR over time.

The coefficients âj indicates whether the changes in the expected duration will be statistically significant or not. The HR, expressed as the exponentials of the coefficients, indicates a higher likelihood of exposure to the event of interest if it is >1, HR < 1 implies lower exposure, while HR=1 suggest no difference. The log-rank test was used to compare the survival experience between different categories of the characteristics studied. Variables significant in the independent Cox regression were used in the multiple Cox regression while controlling for confounders.

The data owners have already made provision to minimize intracluster correlation through the use of effective sampling and thereby reduced correlations among subjects from the same cluster and also weighed the data to adjust for differences in population sizes of each state in Nigeria. Statistical significance was determined at 5%.

Ethical Approval

The Institutional Review Board (IRB) of the National Institute of Medical Research, Nigeria approved the

study protocol, survey instruments, and materials before the data were collected. Details of the ethical approvals have been reported earlier [27]. Also, informed consents were received from the participants before interviewing them. The researchers obtained approval from Measure of DHS for permission to use the data before analysis.

Results

Our analysis was restricted to 27451 married women who had had at least a child-birth and supplied all required dates for relevant events among the 38948 women who participated in the 2013 NDHS. Among these, 22,434 (81.7%) had had second birth as of the survey date. As showed in Table 1, 9778 (35.6%) women were from urban areas. Nearly a half (43.5%) of the women had no formal education, the majority (83.6%) were not using contraceptive and about 14% had lost a first child with a median SBI of 31 months (34.37–35.3). About 16217(59.1%) women were teenagers compared with only 778(2.8%) at age 40–49 years when they had their first childbirth. The overall MST to second birth was 34 months (95% CI: 33.8-34.2) (Table 1).

different categories of characteristics considered as shown in Table 2.

Table 3 shows the outcome of the Cox regression analyses to identify the crude and adjusted HR of factors affecting SBIs. We found women from the rural area to have a higher risk of earlier second births (HR=1.16; 95% CI: 1.13–1.19) compared to those from the urban areas. Women from middle and richest wealth quintile were 16.4% and 23.5% times more likely to delay second births compared to those in the poorest wealth quintile. The SBI tends to decrease with women educational attainment, with HR=0.79 (95% CI: 0.75–0.82) among women with higher education compared with women with no education. Also, women not using contraceptives (HR=1.06; 95% CI: 1.02–1.10) were more likely to have shorter second birth intervals than those using contraceptives.

However, while controlling for confounders, the Cox proportional model revealed a significant relationship between SBI and the regions where the women reside. While women living in other regions had tendencies to shorten SBI compared with the North Central, those from South West were about 10% times (aHR=0.91; 95% CI: 0.86 – 0.96) less likely to have a

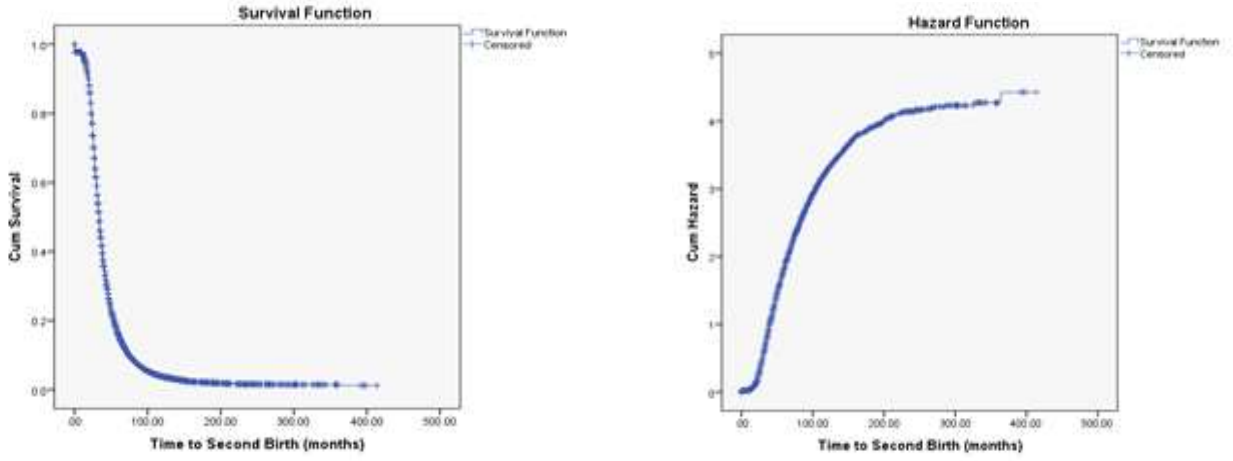


Fig.1: Overall survival and hazard function of SBI

Figure 1 shows the probabilities of the risk of having a second birth after the first birth and the cumulative probability (survival rate). It shows that the overall median survival time is 34 months. In Figures 2a and 2b, we present the survival curves alongside the hazard curves of SBI disaggregated by different categories of selected characteristics of the women.

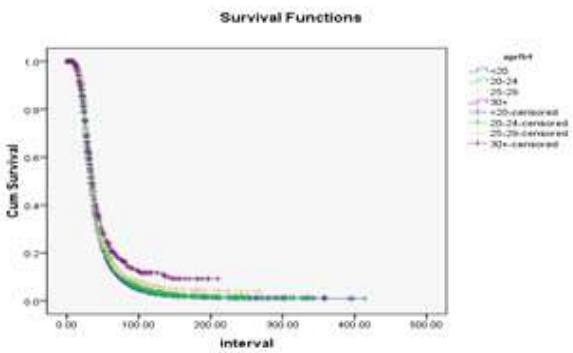
Using the log-rank test, the survival curves of the women's were found to be significant among the second birth. For every one year delay in the age at first birth among the women, the hazard of second birth increased by 1.9%. Employment status of the women was significantly associated with SBI. We found the wealth status of the households from which a woman comes from to be protective of the second birth, with tendencies of longer SBI among richer women. In the same way, the survival of the first child is also protective of SBI (Table 3).

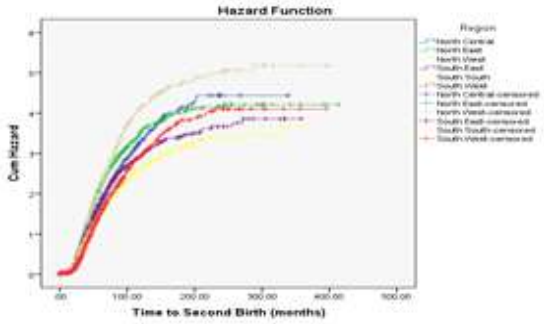
Table 1: Distribution of respondents by some selected characteristics with the median time to second birth

Characteristic's Category	N	%	MST to 2nd Birth (Months)	95% CI for MST to 2nd Birth (Months)
Region				
North Central	4190	15.3	36.0	35.3 - 36.7
North East	5096	18.6	33.0	32.5 - 33.5
North West	7730	28.2	33.0	32.6 - 33.4
South East	2621	9.5	32.0	31.2 - 32.8
South South	3830	14.0	36.0	35.1 – 36.9
South West	3984	14.5	39.0	38.1 - 39.9
Residence				
Urban	9778	35.6	36.0	35.5 - 36.5
Rural	17673	64.4	34.0	33.7 - 34.3
Wealth Index				
Poorest	5543	20.2	33.0	32.5 - 33.5
Poorer	5836	21.2	33.0	32.5 - 33.5
Middle	5588	20.4	35.0	34.4 - 35.6
Richer	5498	20.0	36.0	35.4 - 36.6
Richest	4986	18.2	37.0	36.2 - 37.8
Wife Education				
No Education	11952	43.5	33.0	32.7 - 33.3
Primary	5953	21.7	35.0	34.5 - 35.5
Secondary	7475	27.2	36.0	35.4 - 36.6
Higher	2071	7.5	38.0	36.5 - 39.5
*Husband Education**				
No Education	9700	36.7	33.0	32.6 - 33.4
Primary	5282	20.0	34.0	33.4 - 34.6
Secondary	7631	28.8	35.0	34.5 - 35.5
Higher	3844	14.5	36.0	35.2 - 36.8
*Religion**				
Catholic	2535	9.2	34.0	33.1 - 34.9
Other Christian	10107	36.8	36.0	35.5 - 36.5
Islam	14504	52.9	34.0	33.7 - 34.3
Traditional	293	1.1	33.0	31.2 - 34.8
Age at first birth				
<20	16217	59.1	34.0	33.7 - 34.3
20-24	7754	28.2	35.0	34.5 - 35.5
25-29	2702	9.8	34.0	33.1 - 34.9
30+	778	2.8	35.0	33.3 - 36.7
Marital Status at FB				
FB before Cohabiting	25025	91.2	34	33.7-34.3
Cohabiting before FB	1682	6.1	38	36.7-39.3
Never Married	744	2.7	NA	NA
Employment Status				
Working	20354	74.4	35.0	34.7 – 35.3
Not working	6987	25.6	33.0	32.5 – 33.5
First Child Survived				
Yes	25329	92.3	35.0	34.7 - 35.3
No	2122	7.7	31.0	30.0 - 32.0
Contraceptive use				
Using	4501	16.4	36.0	35.3 – 36.7
Not using	22950	83.6	34.0	33.7 – 34.3
Total	27451		34.0	33.8 – 34.2

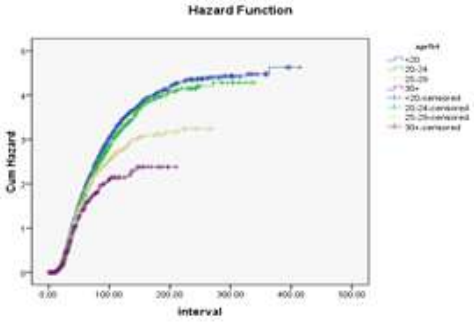
* missing values; CI – Confidence interval; NA – Can't be computed; N – number of women; FB - First Birth; MST - Median Survival Time

Region

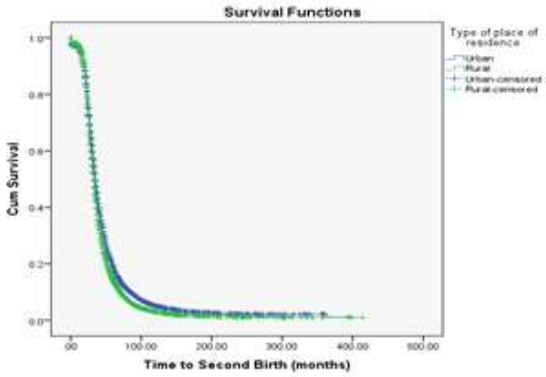


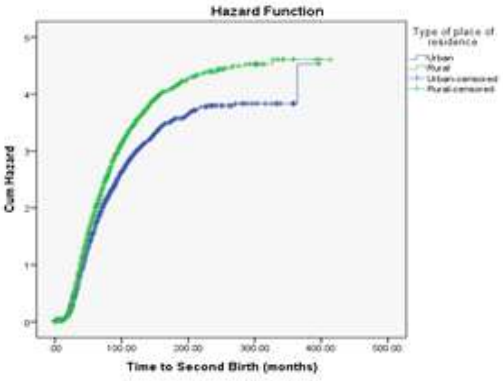


Age at first birth

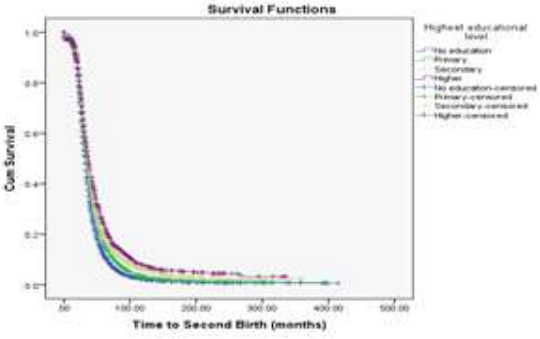


Residence





Educational attainment



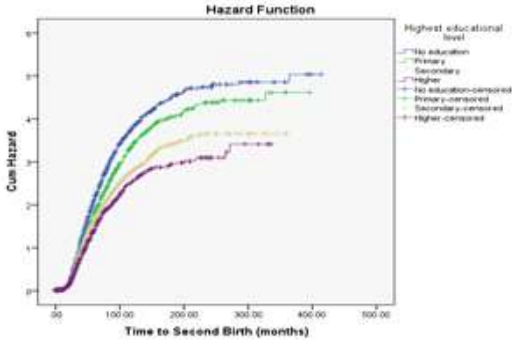
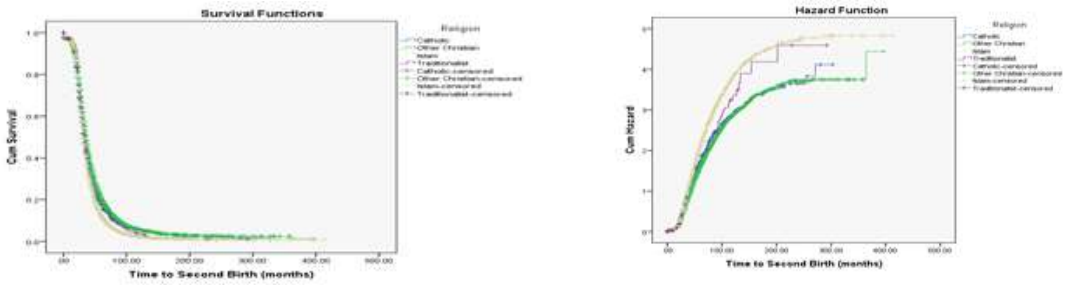
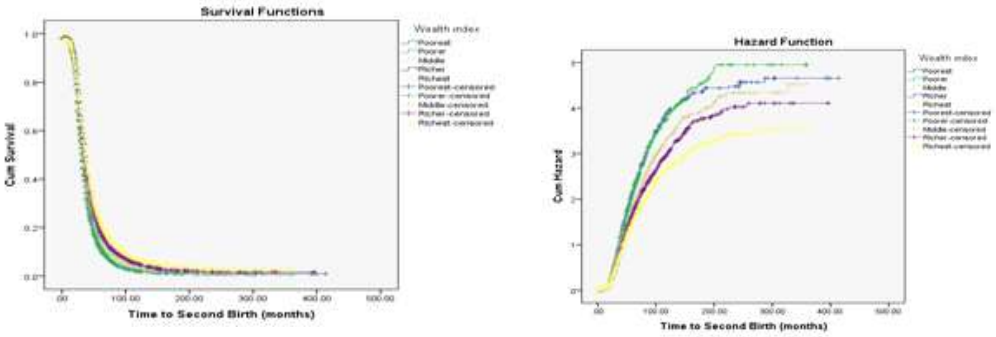


Fig. 2a: Survival and hazard functions of the second birth interval by selected characteristics

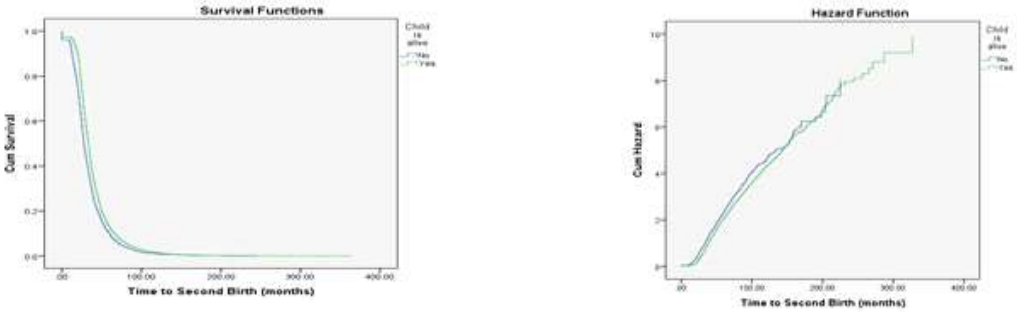
Religion



Wealth index



First child survival



Contraceptive Use

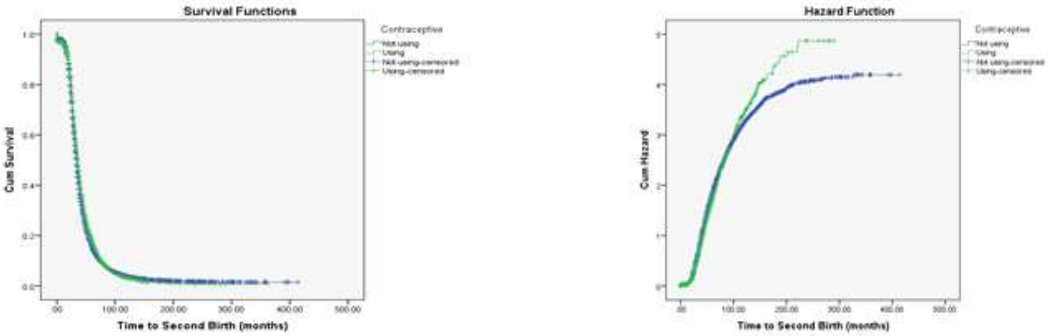


Fig. 2b: Survival and hazard functions of the second birth interval by selected characteristics

Table 2: Comparison of the survival curves of SBI by selected explanatory variables using the Log-rank test

Variable	Chi-square	p-value
Region	464.538	<0.0001*
Religion	320.994	<0.0001*
Education	359.015	<0.0001*
Partner education	170.912	<0.0001*
Wealth index	392.927	<0.0001*
Type of residence	138.508	<0.0001*
Age at first birth	38.568	<0.0001*
First Birth Survived	13.317	<0.0001*
Employment status	68.608	<0.0001*
Contraceptive use	16.205	<0.0001*

**significance at 5%*

Discussions

The aim of this study was to assess the timing of second birth among women of reproductive age in Nigeria. The overall median survival time between first and second birth among women in Nigeria is 34 months which varied across the characteristics considered in this study. Our finding is similar to the outcomes of an Ethiopian study which found that about 57% of Ethiopian women practice short birth interval with the median birth interval of 33 months[7]. The authors noted that the actual birth interval is significantly shorter than the preferred birth interval among the women studied. The likelihood of mothers to have delayed SBI is higher among those whose first child survived as corroborated in earlier studies [5,36,37].

We found the geographical zones of residence, employment status, educational attainment as well as age at first birth to have a significant impact on SBI. These outcomes are similar to the findings of Yohannes et al which reported that significant birth interval variations by contraceptive use, residence, wealth index and occupation of husbands [7]. While adjusting for other variables, we found the educational attainment of the spouses to be significantly associated with SBI whereas women education was not significant. This could be attributed to the tendencies of men to have higher decision making power on fertility issues than the women [27,38]. Women whose husband had higher education had a higher likelihood of delaying second births. Our finding on the significance of education on SBI is further corroborated by some earlier studies [13–15]. Education for both males and females is, therefore, a potent trigger for the delay in second childbirth and can help reduce fertility in the long run.

As shown in the adjusted model, the women' household wealth quintile is a determinant of SBI. Generally, women from poorest households had higher odds of shortened SBI compared to those from richer wealth quintiles [5,39]. Women wealth quintiles have an interwoven relationship with other predictors of SBI. For instance, wealth status often predicts and as well associated with educational attainment and employment status of women [40] and also impacts on contraceptive use and unwanted pregnancies [16,41]. The low educational level may trigger unemployment and lead to poor wealth status, causes unwanted pregnancies [42] and consequently affect SBI. Thus, empowerment strategies should focus on education and employment as a means of increasing SBI. Again, wealth status might have affected the use of contraceptives by women. This was already established in the literature [4,43]. The inability of women to purchase the commodity might be detrimental to their intention-to-use. Respondents who were not using contraceptives were less likely to have shorter SBI compared to those using it. This shows that contraceptives use among women will prolong the SBI and check high fertility among women. This is in agreement with Creanga, *et al.* study which identified wealth status to influence contraceptive use and by extension, the SBI [16,17].

As reported in some earlier studies [18,19] that religion is significant to birth intervals, we found religion to be significant in the current study. This significance of religion could be linked to the region from which the women come from. Nigeria Northern regions are mostly occupied by Muslims while Christianity is dominant in the south. Our study found significant differences in the SBI across the regions where the women live with women from the North East, North West, South East, and South-South having longer SBI than the North Central. But, women from the South West had shorter SBI than those from the North Central.

We found out that women from the rural areas had an earlier risk of the second birth compared to those from the urban areas. This is similar to the findings of Andi, et al. which concluded that rural-urban differential is a significant predictor of SBI among Uganda women [13]. These findings further support our other findings that SBIs are usually shorter among unemployed women, and those either primary or

Table 3: Crude and adjusted determinants of the time interval between the first and second childbirth among women in Nigeria

Characteristics	HR	HR 95% CI	aHR	aHR 95% CI
Region				
North Central	Ref			
North East	1.21	*1.16 - 1.27	1.16	*1.10 - 1.22
North West	1.23	*1.18 - 1.29	1.12	*1.06 - 1.17
South East	1.10	*1.04 - 1.16	1.17	*1.10 - 1.24
South South	0.91	*0.87 - 0.96	1.06	*1.01 - 1.12
South West	0.89	*0.85 - 0.93	0.91	*0.86 - 0.96
Religion				
Catholic	Ref			
Other Christian	0.90	*0.86 - 0.95	0.95	0.90 – 1.01
Islam	1.15	*1.09 - 1.20	1.07	*1.01 - 1.13
Traditionalist	1.03	0.91 - 1.17	0.94	0.82 - 1.07
Residence				
Urban	Ref			
Rural	1.16	*1.13 - 1.19	1.02	0.99 - 1.06
Wealth index				
Poor	Ref			
Middle	0.86	*0.83 - 0.89	0.93	*0.89 - 0.96
Richest	0.77	*0.74 - 0.79	0.89	*0.85 - 0.93
Education				
No education	Ref			
Primary	0.87	*0.84 - 0.90	0.99	0.94 - 1.03
Secondary	0.79	*0.76 - 0.81	1.04	0.99 - 1.10
Higher	0.71	*0.67 - 0.74	0.98	0.91 - 1.05
Husband education				
No education	Ref			
Primary	0.92	*0.89 - 0.96	1.06	*1.02 - 1.11
Secondary	0.87	*0.85 - 0.90	1.11	*1.06 - 1.16
Higher	0.79	*0.75 - 0.82	1.01	0.96 - 1.07
Marital status at FB				
FB before Cohabiting	4.94	*4.19-5.82	2.87	*2.51-3.34
Cohabiting before FB	3.79	*3.20-4.51	2.13	*1.98-2.56
Never married	Ref			
Employment Status				
Working	Ref			
Not working	1.12	*1.09 - 1.16	1.10	*1.07 - 1.14
Contraceptive use				
Using	Ref			
Not using	1.06	*1.02 - 1.10	0.99	0.95 - 1.03
Age at first birth				
Age (Years)**	0.99	0.99 – 1.00	1.02	*1.01 - 1.03
<20	Ref			
20 – 24	0.94	*0.92 - 0.97	1.04	*1.01 - 1.08
25 – 29	0.93	*0.88 - 0.97	1.20	*1.14 - 1.25
e”30	0.82	*0.75 - 0.90	1.29	*1.18 - 1.41
First child survived				
Yes	0.78	*0.75 - 0.81	0.81	*0.78 - 0.84
No	Ref			

*Significant at 5%; ** Continuous variable; HR- Hazard Ratio; aHR - adjusted Hazard Ratio; FB- First Birth

secondary education than those with no education. Also, women in one form of relationship or the other had a higher likelihood of shorter SBI than the never-married women. In particular, women who were cohabiting before having a first child were about 200% more likely to quicken second births.

Besides, every additional year delay in the age at first birth is protective of the time of second birth. That is, teen mothers had a higher risk of earlier second births than those who started childbearing at older ages. Bearing a second child while still an adolescent, however, increases the probability of mental and physical problems for themselves and their children. Thus it is a public health concern to decrease the percentage of short birth intervals, particularly among younger women [44]. Our finding seems to be at odds to the belief that women who have delayed the start of their childbearing might have a short SBI simply because their reproductive ages have been "telescoped" into fewer years. There is also public health concerns regarding mothers that delayed childbearing. The delays are as a result of different factors. Some are increased risk of fertility problems and pregnancy loss associated with maternal age, children with disability, and economic strategy [45].

Often, the rational choice strategy of SBI is to maximize the use of baby equipment and clothing of the first child and/or minimize opportunity costs of being out of the labour force if the mother had been in the labour force prior to the birth of the first child and left the labour force after the birth of the first child. At the other end of the continuum are long birth intervals, two primary factors that could potentially lead to long birth intervals are marital/cohabitation disruption and fertility problems, including pregnancy loss [46].

This study might be limited by its cross-sectional design. Self-reported data without any means of verification could be affected by recall bias. However, it has been strengthened by the use of large nationally representative data.

We conclude that the average SBI found in the current study is relatively large but varied across the women social-economic characteristics. Women with lower educational attainment, without employment, not using contraceptives and mainly in the rural parts of the country had shorter SBI compared to others. A long enough birth interval reduces the chances of the subsequent baby being premature and having low birthweight, ensures that women body is strong and healthy enough to successfully carry another pregnancy

The SBI is a function of birth control and fertility planning. The advantage of birth spacing using family planning methods to promote safe motherhood and achieve better child survival cannot be overemphasized. The finding that the birth interval has been influenced by educational attainment is consistent with the hypothesis that better-educated women have a higher preponderance of increasing birth interval. The policy implication is that investment in education complements family planning interventions and by an extension, child spacing. There is a need to empower the entire population in the area of education and employment in addition to health education on the use of contraceptives to space childbirths.

Acknowledgements

We acknowledge the ICF Macro and the Nigeria Population Commission for for granting us right and access to the data used for our study.

References

1. Simeon AA and Khalid ZM. Survival Modeling of First Birth Interval After Marriage. Life Sci J. 2014;11:11–14.
2. Population Reference Bureau. PRB 2014 and 2015 World Population Data Sheets. Washington, DC; 2016.
3. United Nation. Total Fertility Rate: Recent rate compare 1970 rate from countries across the world. 2015.
4. Fagbamigbe AF, Afolabi RF and Idemudia ES. Demand and Unmet Needs of Contraception Among Sexually Active In-Union Women in Nigeria: Distribution, Associated Characteristics, Barriers, and Program Implications. SAGE Open. SAGE PublicationsSage CA: Los Angeles, CA; 2018;8:215824401775402.
5. Adebowale SA, Adepoju OT and Fagbamigbe AF. Child Spacing and Parity Progression: Implication for Maternal Nutritional Status among Women in Ekiti Communities, Southwestern Nigeria. Pakistan J Nutr. 2011;10:485–491.
6. Newman JL and McCulloch C. A Hazard Rate Approach to the Timing of Births. Econometrica. 1984;52:939–962.
7. Yohannes S, Wondafrash M, Abera M and Girma E. Duration and determinants of birth Interval among women of child bearing age in Southern Ethiopia. BMC Pregnancy Childbirth. 2011;11:1–8.

8. Moultrie TA, Sayi TS and Timæus IM. Birth intervals, postponement, and fertility decline in Africa: A new type of transition? Popul Stud (NY). 2012;66:241–258.
9. Zhang Y, Quist A and Enquobahrie D. Short birth-to-pregnancy intervals among African-born black women in Washington State. J Matern Neonatal Med. 2017;2017:1–5.
10. Ball SJ, Pereira G, Jacoby P, de Klerk N and Stanley FJ. Re-evaluation of link between interpregnancy interval and adverse birth outcomes/ : Retrospective cohort study. BMJ. 2014;349:g4333.
11. Chen I, Jhangri GS and Chandra S. Relationship between interpregnancy interval and congenital anomalies. Am J Obstet Gynecol. Elsevier Inc; 2014;210:564.e1-564.e8.
12. States U. AJPH PERSPECTIVES Brief Interpregnancy Interval/ : Are 75 % of Adolescent Mothers Unaware of the Prematurity Risk/ ? 2018;108:11–12.
13. Andi JR, Wamala R, Ocaya B and Kabagenyi A. Modern Contraceptive Use Among Women in Uganda: An Analysis of Trend and Patterns (1995-2011). Afr Popul Stud. 2014;28:1009–1015.
14. ICF International Inc. Uganda Demographic and Health Survey 2011. Kampala, Uganda: UBOS and Calverton, Maryland:; 2012.
15. Stephenson R, Baschieri A, Clements S, Hennink M and Madise N. Contextual Influences on Modern Contraceptive Use in sub-Saharan Africa. Am J Public Heal. 2007;97:12–33.
16. Creanga AA, Gillespie D, Karklins S and Tsui AO. Low Use of Contraception among Poor Women in Africa: An Equity Issue. Bull WHO. 2011;89:258–266.
17. Family Health Initiative. Expanding Contraceptive Use in Urban Uttar Pradesh: Family Planning: Effect of Data Driven Strategies [Internet]. Policy Br. 2010 [cited 2017 May 23]. p. 1–3. Available from: www.uhi-india.org/
18. Olaitan OL. Factors Influencing the Choice of Family Planning among Couples in South West Nigeria. Int J Med Med Sci. 3AD;7:227–232.
19. Ntozi JPM, Ahimbisibwe FE, Ayiga N, Odwee J and Mulindwa IN. Has AIDS Awareness Changed Sexual Behaviour in Uganda. Towards the Containment of the AIDS Epidemic:/ : 63-77. Soc Behav Res. 2000;63.
20. Cohen B. Family Planning Programs, Socio-economic Characteristics, and contraceptive use in Malawi. World Dev. 2000;28:843–860.
21. Kim J. Women's Education in the Fertility Transition: An Analysis of the Second Birth Interval in Indonesia. Brown, USA; 2003.
22. Johnson K, Posner SF, Biermann J, *et al.* Recommendations to Improve Preconception Health and Health Care— United States. Morb Mortal Wkly Rep. 2006;55:1–13.
23. Cleland J, Conde-Agudelo A, Peterson H, Ross J and Tsui A. Contraception and health. Lancet. 2012. p. 149–156.
24. Campbell D. Women risk premature birth if they have second child too quickly [Internet]. Guard. 2014 [cited 2017 May 27]. Available from: www.theguardian.com/society/2014/jun/04/women-premature-birth-second-child-quickly.
25. O'Brien P. Interpregnancy interval. An Intl J O G. 2014;
26. Society for Maternal-Fetal Medicine. Interval between first and second pregnancy strongly impacts preterm birth risk [Internet]. Sci. Dly. 2015 [cited 2018 May 21]. p. 1–2. Available from: www.sciencedaily.com/releases/2015/02/150202123641.htm
27. National Population Commission (Nigeria) and ICF International. Nigeria Demographic and Health Survey 2013. Abuja, Nigeria; 2014.
28. Fagbamigbe AF, Adebowale AS and Morhason-Bello IO. Survival analysis of time to uptake of modern contraceptives among sexually active women of reproductive age in Nigeria. BMJ Open. 2015;5:1–8.
29. Fagbamigbe AF and Idemudia ES. Survival analysis and determinants of timing of first birth after marriage in Nigeria. Afr Popul Stud. 2016;30:2444–2457.
30. Batyra E. Fertility and the changing pattern of the timing of childbearing in Colombia. Demogr Res. 2016;35:1343–1372.
31. Fagbamigbe AF and Idemudia ES. Survival analysis and prognostic factors of timing of first childbirth among women in Nigeria. BMC Pregnancy Childbirth. BMC Pregnancy and Childbirth; 2016;16:1–12.
32. Adebowale AS, Fagbamigbe AF, Okareh TO and Lawal GO. Survival Analysis of Timing of First Marriage among Women of Reproductive age in

Nigeria/ : Regional Differences. Afr J Reprod Health. 2012;16:95–107.
33. Adebowale AS, Yusuf BO and Fagbamigbe AF. Survival probability and predictors for woman experience childhood death in Nigeria: analysis of North-South differentials. BMC Public Health. 2012;12:430.
34. Trussell J, Martin LG, Feldman R, *et al*.. Determinants of birth-interval length in the Philippines, Malaysia, and Indonesia: A hazard-model analysis. Demography. 1985;22:145–168.
35. Shayan Z, Mohammad S, Ayatollahi T and Zare N. Prognostic factors of first birth interval using the parametric survival models. Iran J Reprod Med. 2014;12:125–130.
36. Fagbemigbe AF and Alabi O. Differentials and Correlates of Infant Mortality in Nigeria: A Comparative Survival Analysis Between North-East and South-West. Int J Trop Dis Heal. 2014;4:869–886.
37. Morakinyo OM and Fagbamigbe AF. Neonatal , infant and under-five mortalities in Nigeria/ : An examination of trends and drivers (2003-2013). PLoS One. 2017;12:e0182990.
38. Fagbamigbe AF and Idemudia ES. Wealth and antenatal care utilization in Nigeria: Policy implications. Health Care Women Int. Taylor & Francis; 2016;38:17–37.
39. Fagbamigbe AF and Adebowale AS. Current and Predicted Fertility using Poisson Regression Model/ : Evidence from 2008 Nigerian Demographic Health Survey. Afr J Reprod Heal. 2014;18:71–83.
40. Fagbamigbe AF, Bamgboye EA, Yusuf BO, *et al*. The Nigeria wealth distribution and health seeking behaviour/ : evidence from the 2012 national HIV / AIDS and reproductive health survey. Health Econ Rev. 2015;5:e1–10.
41. Gakidou E and Vayena E. Use of modern contraception by the poor is falling behind. Gillespie D, editor. PLoS Med. 2007;4:e31.
42. Gillespie D, Saifuddin A, Tsui A and Radloff S. Unwanted fertility among the poor: an inequity? Bull WHO. 2007;85:100–107.
43. Austin A. Unmet contraceptive need among married Nigerian women: an examination of trends and drivers. Contraception. 2015;91:31–38.
44. U.S. Department of Health and Human Services. Healthy People 2010: Understanding and Improving Health. 2nd ed. Washington, DC: ./ : U.S. Government Printing Office; 2000.
45. Chandra A, Martinez GM, Mosher WD, Abma JC and Jones J. Fertility Family Planning and Reproductive Health of U.S. Women: Data from the 2002 National Survey of Family Grown.". Vital Heal Stat. 2006;23:1–15.
46. Simmons T and O'Connell M. Married-Couple and Unmarried-Partner Households. New York; 2003.

Afr. J. Med. Med. Sci. (2020) **49,** 253-262

Drug utilisation pattern in South- South Nigeria using the WHO core dug prescribing indicators

AO Opadeyi [1,2], A Fourrier-Réglat[3,4,5] and AO Isah[1,2,6]

Departments of Clinical Pharmacology and Therapeutics[1] and Medicine[2], University of Benin/Benin Teaching Hospital, Benin-City, Edo State, Université de Bordeaux[3], Inserm, Bordeaux Population Health Research Center team, Pharmacoepidemiology, UMR 1219, F-33000 Bordeaux, France, Bordeaux PharmcoEpi[4],INSERM CIC1401 and CHU de Bordeaux[5], Pole de sante publique, Service de Pharmacologic medicale and Department of Clinical Pharmacology and Therapeutics[3], University of Benin, Benin-City, Edo State and National Drug Safety Advisory Committee[6], Natioal Agency for Food abd Drug Administration and Control, Federal Ministry of Health, Abuja, Nigeria

Abstract

Purpose: The WHO core drug prescribing indicators has\ve been shown to be useful in understanding drug use patterns and determining the extent of irrational use of medicines in different settings.

Objective: The aim of this study was to evaluate the prescription pattern using the WHO core drug prescribing indicators in the outpatient departments of teaching hospitals in the South-South zone of Nigeria.

Methods: Filled patients' prescriptions sheets from January 2015 to December 2015 were accessed from the records using systematic random sampling method and entered into a data collection sheets. They were evaluated using the WHO core drug prescribing indicators.

Results: Six teaching hospitals were randomly selected and included into the study with a total of 1437 patient encounters and 4635 medicinal products prescribed in 2015. The average number of medicines per patient prescribed was 3.3 (range 1-9). The proportion of medicinal products prescribed with a generic name was 42.5% and the percentage of medicines in the essential medicines list (EML) was 73.5%. The percentage of encounters that included an antibiotic agent was 22.5% and the percentage that included an injection was 6.5%. The most prescribed medicine was paracetamol (25.5%) closely followed by diclofenac (16%).The most prescribed injectable medicine was artemether.

Conclusion: This study showed good prescribing indices regarding injections and antibiotics but a higher index of polypharmacy, poor utilisation of the EML and lack of adherence regarding generic prescribing compared with previously obtained regional recommended optimal values. It is important to identify safety concerns regarding the commonly used medicines in our environment.

Correspondence: Dr Abimbola O. Opadeyi, Department of Clinical Pharmacology and Therapeutics, University of Benin, Benin City, Nigeria. E-mail: felabimbola@yahoo.com.

Keywords: *WHO core prescribing indicators, drug prescribing, rational drug use, teaching hospitals, prescription pattern, Nigeria.*

Résumé

Objectif : Les indicateurs de base de l'OMS en matière de prescription de médicaments se sont révélés utiles pour comprendre les modes de consommation de médicaments et déterminer l'étendue de l'utilisation irrationnelle des médicaments dans différents contextes.

Objectif : Le but de cette étude était d'évaluer le schéma de prescription en utilisant les principaux indicateurs OMS de prescription de médicaments dans les services de consultations externes des hôpitaux d'enseignement universitaires de la région Sud-Sud du Nigéria.

Méthodes : Les fiches de prescription des patients remplies de janvier 2015 à décembre 2015 ont été consultées à partir des enregistrements à l'aide d'une méthode d'échantillonnage aléatoire systématique et entrées dans des fiches de collecte de données. Elles ont été évaluées à l'aide des principaux indicateurs de prescription des médicaments de l'OMS.

Résultats : Six hôpitaux universitaires ont été sélectionnés aléatoirement et inclus dans l'étude avec un total de 1437 rencontres de patients et 4635 médicaments prescrits en 2015. Le nombre moyen de médicaments par patient prescrit était de 3,3 (gamme 1 à 9). La proportion de médicaments prescrits avec un nom générique était de 42,5% et le pourcentage de médicaments dans la liste des médicaments essentiels (LME) était de 73,5%. Le pourcentage de rencontres qui comprenait un agent antibiotique était de 22,5% et le pourcentage qui comprenait une injection était de 6,5%. Le médicament le plus prescrit était le paracétamol (25,5%) suivi de près par le diclofénac (16%). Le médicament injectable le plus prescrit était l'artéméther.

Conclusion : Cette étude a montré de bons indices de prescription concernant les injections et les antibiotiques mais un indice de polypharmacie plus élevé, une mauvaise utilisation de LME et un manque d'adhérence concernant la prescription générique par

rapport aux valeurs optimales régionales recommandées précédemment obtenues. Il est important d'identifier les problèmes de sécurité concernant les médicaments couramment utilisés dans notre environnement.

Mots-clés : *Indicateurs fondamentaux de prescription de l'OMS, prescription de médicaments, utilisation rationnelle des médicaments, hôpitaux universitaires, schéma de prescription, Nigéria.*

Introduction

Irrational use of medicines is a major factor in the development of adverse drug reactions (ADRs) [1]. It may serve as a major area for intervention in the prevention of ADRs which to a significant extent can be a consequence of irrational use. The broadened scope of pharmacovigilance includes acknowledgement of the contributions of medication errors, misuse and abuse of medicines, poisoning and even more recently the development of antimicrobial resistance [2,3]. It is imperative to examine the irrational use of medicines in order to improve drug safety.

Treatment of diseases should follow Standard Treatment Guidelines (STG) and rational pharmacotherapy. However, it has been shown that poor prescribing practices, poor knowledge of the pharmacology of medicines, lack of awareness of availability of the STGs and of the medicines in the Essential Medicines List (EML), unavailability of the STG and EML are a few of the factors limiting rational pharmacotherapy [4-6].

Drug utilisation studies are usually conducted to review the rational use of medicines in any setting. This could be done on a country wide basis, across regions or in facilities; these studies could be carried out either retrospectively or prospectively using well established registries or databases [7]. In a resource constrained setting like Nigeria, such databases do not exist or are in the elementary forms in most parts of the country. The WHO/International Network of Rational Use of Drugs (INRUD) had advocated a simple means of reviewing drug utilisation of medicines in low resource setting through the application of core drug use prescribing indicators [8].

The indicators allow for comparisons between facilities, regions and countries. They also help hospitals in performing self-audits [8]. These evaluations are best carried out periodically to allow for prompt intervention as needed. To conduct a medicine utilization study, associating the medicines with diagnosis would have yielded much better data to enable proper pharmacoepidemiological assessment but there is poor documentation of data in this setting regarding drug use patterns relating to diagnosis and disease patterns. Prescriptions and pharmacy bulk purchase data are all that may be readily available to review the utilization of medicines in Nigeria as the regulations state that these should be retained for some time. Therefore, using the WHO core prescribing indicators are appropriate for use in this setting [8]. Earlier studies in Nigeria, have reported analgesics, antibiotics, multivitamins and antihypertensives as the common medicines in use in Nigeria [9,10] reflecting the health burden seen in a developing world setting.

To enable for appropriate monitoring and comparison, reference values had been established based on a morbidity mix found in the outpatient setting of healthcare facilities in Nigeria [11]. Studies carried out in various setting have highlighted the high prescribing of medicines with the values for the number of medicines, injections exceeding the reference values [12,13]. However, most of the earlier studies were carried out in different settings including primary health care centres [9,14,15] and very few, if any comparing teaching hospitals within a geo-political zone. It is expected that general outpatient departments of teaching hospitals which are centres of learning should have better prescribing practices. This study was therefore directed at teaching hospitals in a geo-political area in order to determine the compliance with the reference values [11] and profiles of drug prescribing practices in their general out-patient departments. This is to enable identification of areas requiring targeted intervention and generally improve patient safety.

Methods

Setting: This study was carried out in six teaching hospitals in the South-South geo-political zone of Nigeria which is located in the coastal region of Nigeria and home to about 21 million residents (National census 2006). The teaching hospitals are centres of teaching, research, clinical services and cater for a wide variety of patients. The government owned randomly selected teaching hospitals included in the study are as follows: University of Benin Teaching Hospital Benin-City, Edo State, (UBTH); Delta State University Teaching Hospital Oghara, Delta State (DELSUTH); Niger Delta University Teaching Hospital Okolobri, Bayelsa State, (NDUTH); University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State,

(UPTH); University of Uyo Teaching Hospital, Uyo, Akwa- Ibom State (UUTH) and University of Calabar Teaching Hospital, Calabar Cross-River State, (UCTH)). The bed complement ranged from 148 to 701 beds per hospital as at 2015. A retrospective evaluation of prescriptions from the out-patient departments was carried out using the WHO core prescribing indicators in all the centres.

Study population

Prescription sheets of patients who attended the general out-patient clinic during the year 2015 (January to December 2015) were obtained from the hospital pharmacy. The general out-patient departments in teaching hospitals attend to various patients in different age groups and therefore have a general morbidity mix pattern. Prescription sheets of patients who visited the other specialist clinics were excluded from this study.

Sample size determination

The WHO/INRUD core drug prescribing indicators manual recommendations were followed in this study. [8] The recommendations dictate that to review prescribing indices, a minimum of 600 prescriptions be sampled from all centres. To improve the reliability of these estimates, a minimum of 1200 prescriptions was overall sampled from the six institutions.

Data collection and analysis

Using the WHO core drug use indicators recommendations to ensure reliability, prescriptions of patients who had visited the pharmacy department after attending the general outpatient department clinic with a varied morbidity mix in the year 2015 were selected from the pharmacy records using a systematic random sampling method. The sampling was done in accordance with the WHO/INRUD core drug prescribing indicators manual. Prescriptions for the whole year were included in the sampling frame to avoid seasonal bias. A minimum of 200 prescriptions were selected for the past year. In all selected prescriptions; the medicine, formulation, and route were recorded. Only torn or faded prescriptions were excluded and substituted according to the sampling formula. The generic names when unavailable were determined using standard formularies. All medicines were classified using the Anatomical Therapeutic Chemical (ATC) classification system level 2 [16]. The Nigerian national Essential Medicines List (EML) 5th Edition 2010 [17] was used to determine the medicines prescribed from the EML as this was the latest list prior to the study period. The EML was also used to determine which medicines were to be counted as generics. All fixed dose combination (FDC) medicines were counted as one as recommended, also medicines such as metronidazole was regarded as antibiotics in this study due to their use in the context. The WHO prescribing indicators were used to assess rational use with the reference values previously determined [11].

One of the authors (AOO) as well as a research assistant (trained prior to commencement of study) collected the retrospective data using prescription sheets. All data was entered into Microsoft excel and later analyzed using SPSS version 21 and represented as frequencies, means, standard deviation and percentages.

Ethical considerations

Ethical approval was sought and obtained from the ethics and research committees of all the participating institutions. Institutional approval for the study was obtained from the Hospital Head and Management. The patients' details on the prescriptions were coded and anonymised as appropriate and not shared with a third party. All other ethical considerations were met.

Results

A total of six teaching hospitals were included in the study. The number of beds ranged from 148 to 782 and average overall out-patient attendance in 2015was about 91,000 patients (range 22540-179255 patients; including specialist clinics) are described in table 1.

Using the WHO prescribing indicators, a total of 1437 patient encounters were assessed in this study, with 434 males, 591females and 412 with no sex documented. There were also more adults 991(69%) than children 336 (23.4%); age was not specified in 110 encounters (7.6%).

A total of 4635 medicinal products were prescribed over the study period and the average number (Standard Deviation (SD)) of medicines prescribed were 3.3 (1.7) and this ranged from 1-9 medicines. UCTH had the lowest average number of medicines per prescription Table 1.

The percentage of generic drugs prescribing was 42.5% overall with a range of 37.3% to 49.4% in the institutions and UUTH being the most adherent with 49.4%. The percentage of encounters with antibiotics was 22.5% (13.4% to 35%) and UPTH had the largest number of encounters that included an antibiotic. The

Table 1: Characteristics and summary of the WHO Core prescribing indicators of six teaching hospitals in the South-South Zone of Nigeria from January to December 2015.

	UCTH	UUTH	UPTH	NDUTH	DELSUTH	UBTH	Total	WHO optimal values
Number of beds	610	499	782	148	250	701		
Out-patient attendance (2015)	81,624	114,523	114,277	32,906	22,540	179,255		
Total number of encounters	216	236	223	299	262	201	1437	
Total number of medicinal products	502	956	696	900	822	759	4635	
Average number of medicines per encounter	2.4	4.0	3.2	3.1	3.2	3.8	3.3	1.6-1.8
Range of number of medicines per prescription	1-7	1-9	1-8	1-8	1-9	1-9	1-9	
Percentage of medicines prescribed by generic name	37.3	49.4	37.4	40	46.4	40.6	42.5	100%
Percentage of encounters with an antibiotic prescribed	27.8	14.9	35.0	24.1	19.8	13.4	22.5	20.0-26.8%
Percentage of encounters with an injection prescribed	6.5	3.0	6.3	3.7	8.0	14.4	6.7	13.4-24.1
Percentage of medicines in the National EML (5th Ed)	76.1	66.4	78.0	79.7	77.9	72.3	73.5	100%

Abbreviations: UBTH-.University of Benin Teaching Hospital Benin-City, Edo State, UCTH -University of Calabar Teaching Hospital, Calabar, Cross-River State. UPTH -University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, UUTH - University of Uyo Teaching Hospital, Uyo, Akwa- Ibom State. DELSUTH- Delta State University Teaching Hospital Oghara, Delta State, NDUTH- Niger Delta University Teaching Hospital Okolobri, Bayelsa State.EML: Essential Medicines List

percentage of injection prescribed was 6.7% (3.7% to 14.4%) and highest in UBTH. The proportion of medicines prescribed from the EML was 73.5% and UPTH was the most adherent hospital. Table 1.

Profile of prescribed medicinal products

The twenty (20) most prescribed classes of medicines using the ATC classifications levels 2 are as shown in Table 2. Antibacterial (16.9%) being the most prescribed class and they were mostly for systemic use (96.2%). There were no prescriptions for antiviral agents in this study. Medicines acting on the cardiovascular system (antihypertensive agents and diuretics) were also commonly prescribed.

the most prescribed antihypertensives were amlodipine (3%) and lisinopril (1.7%). Table 3 describes the 20 most prescribed medicines in the zone. The most prescribed injectable medicine was intramuscular artemether 25.5% followed by paracetamol (16%), and these were mostly from DELSUTH and UBTH (Table 4).

Discussion

This study on the assessment of utilization of medicines in the South –South zone of Nigeria using the WHO core prescribing indicators may be the first to be conducted in teaching hospitals across a geo-political zone in Nigeria and it has shown that elements of irrational prescribing practices are still prevalent in the

Table 2: Most prescribed medicine classes using the Anatomic Therapeutic Chemical classification (ATC) Levels 2 in the general out-patient departments of six teaching hospitals in the South- South Zone of Nigeria

Medicinal classes (ATC Level 2)	Number of prescriptions n=4635	Proportion of total prescriptions (%)
Antibacterials (systemic use and topical)	781	16.9
Vitamins	453	9.8
Analgesics	405	8.7
Antiprotozoals (Antimalarials)	368	8.0
Anti-inflammatory and antirheumatic products	313	6.8
Drugs for acid related disorders (Proton pump inhibitors + Combinations and complexes of aluminium, calcium and magnesium compounds)	212	4.6
Agents acting on the renin-angiotensin system,	210	4.5
Calcium channel blockers	163	3.5
Drugs used in Diabetes	152	3.4
Mineral supplement	145	3.1
Anti-anaemic preparations	144	3.1
Antithrombotic agents	135	2.9
Diuretics	133	2.9
Psycholeptics (Benzodiazepine derivatives)	98	2.1
Antiepileptics	90	1.9
Muscle relaxants	77	1.7
Antihistamine for systemic use	68	1.5
Cough and cold preparations	45	1.0
Antihelminthics	42	0.9
Psychoanaleptics	41	0.9

On further evaluation, of the 4635 prescribed medicinal products, the most prescribed medicine from reviewed prescriptions was paracetamol (8.0%) closely followed by diclofenac (4.3%). Others were vitamins in different forms. The most prescribed antibiotic was amoxicillin/clavulanic acid (2.9%), the most prescribed antimalarial was artemether-lumenfantrine (4%) and

region with a high number of medicines per prescription, poor prescribing using brand names and sub-optimal use of the EML compared with the reference values. There appears to be some modest improvement compared with previous studies especially regarding use of antibiotics and injections [9,14].

Table 3: Twenty most prescribed medicines in the general out-patient departments of six teaching hospitals in the South-South Zone of Nigeria

Medicine	Total number (n)1437	Proportion (%)
Paracetamol	370	8.0
Diclofenac	199	4.3
Ascorbic Acid	190	4.1
Artemether/Lumenfantrine	186	4.0
Multivitamin/Vitamin B complex	174	3.8
Amlodipine	140	3.0
Amoxicillin/Clavulanic Acid	136	2.9
Metronidazole	117	2.5
Cefuroxime axetil	92	1.9
Amoxicillin	90	1.9
Ciprofloxacin	88	1.9
Omeprazole	87	1.8
Lisinopril	82	1.7
Acetylsalicyclic acid (75mg strength)	80	1.7
Metformin	71	1.5
Hydrochlorothiazide	69	1.5
Bromazepam	64	1.4
Aluminium Hydroxide/Magnesium Hydroxide	58	1.2
Clopidogrel	56	1.2
Tramadol	55	1.2

There were more adults in this study as shown by the age distribution in this study and more identified females than males consistent with the clientele seen in the clinics. A significant number of patients did not document their age and gender. The average number of medicines prescribed per encounter in this study was 3.3, which is slightly lower than values in earlier studies but exceeds the existing reference values (1.6 to 1.8) set almost 2 decades ago in two of the states in the same South-South zone [11]. Other studies that have been carried out in similar settings in Nigeria [18,19] since the baseline studies have recorded initial higher mean values than what was observed in this study while some others recorded lower mean values of about 3 per prescription [20].

These values are still quite suboptimal considering that the institutions are tertiary care hospitals with high quality staff. The lack of diagnostic facilities and symptomatic treatment mindset of prescribers may be responsible for the polypharmacy still observed in this study, 20 years after one of the earliest studies in the same geographical area [9]. In another developing country, the mean number of medicine per prescription is lower than what obtained in this study [21]. Furthermore, this also suggests that various interventional strategies to reduce the burden of drug related events may be needed since polypharmacy as depicted by the average number of medicines per prescription is rife in the zone and may contribute to drug related events and increased cost of treatment [1].

The study showed there was a discrepancy between the values obtained in this study and the derived ideal standard [11] that medicines should be prescribed with their generic names as only 42.5% of all medicinal products were prescribed in the generic format. This may be due to undue influences of poor drug promotion practices in the zone [22]. This may also increase the risk of medication errors [23]. This was also seen in the previous studies in the area [9,14].

Antibiotic over-utilization in non-infective conditions is a leading cause of antibiotics resistance and this has been described as a marginalized area in pharmacovigilance [3]. Accordingly, it is suggested that antibiotics usage should be evaluated in any drug use indicator study [8]. The study showed that there was good adherence with the recommended optimal values of 20 to 26.8% of encounters including an antibiotic as only 22.5% of the encounters in this study included an antibiotic. This is very encouraging especially when

Table 4: List of injectable medicines in the general out-patient departments of six teaching hospitals in the South- South Zone of Nigeria

	DELSUTH (n)	NDUTH (n)	UBTH (n)	UCTH (n)	UPTH (n)	UUTH (n)	Total (%)
Artemether	8		14	1		1	24 (25.5)
Paracetamol	3		10		2		15 (16)
Ceftriaxone		2		4	6	1	13 (13.8)
Artesunate	1	2				1	4 (4.3)
Promethazine		1	3				4 (4.3)
Furosemide				2	1	1	4 (4.3)
Tetanus toxoid	3					1	4 (4.3)
Ciprofloxacin		2		1			3 (3.2)
Pentazocine			1	2			3 (3.2)
Diclofenac	2						2 (2.1)
Normal saline	1			1			2 (2.1)
Cefuroxime		1			1		2 (2.1)
Gentamicin		1				1	2 (2.1)
Hydrocortisone		1			1		2 (2.1)
Diazepam			1			1	2 (2.1)
Iron Sucrose	1						1 (1.1)
Pethidine	1						1 (1.1)
Ceftazidime	1						1 (1.1)
Arteether		1					1 (1.1)
Calcium gluconate				1			1 (1.1)
Vitamin B1				1			1 (1.1)
Ringers lactate				1			1 (1.1)
Metronidazole					1		1 (1.1)
Phenobarbitone					1		1 (1.1)
Total	21	11	29	13	13	7	94

***Abbreviations: UBTH**-.University of Benin Teaching Hospital Benin-City, Edo State, **UCTH** -University of Calabar Teaching Hospital, Calabar, Cross-River State.**UPTH** -University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, **UUTH** - University of Uyo Teaching Hospital, Uyo, Akwa- Ibom State.**DELSUTH-** Delta State University Teaching Hospital Oghara, Delta State, **NDUTH-** Niger Delta University Teaching Hospital Okolobri, Bayelsa State*

compared with earlier studies in some states in the zone where antibiotics use had exceeded optimal values [9,12,14]. However, most of these studies were conducted in primary care centres and private hospitals. Other in-country studies also reported a high use of antibiotics [24,25] but studies from other developing countries show lower usage of antibiotics [26]. The result from this study could be due to previous trainings and education of the physicians on the need to prescribe antibiotics only when needed. Although one of the institutions still showed poor indices of antibiotics over-prescribing, it is believed that this can be remedied with adequate training and other intervention strategies.

All centres displayed good injections safety practices, which is not unexpected considering the risk of infectious diseases such as HIV/AIDS, Hepatitis B that are transmissible via blood and other body fluids. [27] As such, physicians are less likely to prescribe injections in view of the attendant risks to the healthcare personnel. Again, it may be due to a changing morbidity profile in Nigeria with the increase in non-communicable disease such as hypertension [28] and the change in antimalarial medicine policy that led to the removal of chloroquine from the recommended antimalarial medications [29] when compared with the time the reference values were developed[11]. There may be a need to revise the reference values in view of this change. We however note a higher than prevailing averages for UBTH and on further evaluation this was adduced to injections of antimalarial- artemether and

use of paracetamol. There appears to be an urgent need to conduct another interventional study in antimalarial prescribing in that centre despite an initial study[30], especially since there has been a paradigm shift in the prescriptions of antimalarials to Artemisinin-based combination therapy (ACTs) in out-patient care than injectables [29]. It is assumed that for patients requiring injections, they would be referred to the appropriate points of care. The use of intramuscular antimalarials in out-patient care was also seen in a study in the Northern part of the country [31].

All institutions performed below 80% in prescribing medicines in the National Essential Medicines List. The EML is backed by law and is meant to encourage rational prescribing and reduce cost (direct and indirect) [32]. An earlier study had shown a high adherence to the EML up to 95% [12]. Non-adherence to this important policy may be an indication of the physician's preference for newer drugs as a consequence of drug promotion or it could be from personal research suggesting the superiority of newer molecules over the medicines in the national EML. Again, it may be due to lack of awareness of the Standard Treatment Guidelines (STG) as well as the EML. It has been demonstrated that most prescribers are unaware of the availability and usefulness of the EML, and for others, the list is unavailable for their use [6]. The results from this study has great implication for a developing nation with numerous drug challenges as it may lead to poor drug stocking practices, limiting access to real essential medicines. Worthy of note is the fact that a newer edition of the national EML was released recently after the completion of this study. A systematic review had shown that a less than optimal adherence is not an uncommon occurrence in sub-Saharan Africa [33].

The study showed that antiviral agents were not found in the evaluated prescriptions. This may be due to a possible lack of diagnostic facilities in the setting or under-recognition of viral diseases by the prescribers or it could be due to the fact that most viral illnesses are self-limiting and as such most prescribers are unwilling to prescribe antiviral agents. Again, antiretroviral agents used in treating HIV infections are prescribed in specialised clinics which were excluded from this study. An absence of antiviral agents was also noted in other studies involving similar settings in Nigeria. [24,34]. Availability of the required diagnostic facilities may improve diagnosis of viral infections and aid the treatment.

We note the high use of paracetamol and diclofenac in this study as the singular most prescribed medications. Paracetamol is considered to be safe and this may explain the high rate of prescriptions, but it has been recently shown that long term usage of paracetamol may have adverse consequences [35] and although the safety concerns regarding use of Non-Steroidal Anti-inflammatory Drugs(NSAIDs) are relatively well known, the high rate of prescriptions in this study suggests there may be a need to retrain prescribers on other lesser known risks and evaluate other commonly used medicines for their safety profile in this relatively homogenous population. Overall, this study has shown that medicines used in the treatment of non-communicable diseases may require close observations in view of the number of prescriptions seen in this study, without de-emphasizing the surveillance on antimicrobials especially antibiotics.

Limitations

This study was not intended to address the characteristics of prescribers which should have shed more light into prescriber factors that impact on the quality of the usage of medicines. Again, the study did not capture some medicines (e.g. some antimicrobials) which are used largely or exclusively in the public health programs and are not seen in the out-patient departments.

Conclusion

This drug utilization study in teaching hospitals in the South-South zone of Nigeria still showed a less than optimal adherence to rational prescribing as evaluated with the use of the WHO-INRUD Prescribing Indicators as tool for the assessment. Observed values were not markedly different from those found in earlier studies two to three decades ago. However, lower rates of use of injections and antibiotic prescribing was observed despite outliers in a few centres. There is need for an intensive, sustained intervention measures with reinforcement to effect a change in knowledge, attitude and practice.

Acknowledgements

We thank the management and staff of the various teaching hospitals especially the pharmacy departments for their kind assistance in carrying out this study.

References

1. Meyboom RH, Lindquist M and Egberts AC. An ABC of drug-related problems. Drug Saf. 2000;22(6):415–423.
2. World Health Organization. The importance of pharmacovigilance- Safety monitoring of medicinal products. WHO. Geneva: World Health Organisation; 2002.
3. World Health Organization-Uppsala Monitoring Centre. Antimicrobial resistance- An overlooked adverse event. Uppsala Reports, Issue 74, Uppsala Sweden; 2017.
4. World Health Organization. Promoting rational use of medicines: Core components- WHO Policy Perspectives on Medicines No.5. Geneva Switzerland; 2002.
5. Ofori-Asenso R and Agyeman A. Irrational Use of Medicines—A Summary of Key Concepts. Pharmacy. 2016;4(4):35.
6. Hassan A, Abdullahi GA, Ahmed AA, *et al*. Assessing prescriber's awareness of essential medicine list, hospital drug formulary and utilization of standard treatment guidelines in a tertiary healthcare facility in North-Central Nigeria. Alexandria J Med. 2018;54(1):81–84.
7. Lee D and Bergman U. Studies of Drug Utilization. In: Pharmacoepidemiology. Wiley-Blackwell; 2012. p. 377–401.
8. World Health Organisation. WHO drug use in health facilites. Geneva Switzerland; 1993.
9. Isah AO, Ohaju-Obodo J, Isah EC and Ozemoya O. Drug use profile in a Nigerian city hospital. Pharmacoepidemiol Drug Saf. 1997;6(5):319–324.
10. Adebayo ET and Hussain NA. Pattern of prescription drug use in Nigerian army hospitals. Ann Afr Med. 2010;9(3):152–158.
11. Isah A, Laing R, Quick J, *et al*. The Development of Reference Values for the WHO Health Facility Core Prescribing Indicators. West Afr J Pharmacol Drug Res. 2001;18(1):6–11.
12. Akoria OA and Isah A. An evaluation of doctors' prescribing performance in Nigeria. Pakistan J Med Sci. 2009;25(4):533–538.
13. Desalegn AA. Assessment of drug use pattern using WHO prescribing indicators at Hawassa University teaching and referral hospital, south Ethiopia: a cross-sectional study. BMC Health Serv Res. 2013;13(1):170.
14. Okoli RI, Isah AO, Ozolua RI, *et al*. Drug prescribing pattern in three levels of health care facilities in the north and central senatorial districts of Edo State, Nigeria. Int J Herbs Pharmacol Res. 2015;4(3):46–57.
15. Adisa R, Fakeye TO and Aindero VO. Evaluation of prescription pattern and patients ' opinion on healthcare practices in selected primary healthcare facilities in Ibadan , South-Western Nigeria. Afri Heal Sci. 2015;15(4):1318–1329.
16. World Health Organization Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment 2018. Oslo Norway; 2017.
17. Federal Ministry of Health. Essential Medicines List. Abuja, Nigeria; 2010. (5th Edition).
18. Ibrahim M. Physicians' prescribing behaviour in two tertiary health care facilities in north-western Nigeria -- Analysis of 518 prescriptions. Sahel Med J. 2004;7(4):115–118.
19. Jimoh AO, Omar I, Adebisi IM, *et al*. Review of Morbidity Profiles and Drug Prescribing Patterns of a University Clinic in North-Western Nigeria. Int J Med Med Sci. 2014;1(8):107–115.
20. Enato EFO and Chima IE. Evaluation of drug utilization patterns and patient care practices. West African J Pharm. 2011;22(1):36–41.
21. Sisay M, Mengistu G, Molla B, Amare F and Gabriel T. Evaluation of rational drug use based on World Health Organization core drug use indicators in selected public hospitals of eastern Ethiopia: a cross sectional study. BMC Health Serv Res. 2017;17(1):161.
22. Ijoma U, Onwuekwe I, Onodugo O, *et al*. Effect of promotional strategies of pharmaceutical companies on doctors' prescription pattern in South East Nigeria. Turk Silahl Kuvvetleri, Koruyucu Hekim Bul. 2010;9(1):1–6.
23. Velo GP and Minuz P. Medication errors: prescribing faults and prescription errors. Br J Clin Pharmacol. 2009;67(6):624–628.
24. Tamuno I and Fadare JO. Drug prescription pattern in a Nigerian Tertiary hospital. Trop J Pharm Res. 2012;11:146–152.
25. Ndukwe HC and Ogaji J ISCN. Drug Use pattern with standard indicators in Jos University Hospital Nigeria. West African J Pharm. 2013;24(1):88–93.
26. Ragam A, Acharya S and Holla R. Assessment of drug use pattern using World Health Organization prescribing indicators in a tertiary care hospital in Mangalore: A cross-sectional study. Natl J Physiol Pharm Pharmacol. 2017;7(10):1.

27. Maiyaki MB and Garbati MA. The burden of non-communicable diseases in Nigeria; in the context of globalization. Ann Afr Med. 2014;13(1):1–10.
28. Federal Ministry of Health. National antimalarial treatment policy. Abuja; 2005.
29. Akoria OA and Olowofela A. Impact of an educational intervention on the prescribing of antimalarials at the University of Benin Teaching Hospital. Int J Heal Res. 2011;4(3):117–122.
30. Maryah P, Denue B, Ikunaiye N, Aderemi-Williams R and Akawu C. Evaluation of antimalarial drugs usage according to WHO prescribing indicators in a tertiary health facility in Maiduguri, Northeastern Nigeria. Port Harcourt Med J. 2017;11(2):67.
31. Federal Republic of Nigeria. National Drug Formulary and Essential Drug List Act. Decree 43 Nigeria; 1989.
32. Atif M, Scahill S, Azeem M, Rehan Sarwar M and Din Babar Z-U. Drug utilization patterns in the global context: A systematic review. Heal Policy Technol. 2017;6(4):457–470.
33. Gulmez SE, Larrey D, Pageaux G-P, *et al.* Transplantation for Acute Liver Failure in Patients Exposed to NSAIDs or Paracetamol (Acetaminophen). Drug Saf. 2013;36(2):135–144.

Afr. J. Med. Med. Sci. (2020) **49,** 271-280

Prevalence and distribution of tinea infections among primary school children in a rural setting of South-West Nigeria

AM Adebayo, AA Adelodun, OO Olabumuyi and AM Adelabu
Department of Community Medicine,
University College Hospital, Ibadan

Abstract
Background: Tinea infections continue to be an important public health problem among children. Evidence has shown an increasing incidence among primary school pupils, as well as poor treatment-seeking attitude of their wards. The aim of this study was to determine the prevalence and the distribution of tinea infections among primary school children in a rural setting of South-west Nigeria.
Methods: A community-based cross-sectional study design using multi-stage sampling technique was used to select children aged 6 to 12 years. A semi-structured interviewer-administered questionnaire was used for data collection. The tinea infection diagnostic criteria by the primary care dermatology society was used for diagnosis of tinea infection. Data was analysed with descriptive statistics and associations tested using Chi-square and binary logistic regression at 5% level of statistical significance.
Results: The mean age of the children was 8.5 years (SD = 2.1) and 55.9% of them were males. Nearly one-half, 48.3%, had tinea infections with tinea capitis being the commonest type of tinea infection found among 38.5% of the children. Tinea infection was found among a significantly higher proportion (57.5%) of male children compared to 36.7% of female children ($p<0.001$). Mothers'/caregivers' age (OR 2.6 and 5.2 for middle aged and elderly, respectively), relationship with child (OR=0.2), income (OR=1.9) and level of education (OR=2.1) were all found to be predictors of tinea infections.
Conclusion: The prevalence of tinea infections was high with tinea capitis being the commonest and it was associated with low socio-economic conditions. School-based health education services are therefore needed as well as the improvement of the residents' social status.

Keywords: *Tinea infections, tinea capitis, primary school pupil, Mothers/Caregivers, rural setting, South-West Nigeria*

Correspondence: Dr. A.A. Adelodun, Department of Community Medicine, University College Hospital, Ibadan, Nigeria. E-mail: checkgannya@yahoo.com;

Résumé
Contexte : Les infections à teigne continuent d'être un important problème de santé publique chez les enfants. Les preuves ont montré une incidence croissante parmi les élèves du primaire, ainsi qu'une mauvaise attitude de recherche de traitement de la part de leurs tuteurs. Le but de cette étude était de déterminer la prévalence et la répartition des infections à teigne parmi les enfants des écoles primaires dans un environnement rural du sud-ouest du Nigeria.
Méthodes : Un plan d'étude transversale à base communautaire utilisant une technique d'échantillonnage en plusieurs étapes a été utilisé pour sélectionner les enfants âgés de 6 à 12 ans. Un questionnaire semi-structuré, administré par intervieweur, a été utilisé pour la collecte des données. Les critères de diagnostic de l'infection à teigne par la société de dermatologie de soins primaires ont été utilisés pour le diagnostic de l'infection à teigne. Les données ont été analysées à l'aide de statistiques descriptives et association testée en utilisant le chi carré et la régression logistique binaire à un niveau de signification statistique de 5%.
Résultats : L'âge moyen des enfants était de 8,5 ans (ET = 2,1) et 55,9% d'entre eux étaient des garçons. Près de la moitié, 48,3% avaient une infection à teigne avec teigne capitis étant le type le plus commun d'infection à teigne trouvé chez 38,5% des enfants. L'infection à la teigne a été trouvée parmi une proportion significativement plus élevée (57,5%) d'enfants de sexe masculin contre 36,7% d'enfants de sexe féminin ($p <0,001$). L'âge de la mère/tutrice (OR 2,6 et 5,2 respectivement pour les personnes d'âge moyen et les personnes âgées), la relation avec l'enfant (OR = 0,2), le revenu (OR = 1,9) et le niveau d'éducation (OR = 2,1) se sont tous révélés être des prédicteurs de l'infection à teigne.
Conclusion : La prévalence des infections à teigne était élevée, la teigne capitis étant la plus courante et elle est associée à de faibles conditions socio-économiques. Des services d'éducation sanitaire en milieu scolaire sont donc nécessaires ainsi qu'une amélioration du statut social des résidents.

Mots-clés : *infections à teigne, teigne capitis, élève du primaire, mères/tutrice, milieu rural, sud-ouest du Nigéria*

Introduction

Tinea infections (dermatophytoses) are a group of fungal infections that affect the superficial keratinized tissue (skin, hair and nails) of man and animals, often called ring worm because of its characteristic circular, ring-like appearance. These fungi require keratin to grow and, therefore, they are unable to infect mucosal surfaces [1]. They are usually named according to the part of the body affected and appearance and include tinea capitis (scalp), tinea faciei (face), tinea corporis (body), tinea manuum (hands), tinea cruris (groin), tinea pedis (foot), tinea unguim (nails). These infections have different clinical presentations depending on site affected. They are highly contagious and spread by direct contact from other people, animals, and soil, as well as indirectly from fomites like clothes, combs or hair dresser's equipment [2].

These infections have a global distribution but are especially more common in the tropics due to prevalent humidity and elevated temperature with about 20-25 % of the world's population having skin mycoses [3]. Children are most affected by the menace because of their interaction pattern which includes sharing personal belongings like combs, toys, clothes, hats etc. Tinea Capitis (T Capitis) was the most frequent type in most studies involving children, a prevalence of 25% reported in a study in Senegal [4]. The picture in Nigeria is quite similar with a prevalence of 20% to 35.3% among children in south-eastern Nigeria [5,6].

These infections though not usually life threatening represent a significant public health problem particularly among in-school children especially in low- and middle-income countries like Nigeria where pre-disposing factors to acquiring the infection such as poor hygiene, overcrowding and low socioeconomic factors abound. This is because they are highly contagious, widely distributed geographically and are capable of leading to complications like superimposed bacterial infections and ulceration [6]. Furthermore, they can be unsightly or disfiguring, are prone to recurrence and can affect student's concentration thereby affecting school performance.

Little attention has been given to dermatophytoses in recent times, however, recent data from elsewhere suggest an increasing incidence [7] therefore, it has become imperative to ascertain the burden of the problem amongst in-school children in order to advocate for school health interventions that will prevent its spread among school children and ensure treatment for those infected. Also, because it usually affects children who cannot seek treatment on their own and the parents really do not see tinea infections as serious and life threatening, treatment seeking attitude can be very poor. Tinea infections in children can be a pointer to other salient diseases like malnutrition and Human Immunodeficiency Virus (HIV) [8].

Epidemiology of tinea infections has continuously changed over the years due to changing socioeconomic status, migration and improved healthcare [3,7]. This makes it vital to look at the current burden and prevalent sites affected in this part of the world. Poor hygiene, water scarcity and poor and overcrowded buildings associated with low socio-economic status are important risk factors that have been linked with tinea infections [3].

The aim of the study was to estimate the prevalence and determine the predominant anatomical sites of tinea infections amongst in-school children in a rural setting of South-west Nigeria.

Methods

This research was conducted in Igbo-Ora in Ibarapa Centra local government area (LGA), Oyo State and it is a rural town in Oyo State, South-western Nigeria. Igbo-Ora was located about 80km North of Lagos State with geographical coordinates of latitude 7.43333 and longitude 3.28333 and an average population of was 92,719 [9]. Igbo-Ora is the headquarters of Ibarapa Central LGA the local government has ten wards and seven out of the ten wards are in Igbo-Ora community. The inhabitants are majorly of the Yoruba tribe, predominant religion is Islam and major occupations of the adult population are farming, civil service and trading. It is a patriarchal community but women are known to contribute enormously to the care and upbringing of children [10].

Participants in this study were consenting caregivers/mothers with primary school children within the age of 6-12years, while caregivers/ mothers whose child/children were not available at the time of interview were excluded. Sample size was determined using the L-K formula for estimating single proportion [11], with Z_{α} set at 1.96, prevalence of 30.4% (proportion of children with tinea capitis) [5,6] and degree of error set at 5%. Study participants were selected using a multistage sampling technique.

The first stage involved selection of three out of the seven wards in Igbo-Ora by balloting. At the second stage, using the house numbering done by the Department of Community Medicine, College of Medicine, University of Ibadan, systematic sampling technique was used to select alternate houses in the selected wards. If the selected house did not have an eligible caregiver/mother, the next house with an eligible respondent was selected. The third stage involved the selection of a household from each house using balloting while at the last stage, an eligible caregiver/mother was selected by balloting (in cases in which more than one caregiver/woman were eligible per household).

An interviewer-administered questionnaire, developed from extensive literature review was used for data collection. The study instrument was translated into the predominant local language (Yoruba) and back translated into English to ensure retention of the original meaning. Instrument was thereafter pre-tested among caregivers/mothers in another community in Ibarapa that is comparable to the study area in socio-cultural practices and amendments were made as necessary. The tinea infections diagnostic criteria by the primary care dermatology society, United Kingdom was used for making diagnosis of tinea infections on various parts of the body [12].

Research assistants were undergraduate medical students who had training on study instruments, diagnostic tool and research ethics prior to commencement of data collection for uniformity of data collection. Training was facilitated by a senior resident in dermatology medicine and a researcher with the use of posters, pictures and videos as teaching aids. Information on socio-demographic characteristics, knowledge and prevalence of tinea infections, predisposing factors and physical examination records were collected.

Data analysis

Outcome variable: The outcome variable for this study was prevalence of tinea infections and prevalence of each type of tinea infections among children of the caregivers.

Prevalence of tinea infections was assessed among all the children using a "Yes" or "No" option to the question "Was tinea infection found on the child's body during examination." Prevalence of each type of tinea infection was assessed using the response to the open-ended question: "What part of the body was tinea infection found on the child during examination?"

Independent variables: The following variables were categorized as shown in table 1 and used to determine the factors associated with the tinea infection:

Mothers'/Caregiver's age was dichotonized into "young people" that is 15-24 years, "young adult" that is 25-44 years, middle aged" that is 45-64years and "elderly" those who were ≥65 years. Child's age was grouped into those between "6-8 years" and those between "9-12 years". Mothers'/Caregiver's income was categorized into two; "those earning less than 15,000 naira" and "those earning 15,000 naira or more" in a month. (N15.000 naira is equivalent to $41.67 at N360: $1).

Family size was dichotomized using both parents and the expected maximum number of children per family in Nigeria [13] into those with "6 members or less" and "more than 6 members". Mothers'/ Caregiver's knowledge was assessed among mothers/ caregivers' that reported that they were aware of tinea infection using three questions on the mode of transmission of tinea infections with "Yes" or "No" options. A response of "Yes" to any of the three questions was categorized as "knowledgeable" while a response of "No" to all three question was categorized as "not knowledgeable". Mothers'/Caregiver's occupation was assessed using appropriate answer to a question on type of occupation with "Unemployed", "Civil servant" and "Business" options.

Other variables child's gender, caregivers' relationship with child, head of child's household.

Approval for the study was given by the Ibarapa Programme of the College of Medicine of the University of Ibadan. The purpose of the study was explained to the mothers/caregivers and their informed consents were obtained before the commencement of data collection.

Results

Socio-demographic and family characteristics

Mother/caregivers' mean age was 35.9 years (SD = ±11.3), majority (86.8%) of them were mothers. Caregivers with secondary and primary level of education were 39.1% and 33%, respectively while majority 84.3%) of them reported trading as their occupation,. A quarter of the mothers/caregivers earned more than 15,000 naira on a monthly basis (Table 2).

Table 1: Categorization of independent variables

Variable	Categorization
Mothers'/ Caregiver's age	
	15-24 years – Young people
	25-44 years – Young adult
	45-64 years - Middle aged
	≥ 65 years – Elderly
Children's age	
	6-8 years
	9-12 years
Mothers'/Caregivers' income	
	15,000 naira
	≥ 15,000 naira

The mean age of the children examined was 8.5 years (SD = 2.1) and about half (55.9% and 53.9%) of them were males and between 6-8 years, respectively. Majority of the children (78.3%) were from a family with six or less family members (Table 3).

Table 2: Mothers/Caregiver's socio-demographic characteristics

Variable [N=631]	Frequency	Percentage
Age		
Young people	49	7.8
Young adult	486	77.0
Middle aged	65	10.3
Elderly	31	4.9
Mean age (SD)= 35.9years (11.3)		
Caregiver relationship		
Father	19	3.0
Mother	548	86.8
Grandparents	50	7.9
Others	14	2.2
Caregivers' gender		
Female	604	95.7
Male	27	4.3
Caregivers' tribe		
Yoruba	625	99.0
Igbo	4	0.7
Others	2	0.3
Caregivers' religion		
Islam	364	57.7
Christianity	240	38.0
Traditional	26	4.1
Others	1	0.2
Caregivers' highest level of education		
None	114	18.1
Primary	208	33.0
Secondary	247	39.1
Tertiary	62	9.8
Caregivers' occupation		
Unemployed	23	3.6
Civil servant	45	7.1
Business	532	84.3
Others	29	4.7
Missing	2	0.3
Caregivers' monthly income		
≤15,000naira	471	74.6
≥15,000 naira	159	25.2
Missing	1	0.2

Respondents awareness and knowledge of tinea infection

Majority (95.9%) of the mothers/caregivers were aware of tinea infections while 57.8% were found to be knowledgeable on the mode of transmission of the infection being contact, poor hygiene and fomites. Poor hygiene was the mode of transmission reported by (22.8%) of the caregivers (Table 4).

Table 3: Children's socio-demographic and family characteristics

Variable [N=631]	Frequency	Percentage
Age		
6-8 years	340	53.9
9-12 years	291	46.1
Mean (SD) =8.5 years (±2.1)		
Gender		
Male	353	55.9
Female	278	44.1
Family size		
≤ 6	494	78.3
> 6	137	21.7
Head of household		
Father	580	91.9
Mother	21	3.4
Grandparents	28	4.4
Others	2	0.3

Prevalence and pattern of tinea infections among the children

Close to one half (48.3%) of the children examined had one type of tinea infections or the other while the reported prevalence by mothers/caregivers' was 15.1%. Tinea capitis was found among 38.5% (243) of the school children hence it was the type with the highest prevalence while tinea unguium found among 1.1% (7) of the children was the least prevalent type (Figure 1).

Table 4: Knowledge of tinea infection among caregivers'

Variable [N=631]	Frequency	Percentage
Awareness of tinea infections		
Yes	605	95.9
No	26	4.1
Knowledge of transmission (n=605)		
Knowledgeable	365	57.8
Not knowledgeable	240	42.2
Mode of transmission (n=365)		
Contact	94	14.9
Poor hygiene	144	22.8
Fomites	95	15.1
Others	32	5.1
None	266	42.1
Number of parts of body affected (n=605)		
Single body part	359	59.3
Multiple parts	246	40.7

There was gender variation with the distribution of tinea infections as more in male children than female had any type of tinea infections-overall (57.5% vs 36.7%), tinea capitis (46.7% vs 28.1%), tinea corporis (5.4% vs 4.0%) and tinea mannum (2.0% vs 0.4%) (Figure 2). The prevalence of Tinea pedis and tinea unguium were however higher among females compared to males (2.9% vs 2.5% for T. pedis) and (1.4% vs 0.8% for T. unguium) (Figure 2).

Factors associated with tinea infection

Prevalence of tinea infections was found to be significantly higher among the children with elderly caregivers (74.2%) compared to those with middle aged (63.1%); young adult (45.3%) and "young people" (42.9%) (p=0.001) (Table 5). It was also found to be significantly higher among male children (57.5%) compared to the female (36.7%). A higher proportion (52.0%) of the children whose caregiver earned fifteen thousand naira or less monthly were found with tinea infection compared to those earning more than fifteen thousand naira (37.7%) (p=0.002) (Table 5). Caregivers' relationship with child (p=0.001), level of education (p=0.003) and knowledge of tinea (p=0.009) were all significantly associated with tinea infections (Table 5).

On logistic regression however, significantly higher odds of having tinea infections was found among the elderly and middle-aged caregivers compared to the "young people" caregiver (Table 5). Similarly, mothers/caregivers earning less than fifteen thousand naira or less monthly were found to be about two times more likely to have children with tinea infections (OR 1.9; 95% CI 1.23-2.83) while the male children also have higher odds of having tinea infections compared to female children (OR 2.4; 95% CI 1.70-3.35). Children being cared for by the grandparents were less likely to have tinea infections compared to those being cared for by fathers (OR 0.2; 95% CI 0.04-0.67). Children being cared for by mothers were also found to be less likely to have tinea infections compared to those being cared for by fathers (OR 0.2; 95% CI 0.07-0.77) (Table 5).

Discussion

Tinea infections, also commonly referred to as ringworm, is still an important public health problem especially in regions with prevailing poor living conditions including Nigeria. The implicated organisms affect the keratinized tissues of man like the skin, nails and hair(14).

Prevalence of tinea infections

Tinea infections have been shown to be more common among children than adults because the adult sebum is said to contain fatty acids with higher fungistatic activities [15]. This study showed the overall prevalence of tinea infection among the primary school pupils to be 48.3%, which is relatively higher than what was found in some South-western parts of Nigeria

Table 5: Factors associated with and predictors of tinea infection

Variable	Presence of tinea (N=631)			95% CI		
	Yes n (%)	No n (%)	p-value	AOR	Lower	Upper
Caregivers' age						
Young people	21 (42.9)	28 (57.1)		1		
Young adult	220 (45.3)	266 (54.7)	0.001*	1.5	0.73	3.01
Middle aged	41 (63.1)	24 (36.9)		2.6	1.01	6.72*
Elderly	23 (74.2)	8 (25.8)		5.2	1.318	20.847*
Caregivers' monthly income (n=630)						
≤15,000 naira	245 (52.0)	226 (48.0)	0.002*	1.9	1.23	2.83*
>15,000 naira	60 (37.7)	99 (62.3)		1		
Children's age#						
6-8 years	160 (47.1)	180 (52.9)	0.488			
9-12 years	145 (49.8)	146 (50.2)				
Child's gender						
Male	203 (57.5)	150 (42.5)	<0.001*	2.4	1.70	3.35*
Female	102 (36.7)	176 (63.3)		1		
Household head#						
Father	279 (48.1)	301 (51.9)				
Mother	9 (42.9)	12 (57.1)	0.372			
Grandparents	17 (60.7)	11 (39.3)				
Caregivers' relationship (n=629)						
Father	15 (78.9)	4 (21.1)		1		
Mother	251 (45.8)	297 (54.2)	0.001*	0.2	0.07	0.77*
Grandparent	32 (64.0)	18 (36.0)		0.2	0.04	0.67*
Level of education						
None	67 (58.8)	47 (41.2)		2.1	1.02	4.43*
Primary	101 (48.6)	107 (51.4)	0.003*	1.7	0.88	3.26
Secondary	119 (48.2)	128 (51.8)		1.9	0.99	3.58
Tertiary	18 (29.0)	44 (71.0)		1		
Caregivers' occupation# (n=600)						
Unemployed	16 (69.6)	7 (30.4)				
Civil servant	16 (35.6)	29 (64.4)	0.065			
Business	258 (48.5)	274 (51.5)				
Knowledge of tinea						
Knowledgeable	161 (44.1)	204 (55.9)	0.009*	0.9	0.38	2.09
Not knowledgeable	132 (55.0)	108 (45.0)		1		
Family size#						
≤6	239 (48.4)	255 (51.6)	0.966			
>6	66 (48.2)	71 (51.8)				

*** Significant association** **# Not included in regression model**

[16,17] and much higher than the prevalence reported by Adefemi *et al* in Oke-oyi, a North-central part of the country (5%) [18]. The higher prevalence in this study could be due to the differences in methods of diagnosis. This study used an observational method compared to other studies from this region that used laboratory method for making diagnosis of tinea infections. A study in Odisha, India also reported a similar prevalence of tinea infections among school children [19]. This varying prevalence is due to the prevailing geographical and environmental conditions – population growth, close contacts among infected children and poor personal hygiene. The very low prevalence recorded in Oke-Oyi was said to be probably due to conditions favouring the growth of other fungi over dermatophytes, as well as the use of local remedies which may have affected their isolation in vitro [18].

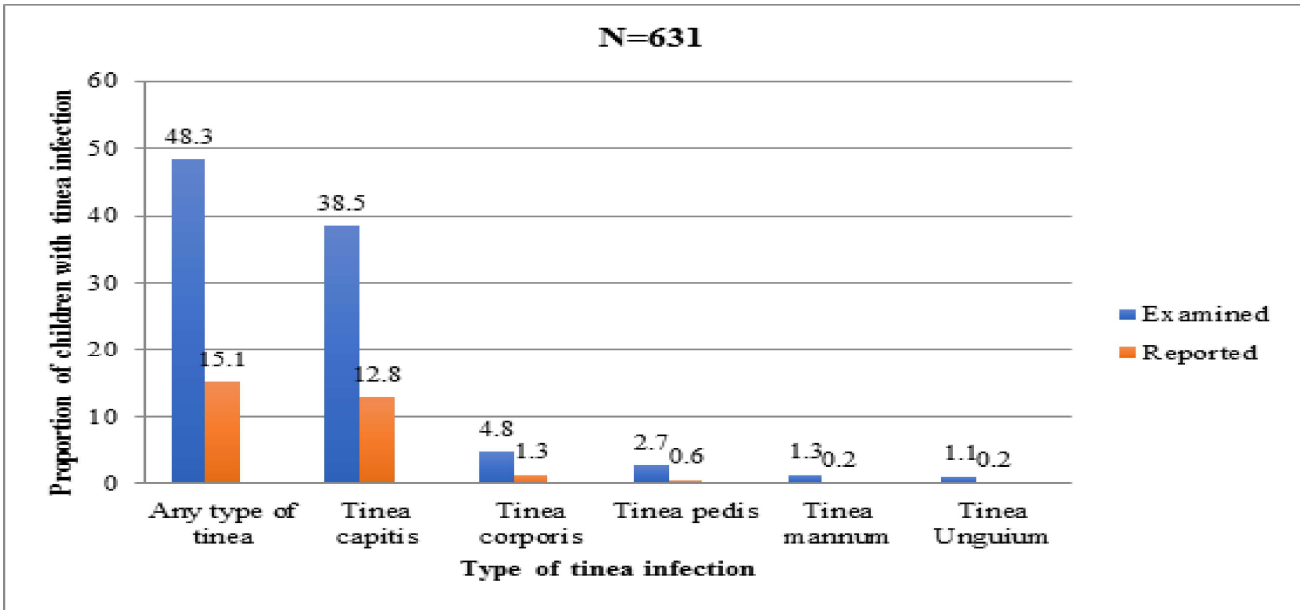


Fig. 1: Prevalence of different types of tinea infection among the children

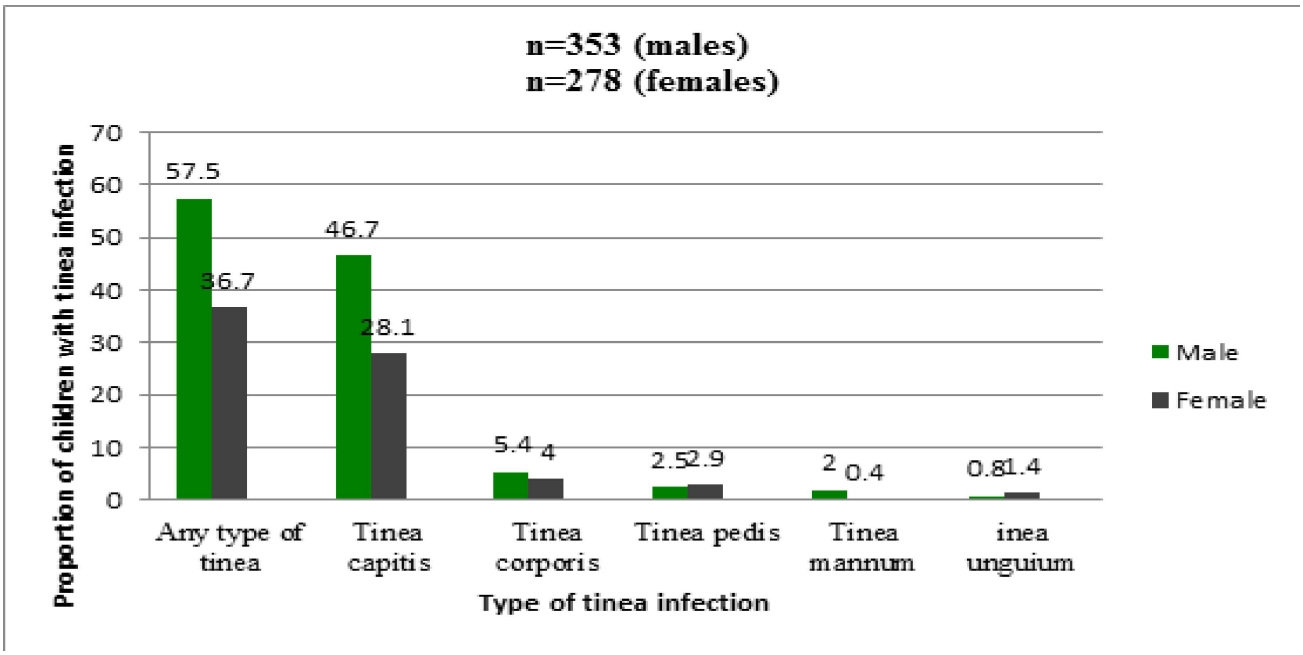


Fig. 2: Gender distribution of tinea infection among the children

These high rates of infections in the country could also be a reflection of a failing or poorly implemented school health programmes.

The reported overall prevalence of tinea infections in this study was also strikingly different from the reported prevalence by the caregivers of these children (15.1%), despite recording a very good awareness of the infections among the caregivers and about a half of them knowing the mode of transmission. This difference might not be unconnected with the fact that most of these infections are not life-threatening and largely asymptomatic, thereby drawing less of their attention. This goes to show how unaware these mothers/caregivers were of the effects of tinea.

Fig. 3: Tinea capitis

Fig. 4: Suppurative tinea capitis

Fig. 5: Tinea corporis

infections on their wards' academic and psychosocial life.

In addition, the study showed that the prevalence was higher among the male children than the female children. This is similar to several studies conducted in different parts of the country [5,15,16,20] except in Oke-Oyi where the prevalence among female was higher [18]. Contact with soil from farming as well as their involvement in a lot of contact games such as football and rough play with peers might be strong reasons why the male children are more affected.

Distribution of tinea infections

Tinea capitis contributed about 38.5% of the overall prevalence of tinea infections among the school pupils. This was followed by tinea corporis and then tinea pedis. Tinea unguium contributed the least (1.1%). A lot of studies showed similar trend with tinea capitis being the commonest form of tinea infection among the children(16,17,20–22). Tinea cruris was however found to be the commonest among children in Odisha in India [19].

Tinea capitis was also commoner among male children than the female children. This was the same for the other types of infection except for tinea pedis and tinea unguium, which were commoner among the female children. Hair care practices like sharing of contaminated equipment at the place of barbing, keeping short hair which promotes easy transmission from scalp to scalp by the males; and tight hair braiding, plaiting and use of hair oil by the females have been implicated in the varying gender distribution of tinea capitis [18,22].

Determinants of tinea infections

The factors found to be associated with primary school pupils having tinea infections like the socio-economic factor, level of education of the caregivers and the caregivers' knowledge of tinea infection, are not different from what have been reported in similar studies [5,6,23]. Ayanlowo *et al* in a study to assess the prevalence of tinea capitis among primary school pupils in a rural setting in South-western Nigeria demonstrated similar association between socio-economic status and tinea infections [23].

Limitations

A main limitation of the study is that diagnosis of Tinea infections was made by clinical examinations as patients were not subjected to further biochemical testing (potassium hydroxide smear, microscopy and cultures) to confirm diagnosis. This could have resulted in an overestimation of the prevalence of infections.

Conclusion

The prevalence of tinea infections among primary school children in Igbo-Ora, South-western Nigeria was quite high with tinea capitis being the commonest form. School-based health services with a dermatological component should be advocated. This will help with the education of teachers and pupils as well as the caregivers on tinea infections and the modes of transmission. Also, an avenue should be created in the form of outreaches to educate the mothers and to improve their level of awareness. Low socio-economic status was also found to be a risk for tinea infection. Efforts at improving the social status of residents will therefore help in no small measure in reducing the prevalence of tinea infections.

Acknowledgements

We would like to thank the undergraduate medical students of the University of Ibadan who helped with data collection. We would also like to thank the caregivers and children that consented to be part of this study.

References

1. Lange L, Huang Y and Busk PK. Microbial decomposition of keratin in nature—a new hypothesis of industrial relevance. Appl Microbiol Biotechnol 2016 Mar 12;100(5):2083–2096.
2. Neela FA. Prevalence and etiology of dermatomycoses in Rajshahi , Bangladesh. J Life Earth Sci. 2007;2(2):75–78.
3. Havlickova B, Czaika VA and Friedrich M. Epidemiological trends in skin mycoses worldwide. Mycoses. 2008 Sep;51:2–15.
4. Badiane AS, Ndiaye D, Denning DW. Burden of fungal infections in Senegal. Mycoses. 2015 Oct;58:63–69.
5. Kalu EI, Wagbatsoma V, Ogbaini-Emovon E, Nwadike VU and Ojide CK. Age and sex prevalence of infectious dermatoses among primary school children in a rural South-Eastern nigerian community. Pan Afr Med J. 2015;20.
6. Oladele RO and Denning DW. Burden of serious fungal infection in Nigeria. West Afr J Med. 2014;33(2):107–14.
7. Ameen M. Epidemiology of superficial fungal infections. Clin Dermatol. 2010 Mar 4;28(2):197–201.
8. Doni SN, Mitchell AL, Bogale Y and Walker SL. Skin disorders affecting human immunodeficiency virus-infected children living in an orphanage in Ethiopia. Clin Exp Dermatol. 2012 Jan;37(1):15–19.
9. Agrawal S, Karan A, Selvaraj S, *et al*. Socio-economic patterning of tobacco use in Indian states. Int J Tuberc Lung Dis. 2013 Aug;17(8):1110–1117.
10. Raley S, Bianchi SM and Wang W. When Do Fathers Care? Mothers' Economic Contribution and Fathers' Involvement in Child Care. Am J Sociol. 2012 Mar 17;117(5):1422–1459.
11. Kirkwood JAS. 2. Essential medical statistics (2nd edn). Blackwell Science, Oxford, 2003. ISBN 0-86542-871-9. Stat Med. 2005;24(5):824–824.
12. Levinson AH, Valverde P, Garrett K, *et al*. Community-based navigators for tobacco cessation treatment: a proof-of-concept pilot study among low-income smokers. BMC Public Health. 2015 Jan;15(1):627.
13. Main C, Thomas S, Ogilvie D, *et al*. Population tobacco control interventions and their effects on social inequalities in smoking: placing an equity lens on existing systematic reviews. BMC Public Health. 2008 Jan;8:178.
14. Wariso KT, Igunma JA, Oboro IL and Wariso KT. Pattern of Dermatophytes Isolated in the Medical Microbiology Laboratory of the University of Port Harcourt Teaching Hospital, Rivers State, Nigeria. Adv Microbiol. 2015;5(5):346–350.
15. Emele F and Oyeka C. Ringworm Infections in Anambra State of Nigeria: Epidemiologic Features and Antifungal Potentials of Local Plant Remedies. Hair Ther Transplant. 2017 Jan 20;7(1):1–5.
16. Hassan S. Distribution And Microbiological Characterisation Of Dermatophytes Infection Among Primary School Children In Ago Iwoye, Ogun State, Nigeria. Niger Res. 2010;22(1212):80–5.
17. Oke OO, Onayemi O, Olasode OA, Omisore AG and Oninla OA. The Prevalence and Pattern of Superficial Fungal Infections among School Children in Ile-Ife, South-Western Nigeria. Dermatol Res Pract. 2014 Dec 10;2014:842917.
18. Adefemi SA, Odeigah LO and Alabi KM. Prevalence of dermatophytosis among primary school children in Oke-Oyi community of Kwara state. Niger J Clin Pract. 2011 [;14(1):23–28.
19. Dash M, Panda M, Patro N and Mohapatra M. Sociodemographic profile and pattern of superficial dermatophytic infections among pediatric population in a tertiary care teaching

hospital in Odisha. Indian J Paediatr Dermatology. 2017;18(3):191.
20. Enemuor SC and Amedu AS. Prevalence of superficial mycoses in primary school children in Anyigba, Kogi State, Nigeria. African J Microbiol Res. 2009;3(2):62–65.
21. Nwadiaro PO and Ogbonna CIC. Patterns of Dermatophytosis in Jos North, Plateau State of Nigeria. Niger J Exp Appl Microbiol. 2009;10(2):73–77.
22. Dogo J, Afegbua SL and Dung EC. Prevalence of Tinea Capitis among School Children in Nok Community of Kaduna State, Nigeria. J Pathog. 2016;2016:9601717.
23. Ayanlowo O, Akinkugbe A, Oladele R and Balogun M. Prevalence of Tinea capitis infection among primary school children in a rural setting in south-west Nigeria. J Public Health Africa. 2014 Mar 17;5(1).

Afr. J. Med. Med. Sci. (2020) **49,** 181-188

Dilated Cardiomyopathy in Ibadan, Nigeria: an echocardiographic study

A Adebiyi[1], OS Ogah[1], A Aje[1], AM Adeoye[2], OO Oladapo[3] and AO Falase[1]
Department of Medicine[1], University of Ibadan, Department of Medicine[2], University College Hospital and Department of Anatomy[3], University of Ibadan, Ibadan, Nigeria

Abstract
Introduction: Dilated Cardiomyopathy (DCM) is a common cause of cardiac related morbidity and mortality in Nigeria. It is ranked second or third in the causes of heart failure in Nigeria behind hypertensive heart failure and rheumatic valvular heart disease. The condition occurs in all age groups and the prognosis is often poor. Previous studies on dilated cardiomyopathy in Ibadan had looked at the role of infection and infestations especially viruses, the possible role of nutritional deficiency, as well as the relationship to hypertension. There is scanty echocardiographic based report on the left ventricular structural and functional alteration in adult dilated cardiomyopathy in Nigeria. The objective of this paper was, therefore, to present the echocardiographic findings in patients with dilated cardiomyopathy in Ibadan, Nigeria.
Methods: The study was carried out at the Cardiology unit, Department of Medicine, University College Hospital, Ibadan. Eligible patients were adult men and women with established clinical diagnosis of DCM. The diagnosis of DCM was based on the exclusion of other causes of heart disease. The echocardiogram was performed with the use of commercially available echo-machines and a 3.5MHz linear array transducer. All measurement were made according to the American Society of Echocardiography leading edge to leading edge criteria.
Results: One hundred and fifty-two cases were identified as DCM. There were 87 (57.2%) men and 65 (42.8%) women. The mean age of the subjects was 44.9 ± 14.5 years (range =20-77 years) The males were significantly older than the female (p= 0.03) The left atrium, left ventricular internal diameter in diastole and LV posterior wall thickness were significantly larger in the males compared to the females- 4.59 ± 1.07cm vs. 4.36 ± 0.59cm, 6.62 ± 0.96 cm vs. 6.37 cm ± 0.64 cm and 0.96 ±0.28 cm vs. 0.87± 0.23 cm respectively. Four (2.6%) subjects had normal geometry. Concentric geometry was observed in ten (6.6%) while majority, 137 (90.7%) had eccentric LVH. Over 80% of the subjects had HF with reduced EF. 10 subjects each (6.7%) had HF with mid-range EF and preserved EF. The frequencies of diastolic dysfunction are pseudonormalised, 79(55.6%), restrictive pattern, 55(38.7%) and impaired relaxation, 8 (5.6%).
Conclusion: Left ventricular echocardiographic assessment of DCM patients indicate that they present with severe functional and structural alterations. Early detection and treatment is therefore recommended.

Keywords: *Dilated cardiomyopathy, Heart muscle disease, myocardial dysfunction, systolic dysfunction, Heart failure, Ibadan, Africa.*

Résumé
Introduction : La cardiomyopathie dilatée (CMD) est une cause courante de morbidité et de mortalité cardiaque au Nigéria. Il est classé deuxième ou troisième pour la cause de l'insuffisance cardiaque au Nigeria derrière l'insuffisance cardiaque hypertensive et la cardiopathie valvulaire rhumatismale. La condition survient dans tous les groupes d'âge et le pronostic est souvent mauvais. Des études antérieures sur la cardiomyopathie dilatée à Ibadan ont examiné le rôle de l'infection et des infestations, en particulier les virus, le rôle possible de la carence nutritionnelle, ainsi que la relation avec l'hypertension. Il existe peu de rapports écho-cardiographiques basés sur l'altération structurale et fonctionnelle du ventricule gauche dans la cardiomyopathie dilatée chez les adultes au Nigeria. L'objectif de cet article est, par conséquent, de présenter les résultats écho-cardiographiques chez les patients atteints de cardiomyopathie dilatée à Ibadan, Nigeria.
Méthodes : L'étude a été réalisée à l'unité de cardiologie, Département de Médecine, Collège Hospitalier Universitaire, Ibadan. Les patients éligibles étaient des hommes et des femmes adultes avec un diagnostic clinique établi de CMD. Le diagnostic de CMD était basé sur l'exclusion d'autres causes de maladie cardiaque. L'échocardiogramme a été réalisé à l'aide d'écho-machines disponibles dans le commerce et d'un transducteur à réseau linéaire à 3,5 MHz. Toutes les mesures ont été effectuées conformément aux

Correspondence: Dr. O.S. Ogah, Department of Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria, E-mail: osogah56156@gmail.com

critères bord a bord de premier plan de la Société Américaine d'Echocardiographie.
Résultats : Cent cinquante-deux cas ont été identifiés comme CMD. Il y avait 87 (57,2%) hommes et 65 (42,8%) femmes. L'âge moyen des sujets était de 44,9 ± 14,5 ans (intervalle = 20-77 ans). Les hommes étaient significativement plus âgés que les femmes (p = 0,03). L'orifice de l'oreillette gauche, le diamètre interne du ventricule gauche dans la diastole et l'épaisseur de la paroi postérieure du VG étaient significativement plus grandes chez les hommes par rapport aux femmes - 4,59 ± 1,07 cm vs 4,36 ± 0,59 cm, 6,62 ± 0,96 cm vs 6,37 cm ± 0,64 cm et 0,96 ± 0,28 cm vs 0,87 ± 0,23 cm respectivement. Quatre (2,6%) sujets avaient une géométrie normale. Une géométrie concentrique a été observée dans dix (6,6%) tandis que la majorité, 137 (90,7%) avaient une VGH excentrique. Plus de 80% des sujets avaient une HF avec une FE réduite. 10 sujets chacun (6,7%) avaient une HF avec une FE moyenne et une FE préservée. Les fréquences sont pseudo-normalisées, 79 (55,6%), motif restrictif, 55 (38,7%) et altération de la relaxation, 8 (5,6%). La dysfonction valvulaire secondaire était courante.
Conclusion : L'évaluation écho-cardiographique ventriculaire gauche des patients atteints de CMD indique qu'ils présentent des altérations fonctionnelles et structurelles sévères. Une détection et un traitement précoces sont donc recommandés.

Mots-clés : *Cardiomyopathie dilatée, maladie du muscle cardiaque, dysfonction myocardique, dysfonction systolique, insuffisance cardiaque, Ibadan, Afrique.*

Introduction

Dilated cardiomyopathy (DCM) is a common cause of cardiac related morbidity and mortality in Africa. It presents many challenges to healthcare providers in the region due to lack of diagnostic tools as well as the multifactorial aetiology such as infections and infestations.

DCM places second or third in the order of aetiological risk factors for heart disease and heart failure in Nigeria in particular and Africa in general after hypertensive heart disease and rheumatic heart disease.

DCM occurs in all age groups and the disease is often fatal. In advanced centres, it is a common reason for heart transplantation. It is characterized by ventricular dilatation and impaired systolic function. Previous studies on DCM in Ibadan had looked at the role of infection and infestations especially viruses [1-3], the possible role of nutritional deficiency [4], as well as the relationship to elevated blood pressure [5, 6].

While there has been several clinical and echocardiographic work on hypertensive heart disease and rheumatic heart disease in Nigeria and sub-Saharan Africa, there are few echocardiographic reports on the left ventricular structure and function in adult patients presenting with clinical features of dilated cardiomyopathy. The main trust of this paper is, therefore, to present the echocardiographic findings in patients with dilated cardiomyopathy in Ibadan, Nigeria.

Material and methods

The study was carried out at the Cardiology unit, Department of Medicine, University College Hospital, Ibadan. Since 2004, the unit has maintained a dedicated electronic registry of echocardiograms performed in the centre. Eligible patients were adult men and women with established clinical diagnosis of DCM. The diagnosis of DCM was based on the exclusion of other causes of heart disease such as hypertension, valvular heart disease, ischaemic heart disease etc. (Table 1 for exclusion criteria) Ethical approval was obtained from the institution's ethical review board.

Clinical evaluation

Baseline clinical characteristics were obtained from the subjects' case notes. These included date of birth (age), gender, blood pressures, pulse rate, body weight and height at the time of echocardiography. Body mass index (BMI) was calculated using the formula: BMI(kg/m^2) = Weight / (height)^2
Body surface area was calculated using the formula of Dubois[7] Body Surface Area (BSA) (in m^2) =0.0001 x (71.84) x (Weight in kilogram) $^{0.425}$ x height in centimetre) $^{0.725}$.

Echocardiography

The echocardiogram was performed with the use of commercially available echo-machines and a 3.5MHz linear array transducer. This was performed on each subject in the left lateral decubitus position. All measurement were made according to the American Society of Echocardiography leading edge to leading edge criteria [8]. LV measurement was obtained at end diastole and end systole. The LV measurements recorded included interventricular septal thickness at end-diastole (IVSTd), the posterior wall thickness at end diastole (PWTd), and the LV internal dimensions at end systole (LVIDs) and end diastole (LVIDd). Other parameters obtained were left atrial diameter, aortic

root diameter, indices of LV diastolic diameter {Early filling velocity (E- velocity), late filling velocity (A-velocity) and Deceleration Time (DT) In our laboratory, the intra-observer concordance correlation coefficient ranged from 0.76 to 0.98 while that of the inter-observer concordance ranged from 0.82 to 0.96 [9].

Calculation of echocardiographically derived variables

Left ventricular mass was calculated using the formula that has been shown to yield values closely related (r=0.90) to necropsy LV weight and that has good inter-study reproducibility[10].

LVM (ASE) = 0.8 [1.04 (IVSTd + LVIDd + PWT d) 3 + 0.6g

Relative wall thickness was calculated as 2 x posterior wall thickness/LV internal dimension in diastole. Relative wall thickness of 0.43 or greater was considered abnormal [11]. LV hypertrophy was considered present when LV mass exceeded 51g/$m^{2.7}$ in both men and women. Left ventricular (LV) volumes were estimated using the formula of Teichholz *et al* [12].

Left ventricular geometric was defined as follows: Normal geometry, when LVMI and RWT were normal; Concentric remodeling, when LVMI was normal and RWT increased; Eccentric hypertrophy, when LVMI was increased but normal RWT; and Concentric hypertrophy, when both LVMI and RWT were increased [13].

Statistical analysis

SPSS version 20.0 software (SPSS, Chicago, IL, USA) was used in the analysis of the data. Continuous variables were expressed as mean $\pm$ SD while categorical variables were expressed as counts (percentages). Normality of continuous variables was assessed using the Kolmogorov- Smirnov statistics. Comparison between two groups was assessed by the Students t- test for independent variables while the chi-square analysis was used to compare proportions. A 2-tailed p-value of 0.05 was assumed statistically significant.

Results

The electronic echocardiography of the Cardiology unit of the University College Hospital commenced on the 4th of March, 2004. As at 4th December, 2014, there were 15,381 records in the registry. After excluding repeated measurements, one hundred and ninety-three records had the diagnosis of dilated cardiomyopathy.

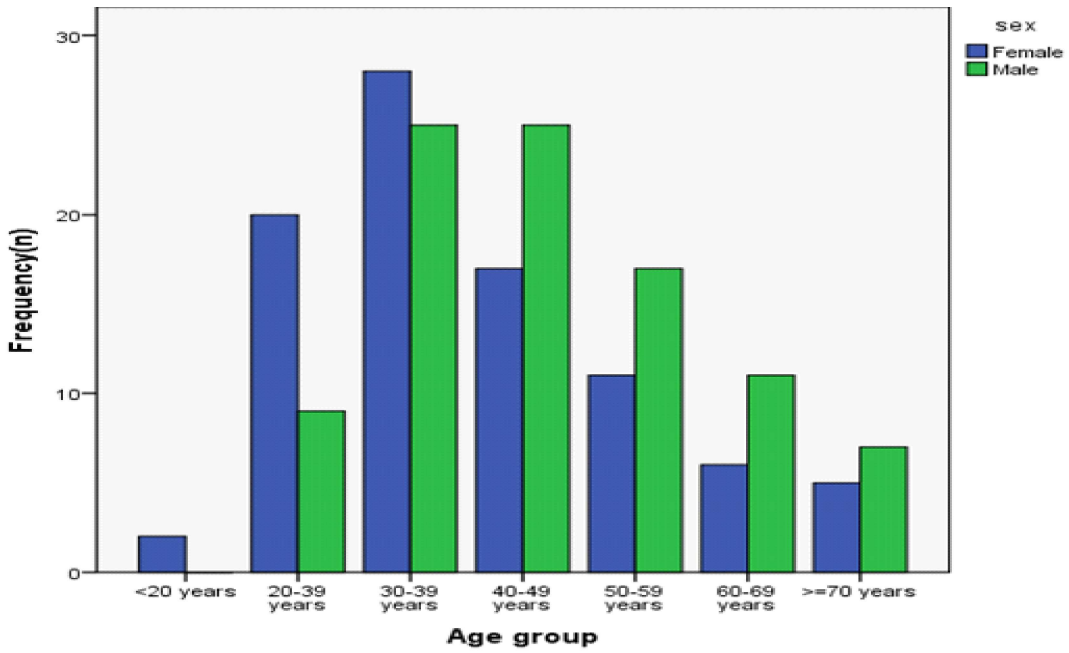


Fig. 1: Histogram showing the age distribution of the subjects by gender

We further excluded 41 records. Seventeen had peripartum cardiomyopathy, 10 had severe hypertensive heart failure, eight had rheumatic valve disease and three each had alcohol induced cardiomyopathy and drug induced cardiomyopathy.

Diagnosis of alcohol induced cardiomyopathy was made in these patients because they had very significant alcohol consumption (and no other risk factors) and their conditions improved remarkably with cessation of alcohol consumption and thiamine therapy. Myocardial biopsy was not done to confirm the diagnosis as the expertise was not available at the centre.

The data of remaining 152 subjects were analyzed. There were 87 (57.2%) men and 65 (42.8%) women. The mean age of the subjects was 44.9 ± 14.5 years (range =20-77 years). The males were significantly older than the female (p= 0.03) The mean age of the males was 47.01±14.1, while that of the females was 42.0±14.7 years. Figure 1 shows the age distribution of the subjects according to gender. Before the age of 40 years more women were diagnosed with DCM but thereafter, males predominated.

Table 1. Definition of case and exclusion criteria

Case definition	Diagnostic criteria
Dilated Cardiomyopathy	Dilated cardiomyopathy was diagnosed when there aredilated heart chambers with normal or decreased wallchambers as well as impaired LV systolic function.
Hypertensive HF	Previous history of hypertension or sustained BP of >140/90 mmHg in the presence of symptoms of HF, increased LV mass LV systolic and/or diastolic dysfunction
Valvular HF (mostly rheumatic)	HF in addition to any of the following: i. Mitral stenosis: – presence of thickened and calcified mitral valve leaflets, loss of the classic M-shaped pattern of a normal mitral valve, diastolic dooming and restriction of the mitral valve leaflet motions. ii. Mitral Regurgitation: Poor coaptation of the mitralvalve leaflets in systole, thickened leaflets, dilated and hyperdynamic left ventricle, iii. Aortic stenosis: Presence of calcified aortic valve,reduction in aortic cusp separation, highly echo reflect antaortic valve leaflets, iv. Aortic regurgitation: Poor coaptation of the aorticcusps in diastole dilated left ventricles and fine fluttering of the anterior mitral valve in diastole.
Endomyocardial Fibrosis	Endomyocardial fibrosis (EMF) was documented in the presence of clinical features coupled with dilated atria and thickening of the endocardium especially at the apices of the ventricles
Pericardial Effusion	Pericardial effusion was diagnosed when there is echo free space between the visceral and parietal pericardium. Diagnosis of constrictive pericarditis was based on standard criteria
Cor-pulmonale or Right Heart Failure	Cor pulmonale was present when there is dilated and hypertrophied right ventricle (RV), evidence of increased RV systolic pressure (D-shaped LV in diastole (diastolic flattening of the LV septum)
Ischaemic Cardiomyopathy	This is based on ECG changes, Cardiac enzyme elevation and regional wall motion abnormality at echocardiography
LV systolic dysfunction	LV ejection fraction (LVEF)< 40%%
Preserved LV systolic function	LVEF >=50
Mid-range LV systolic function	LVEF 40-49%

Table 2: Biophysical characteristics of the 152 DCM patients

Parameter	All(152)	Male(87)	Female(65)	P-valve
Age (Years)	44.9 (14.5)	47.1(14.1)	42.0(14.7)	0.033
Pulse (beats/min)	98.0(21.3)	97.5(21.1)	98.6(21.8)	0.815
Systolic BP	112.3(18.3)	110.2(24.3)	111.7(18.5)	0.738
Diastolic BP	76.1(12.6)	75.3(16.8)	74.7(12.9)	0.268
Pulse pressure (mmHg)	36.6(13.5)	35.9(12.9)	37.3(14.2)	0.549
MAP (mmHg)	85.2(13.2)	89.0(13.2)	87.1(13.2)	0.369
Body weight (kg)	66.1(14.5)	68.0(14.1)	63.4(14.7)	0.056
Height (cm)	167.7(8.6)	170.1(7.6)	164.4(9.0)	<0.001
BSA (m^2)	1.74(1.02)	1.78(0.19)	1.69(0.20)	0.0003
BMI (kg/m^2)	23.4(4.6)	23.4(4.17)	23.4(5.1)	0.949

Table 2 shows the baseline biophysical profile of the

Table 3: Echocardiographic parameters in the 152 DCM patients

Variable	All (n=152)	Male (n=87)	Female (n=65)	P value
Aortic root dimension (cm)	2.82 (0.42)	2.87(0.42)	2.25 (0.41)	0.084
Left atrial dimension (LAD)(cm)	4.49 (0.65)	4.59 (1.07)	4.36(0.59)	0.036
LAD indexed to BSA	2.60(0.43)	2.59(0.43)	2.62(0.44)	0.710
Interventricular septal wall thickness (diastole-cm)	0.91 (0.22)	0.93 (0.21)	0.89 (0.23)	0.325
Interventricular septal wall thickness (systole-cm)	1.09 (0.82)	1.16 (1.04)	1.0 (0.29)	0.262
Left ventricular internal dimension (diastole-cm) (LVIDd)	6.51 (0.84)	6.62 (0.96)	6.37 (0.64)	0.035
LVIDd indexed to BSA	3.78(0.60)	3.75(0.640	3.82(0.55)	0.470
Left ventricular internal dimension(LVIS) (systole-cm)	5.74 (0.95)	5.86 (1.07)	5.58 (0.76)	0.073
LVIDs indexed to BSA	3.34(0.66)	3.32(0.70)	3.35(0.61)	0.792
Left ventricular posterior wall thickness(diastole-cm)	0.92 (0.26)	0.96 (0.28)	0.87 (0.23)	0.035
Left ventricular posterior wall thickness(systole-cm)	1.25 (0.35)	1.26 (0.36)	1.24 (0.33)	0.858
LV fractional shortening (%)	12.8 (7.1)	12.9 (7.5)	12.6 (6.6)	0.824
LV ejection fraction (%)	27.4 (13.9)	27.3 (12.9)	27.5 (15.3)	0.943
LV mass (g)	502.6(172.7)	533.7(192.4)	460.1(132.3)	0.008
LV mass indexed to BSA (g)	290.6(100.5)	302.3(110.5)	275.1(83.9)	0.100
LV mass indexed to height ^2.7(g/m^2.7)	125.1(42.5)	128.3(47.1)	121.0(35.4)	0.296
Relative wall thickness	0.29(0.90)	0.30(0.10)	0.28(0.08)	0.164
Mitral E- velocity (m/sec)	0.83(0.09)	0.23(0.03)	0.24(0.03)	0.249
Mitral A-velocity (m/sec)	0.42(0.18)	0.42(0.19)	0.41(0.16)	0.554
E/A ratio	2.37(1.12)	2.27(1.06)	2.50(1.19)	0.236
Deceleration time (DT) (msec)	119.1(43.7)	116.3(41.2)	112.7(46.9)	0.397
LV filling pattern (n=142)				
Impaired relaxation	8(5.6%)	5(6.1%)	3(5.0%)	$_x2$=1.721
Pseudo-normalization	79(55.6%)	49(59.8%)	30(50%)	p=0.423
Restrictive filling	55(38.7%)	28(34.1%)	27(45%)	
LV geometry (n=151)				
Normal LV geometry	4(2.6%)	3(3.5%)	1(1.5%)	$_x2$=5.470
Concentric LV hypertrophy	10(6.6%)	9(10.5%)	1(1.5%)	p=0.065
Eccentric LV hypertrophy	137(90.9%)	74(86%)	63(96.9%)	

subjects. Males were taller (170.1 ± 7.6 cm vs. 164.4 ± 9.0 cm, p<0.001) and had a significantly larger body surface area (BSA)- 1.76 ± 1.19 m^2 vs. 1.69 ± 0.20 m^2, p=0.003. The pulse rate, blood pressures and body mass index were similar.

Table 3 depicts the echocardiographic variables of the DCM subjects. The left atrium, left ventricular internal diameter in diastole and LV posterior wall thickness were significantly larger in the males compared to the females- 4.59 ± 1.07cm vs. 4.36 ± 0.59cm, 6.62 ± 0.96 cm vs. 6.37 cm ± 0.64 cm and 0.96 ±0.28 cm vs. 0.87± 0.23 cm respectively. All the other variables were not significantly different.

Complete echo data was available for 151 subjects for the evaluation of the LV geometry. Four (2.6%) subjects had normal geometry. Concentric geometry was observed in ten (6.6%) while majority, 137 (90.7%) had eccentric LVH. Over 80% of the subjects had HF with reduced EF. 10 subjects each (6.7%) had HF with mid-range EF and preserved EF. (Figure 2)

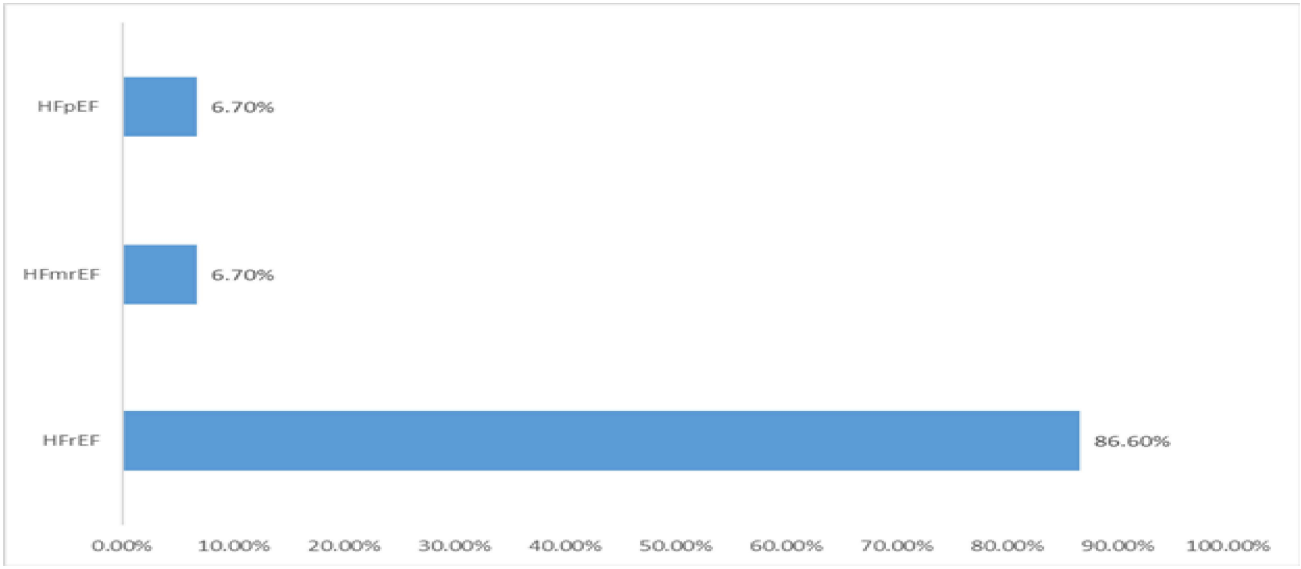


Fig. 2: The distribution of different forms of heart failure in the DCM subjects

LV filling pattern was available in 142 subjects. The frequencies were pseudonormalised, 79(55.6%), restrictive pattern, 55(38.7%) and impaired relaxation: 8 (5.6%)

Thirty subjects had significant mitral regurgitation and/or tricuspid regurgitation. Pulmonary hypertension was documented in nine subjects (5.2%) and there was pericardial effusion in five subjects (3.3%). The pericardial effusion was mild and not beyond what was expected for heart failure.

Other findings included spontaneous echoes in 6 (3.9%) and intramural clot in one (0.7%)

Discussion

In this study, we have described the echocardiographic findings in 152 patients representing 0.98% of Echo studies carried out at the University College Hospital, Ibadan over a 10-year period. We noted that DCM is a disease of young and middle age adults in Ibadan and commoner in males. Females appear to be younger.

Our patients presented in severe heart failure and severely altered cardiac structure and function. Associated conditions included functional valvular dysfunction (mitral and tricuspid re secondary pulmonary hypertension, pericardial effusion, intracardiac spontaneous echoes(echo-smokes) and intracardiac clot.

Our observation that DCM is commoner in young and middle aged adults has been documented by other workers in Africa [14]. This is in contrast to reports from high income countries where DCM patients are relatively older. In one report from Sweden, the mean age of DCM patients was 58years.[15] Similar data have been reported in other parts of Europe and North America [16, 17]. The age disparity in the case between local experience and high income countries

may be due to variations in the exposure to risk factors for DCM in the two regions e.g pathogens such as viruses and toxins.

About 80% of the cases were men. Our patients presented with severe structural and functional impairment. Almost all the patients had eccentric LVH. The mean left ventricular ejection fraction was 27%. Many had severe forms of LV filling pattern. This is similar to reports from elsewhere in sub-Saharan Africa [14, 18]. The reasons for this include the fulminant nature of the disease and late presentation to health facilities. The four subjects who had normal geometry could be cases who a\were showing recovery of LV function and structure following treatment with disease modifying medications or may fall into the category of non-dilated cardiomyopathy [19].

The frequency of valvular dysfunction was also high. This is probably due to the degree of dilation of the ventricles. The mean indexed LV dimensions in our cohort were 3.78cm/sq.metre and 3.34cm/sq.metre for diastole and systole respectively. The indexed left atrial diameter was 2.60cm/sq.metre

The severe LV dysfunction may also be responsible for the presence of spontaneous echoes as well as intracardiac clot formation aside from other inflammatory and clotting abnormalities associated with DCM.

The term DCM indicates heart muscle disease of undetermined origin. Recent advances in diagnosis and genetics have reduced the population of idiopathic DCM. This, however, is still a huge constraint in developing countries especially in sub-Saharan Africa.

Many cardiac conditions such as valvular heart disease, coronary artery disease, alcohol or drug abuse, cytotoxic therapy and severe systemic diseases can lead to heart failure and structural alterations similar to DCM. We have tried as much as possible to exclude these conditions in the selection of subjects for this study. This is, however, limited by the facilities available to us to properly investigate these patients to rule out other conditions, as well as the ability of the patients to afford the cost of these investigations as well as the available skills in our environment.

In conclusion, echocardiographic assessment of DCM patients indicate that they present with severe functional and structural alterations. Early detection and treatment is therefore recommended.

References

1. Falase A.O. Infections and dilated cardiomyopathy in Nigeria. Heart Vessels Suppl, 1985. 1: p. 40-44.
2. Falase A.O., Sekoni G.A and Adenle A.D. Dilated cardiomyopathy in young adult Africans: a sequel to infections? Afr J Med Med Sci, 1982. 11(1): p. 1-5.
3. Falase A.O., A. Fabiyi and O.O. Odegbo-Olukoya, Coxsackie B viruses and heart muscle disease in Nigerian adults. Trop Geogr Med, 1979. 31(2): p. 237-243.
4. Falase A.O., Heart muscle disease among adult Nigerians: role of nutritional factors in its aetiology. Eur J Cardiol, 1979. 10(3): p. 197-204.
5. Falase A.O. Cardiomegaly of unknown origin among Nigerian adults: role of hypertension in its aetiology. Br Heart J, 1977. 39(6): p. 671-679.
6. Lawal S.O., Osotimehin BO and Falase AO. Mild hypertension in patients with suspected dilated cardiomyopathy: cause or consequence? Afr J Med Med Sci, 1988. 17(2): p. 101-112.
7. Du Bois D and Du Bois E. A formula to estimate the approximate surface area if height and weight be known. Arch Intern Med, 1916. 17: p. 863-867.
8. Devereux R.B., *et al*., Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol, 1986. 57: p. 450-458.
9. Adebiyi A.A., *et al*., Correlates of left atrial size in Nigerian hypertensives. Cardiovasc J South Afr, 2005. 16(3): p. 201-204.
10. Devereux R.B., *et al*., Standardization of M-Mode echocardiographic left ventricular anatomic measurements. J Am Coll Cardiol, 1984. 4: p. 1222.
11. Roman M.J., *et al*., Association of carotid atherosclerosis and left ventricular hypertrophy. J Am Coll Cardiol, 1995. 25(1): p. 83-90.
12. Teichholz L.E., *et al*., Problems in echocardiographic volume determination :echocardiographic -angiographic correlations in the presence of absence of asynergy. Am J Cardiol, 1976. 37: p. 7-11.
13. Ganau A., *et al.*, Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. J Am Coll Cardiol, 1992. 19(7): p. 1550-1558.
14. Ntusi N.B., *et al.*, Clinical characteristics and outcomes of familial and idiopathic dilated cardiomyopathy in Cape Town: a comparative study of 120 cases followed up over 14 years. S Afr Med J, 2011. 101(6): p. 399-404.

15. Andersson B., Caidahl K and Waagstein F. Idiopathic dilated cardiomyopathy among Swedish patients with congestive heart failure. Eur Heart J, 1995. 16(1): p. 53-60.
16. Williams D.G. and Olsen E.G. Prevalence of overt dilated cardiomyopathy in two regions of England. Br Heart J, 1985. 54(2): p. 153-155.
17. Vollmar A.C. Use of echocardiography in the diagnosis of dilated cardiomyopathy in Irish wolfhounds. J Am Anim Hosp Assoc, 1999. 35(4): p. 279-283.
18. Ntusi N.B., *et al.* Frequency and clinical genetics of familial dilated cardiomyopathy in Cape Town: implications for the evaluation of patients with unexplained cardiomyopathy. S Afr Med J, 2011. 101(6): p. 394-398.
19. Okeahialam B.N. and Anjorin F.I. Non-dilated cardiomyopathy in Nigerians evaluated by echocardiography. Acta Cardiol, 1998. 53(2): p. 97-100.

Afr. J. Med. Med. Sci. (2020) **49,** 215-223

Oral health knowledge and practice: Influence of socio-demographic factors in rural Nigerian school children

CA Akinyamoju[1], IA Adeoye[2], AO Akinyamoju[3] and DM Dairo[2]

Department of Family Dentistry[1], University College Hospital, Departments of Epidemiology and Medical Statistics[2] and Oral Pathology[3], College of Medicine, University of Ibadan, Ibadan, Nigeria

Abstract

Background: Oral health habits may be influenced by appropriate oral health education leading to change of mind-set and practice. However, majority of African children are said to lack adequate oral health knowledge and children with low oral health knowledge have significantly higher odds of having oral diseases such as dental caries. A strong association has been seen between parent's socio demographic factors and a child's oral health knowledge and practice, with subsequent effect on oral health outcomes.

Aim: To determine the socio-demographic factors that influence knowledge of caries prevention and oral health practice of rural schoolchildren.

Methods: This was a cross sectional study involving 778 schoolchildren from 12 public primary schools in a rural community. A pretested, semi-structured, interviewer-administered questionnaire was used to obtain information on socio-demographics, knowledge of caries prevention and oral health practice of participants. Data were analyzed using descriptive and multivariate analysis at $p< .05$.

Results: The mean age of the children was 11± 1.8 years; the source of oral health information for majority 675(86.8%) of the children was their parents. Mean knowledge score was 4.5±1.7. More (55.6%) 10-12 year olds had fair oral health knowledge, they were 0.4 times more likely to have better oral health knowledge score (p= .003, 95% CI= 0.2–0.7). The gender of the pupil and parents' occupation were predictors of oral health practice.

Conclusion: Participants' knowledge of caries prevention was poor. Similarly, the number of children with good oral health practice was low being lowest among those whose fathers were farmers.

Keywords: *Oral health, schoolchildren, rural, parents*

Correspondence: Dr. A.O. Akinyamoju, Department of Oral Pathology, College of Medicine, University of Ibadan, Ibadan, Ibadan, Nigeria. E-mail: akindayo2002@yahoo.com.

Résumé

Contexte : Les habitudes de santé bucco-dentaire peuvent être influencées par une éducation appropriée en matière de santé bucco-dentaire conduisant à un changement de mentalité et de pratique. Cependant, la majorité des enfants africains ne disposeraient pas de connaissances suffisantes en matière de santé bucco-dentaire, et les enfants ayant de faibles connaissances en matière de santé bucco-dentaire ont des chances significativement plus élevées de souffrir de maladies bucco-dentaires comme les caries dentaires. Une forte association a été observée entre les facteurs sociodémographiques du parent et les connaissances et la pratique de l'enfant en matière de santé bucco-dentaire, avec un effet ultérieur sur les résultats en matière de santé bucco-dentaire.

Objectif : Pour déterminer les facteurs socio-démographiques qui influencent les connaissances sur la prévention de la carie et la pratique de la santé bucco-dentaire des écoliers ruraux.

Méthodes : Ceci était une étude transversale impliquant 778 écoliers provenant de 12 écoles primaires publiques d'une communauté rurale. Un questionnaire prétesté, semi-structuré et administré par un intervieweur a été utilisé pour obtenir des informations sur les caractéristiques sociodémographiques, les connaissances sur la prévention des caries et les pratiques de santé bucco-dentaire des participants. Les données ont été analysées à l'aide d'une analyse descriptive et multivariée à p <0,05.

Résultats : L'âge moyen des enfants était de 11 ± 1,8 ans; la source d'information sur la santé bucco-dentaire pour la majorité 675 (86,8%) des enfants était leurs parents. Le score moyen de connaissances était de 4,5 ± 1,7. Un plus grand nombre (55,6%) de 10 à 12 ans avaient des connaissances en santé bucco-dentaire passables, ils étaient 0,4 fois plus susceptibles d'avoir un meilleur score de connaissances en santé bucco-dentaire (p = 0,003, IC à 95% = 0,2-0,7). Le sexe de l'élève et la profession des parents étaient des prédicteurs de la pratique de la santé bucco-dentaire.

Conclusion : Les connaissances des participants sur la prévention des caries étaient médiocres. De même, le nombre d'enfants ayant de bonnes pratiques de santé bucco-dentaire était faible et plus faible parmi ceux dont les pères étaient agriculteurs.

Mots-clés : *Santé bucco-dentaire, écoliers, rural, parents*

Introduction

Oral health describes the well-being of the oral cavity including the dentition and its supporting tissues [1]. Oral health habits may be influenced by appropriate oral health education, leading to change of mind-set and practice [2]. The introduction of good oral health habits and ample knowledge in childhood is a vital foundation for proper dental norms and their maintenance into adult life [3]. However, majority of African children are said not to have adequate oral health knowledge of whether consumption of sugary products may cause tooth decay nor the role of fluoride in the prevention of dental caries, e.t.c [4]. Children with low oral health knowledge have significantly higher odds of having oral diseases such as dental caries [5]. Various sources of oral health information are available to influence a child's oral health knowledge and practice; Suprabha *et al*. [5] reported dentists, teachers and the media in descending order, as sources of oral health information for a group of Indian school children [5]. However, Varenne *et al.* [6] in a study from Burkina Faso observed that parents had more influence on children's oral health knowledge and practice over teachers and dentists [6]. This may be due to the fact that on a daily basis, parents function as role models for their children, thus influencing their oral health knowledge and practice [5]. In addition, a strong association has been seen between a parent's socio demographic factors and a child's oral health knowledge and practice [7].

Socio-demographic characteristics such as parents' level of education, type of occupation, etc. are said to be important considerations in children's oral health [3]. al-Shammery *et al*., [8] reported a higher prevalence of caries in molar teeth of primary school children whose parents had a primary level of education or were illiterate [8]. Parents with low levels of education may find it challenging to pass on accurate oral health information to their children and hence influence oral health outcomes [9]. A higher knowledge about the prevention of oral diseases has been found among urban compared to rural populations [6]. This could be attributed to the higher level of education of parents in urban settings, active schoolteachers and easier access to information through the media in such places [6].

Thus, this study aimed to determine the socio-demographic factors that may influence the knowledge of caries prevention and oral health practice of rural schoolchildren. This would provide data that can be utilized in planning community and school based oral health promotion activities.

Material and methods

The study was a cross-sectional survey involving pupils from 12 rural primary schools at Obafemi Owode Local Government Area (LGA), Ogun state, Southwest Nigeria. Ethical clearance for the study was obtained from the joint University of Ibadan/University College Hospital ethical review committee (UI/EC/10/0190). Approval for the study was obtained from the Ogun State Universal Basic Education Board, while consent was obtained from the parents of the pupils through the Parents Teachers Association. Also, assent was sought from the pupils before inclusion into the study. Sample size calculation was done using the formula for proportions [10] based on correct knowledge of potential causes of dental caries among rural African children [11]. The calculated sample size was 778 pupils.

Two (Ajebo and Ogunmakin) out of the four educational sectors in the Obafemi zone of the LGA were purposively selected on the basis of proximity to a functional rural health facility in the zone. The health facility is being managed by the Epidemiology and Medical Statistics Department, University of Ibadan. It is a referral and coordinating centre for a proposed School Health Programme. Twelve schools (six from Ajebo and Ogunmakin respectively) were then selected from a list of the 31 schools in the two educational sectors using a table of random numbers. All the pupils in primary 3 to 6 in each school on the day of visiting their schools who gave assent were recruited into the study. Eligible participants absent from school on the day their schools were visited were excluded from the study.

A pre-tested semi-structured interviewer-administered questionnaire was used to obtain data on their socio-demographic characteristics. Participants were also asked their parents' occupation and level of education. The questionnaire also included fourteen statements with responses on knowledge of caries prevention such as causes of tooth decay, care of yellow/ brown deposits on the teeth, effects of cleaning the teeth, causes of dental problems, prevention of dental problems, knowledge of who a dentist is and the functions of a dentist as well as presence of fluoride in toothpaste been used. In addition, it had six statements on oral health practices such as: whether they cleaned their teeth, type of teeth cleaning device used, frequency of teeth cleaning and frequency of change of teeth cleaning device. Also, frequency of sugar snack consumption and their source of

Table 1: Frequency distribution of the schoolchildren by socio demographic characteristics

Socio demographic characteristics	Frequency (N=778)	Percentage (%)
Age group (years)		
7-9	162	20.8
10-12	479	61.6
≥ 13	137	17.6
Gender		
Male	424	54.5
Female	354	45.5
Father's education		
No formal education	68	8.7
Primary school	307	39.5
Secondary school	330	42.4
Post secondary	73	9.4
Mother's education		
No formal education	88	11.3
Primary school	330	42.4
Secondary school	360	46.3
Father's occupation		
Farming	273	35.1
Business/trading	88	11.3
Artisans	215	27.6
Civil servant	63	8.1
Drivers	78	9.9
Others (clergy, security, musician)	61	8.0
Mother's occupation		
Farming	156	20.1
Business	64	8.2
Petty trading	375	48.2
Artisans	95	12.2
Civil servant	23	3.0
Housewife	34	4.4
Others (clergy, traditional birth attendant)	31	3.9

information for oral care were other questions asked. The questionnaire was translated into the local language (Yoruba) and back translated into English by a translator who is a health professional and familiar with the terminologies in the questionnaire. She is a native speaker of the Yoruba language and eloquent in English language. It was administered in the local language where this was preferred by the participant.

The interviewers were an auxiliary nurse and a dental surgeon; both were fluent in speaking the English and Yoruba languages. Before data collection, they were trained on how to administer the questionnaire. The training entailed taking the interviewers through the questions as well as the meaning and interpretation of each question. They administered the questionnaire to a class of twenty pupils and the responses were reviewed then areas of discrepancies were clarified. Periodically, during the course of data collection, the questionnaires were checked to ensure that there were no variations from the initial understanding and interpretation of questions.

Each correct response on knowledge of caries prevention earned a score of 1; some questions had multiple correct responses. Each respondent could obtain a maximum score of 20 and minimum score of 0. Mean knowledge score for participants was calculated and scores were categorized using a scale of ≤9 (poor) and >10 (good) knowledge. Similarly, each correct response on oral health practice earned a score of 1; some questions had multiple correct responses. Acceptable levels of each of the components were brushing more than once a day, eating sugar snacks

less frequently (less than daily), change of toothbrush within three months, using toothpaste that had fluoride and visiting the hospital in the occurrence of a dental problem. Each respondent could obtain a maximum score of 10 and minimum score of 0. Mean practice score for participants was calculated and scores were categorized using a scale of ≤5 (poor) and ≥6 (good) practice [12].

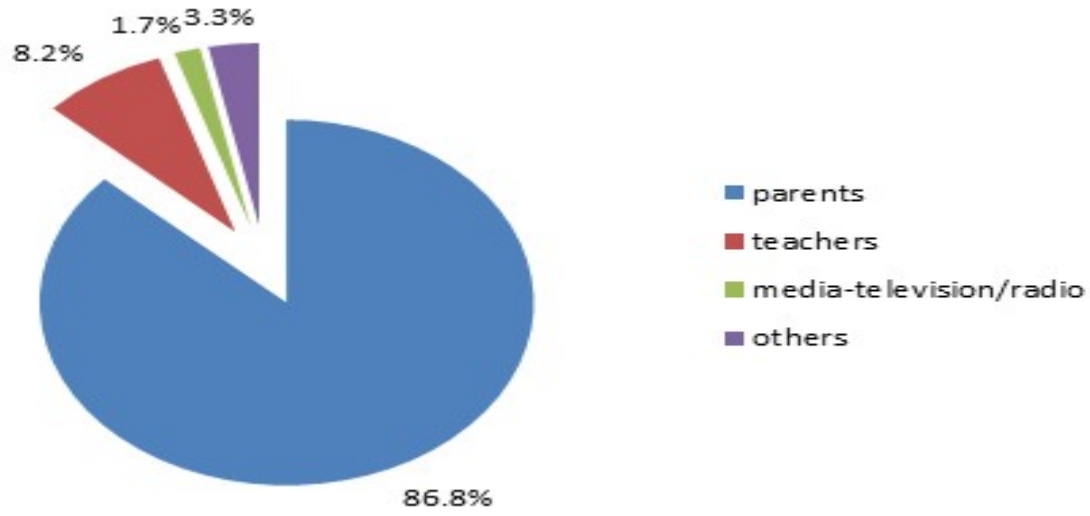


Fig. 1: Source of oral health information of the schoolchildren

Data analysis

The data were analyzed using Statistical Package for Social Sciences version 19, Chicago, IL, USA. The independent variables were age, gender, educational level and occupation of parents while the dependent variables were children's knowledge of caries prevention and their oral health practice.

Chi square test was used to test association between socio-demographic characteristics and categorized scores for knowledge of caries prevention as well as scores for oral health practice. Student's T-test was used to assess the association between mean knowledge and oral health practice scores and gender. Multivariate logistic regression analysis was performed to determine the variables which were potentially significant predictors of children's oral health knowledge and practice. There were three potential independent variables entered in the multivariate regression model for oral health knowledge (age, father's occupation, mother's occupation) and practice (gender, father's occupation, mother's occupation) respectively. The level of significance was set at $p< .05$.

Results

A little above half 424(54.5%) of the participants were males with a male to female ratio of 1.2:1. The ages of the pupils ranged between 7 and 17 years and their mean age was 11± 1.8 years. About a third 273(35.1%) of fathers of the participants were farmers; while many 375(48.2%) of their mothers were petty traders. With respect to the level of education of the parents of the participants, a little less than half 330(42.4%) of the fathers had a secondary school education while 360(46.3%) of mothers had a secondary school education (Table 1).

The source of oral health information for majority 675(86.8%) of the participants was their parents (Fig. 1). Almost all 679(87.3%) of the participants had poor oral health knowledge scores, few 226(29.0%) of them knew that sugar was associated with the cause of tooth decay, while only 42(5.4%) participants knew who a dentist was (Table 2). Concerning their oral health practice, nearly all (99.6%) the participants claimed to clean their teeth. More than half 510(65.5%) claimed to use toothbrush and toothpaste and a little less than half of these participants 332(46.6%) changed their toothbrushes when the bristles of the toothbrush frayed. On the other hand,

Table 2: Number and percentage of schoolchildren by correct knowledge on oral health

Questions	Frequency (N=778)	Percentage (%)
Which of these can cause a hole in the tooth?	226	29.0
How are yellow/brown deposits on the teeth removed?	27	3.5
What does cleaning your teeth help prevent?	264	33.8
Does eating sweets/ sweet foods cause holes in the teeth?	211	27.1
Not brushing properly can cause holes in the teeth	370	47.6
Not visiting the dentist regularly can cause teeth problems	15	1.9
Does avoiding sweets and sticky foods prevent teeth problems?	168	21.6
Does brushing regularly prevent teeth problems?	467	60.0
Does rinsing your after meals prevent holes in the teeth?	77	9.9
Do regular visits to the dentist prevent teeth problems?	11	1.4
Do you know who a dentist is?	42	5.4
Do you know that dentist can clean and polish your teeth?	39	5.0
Can regular cleaning of mouth prevent gum bleeding?	205	26.3
Can regular cleaning of mouth prevent bad smell?	432	55.5

Table 3: Number and percentage of schoolchildren by oral health practice

Questions	Frequency (N=778)	Percentage(%)
Do you clean your teeth		
Yes	775	99.6
No	3	0.4
How often do you clean your teeth		
Not every day	55	7.1
Once daily	577	74.1
Twice daily	108	13.9
More than twice daily	38	4.9
What do you use to clean your teeth		
Chewing stick	48	6.2
Toothbrush and paste	510	65.5
Toothbrush, toothpaste &chewing stick	195	25.1
Others (e.g. ash and cotton wool, cotton wool with water, water only)	25	3.2
Does your toothpaste contain fluoride:		
Yes	139	17.9
No	180	23.1
I don't know	459	59.0
**How often do you change your tooth cleaning device*		
Once in 3 months	104	14.6
Once in 6 months	49	6.9
When bristles get frayed	332	46.6
Once yearly	95	13.3
I don't know exactly	133	18.6
I eat sweet and sweet snacks		
Every day	507	65.2
Once a week	169	21.7
More than three times a week	60	7.7
Not at all	42	5.4

* *n= 713 (those using toothbrush as a teeth cleaning device)*

48(6.2%) used chewing stick only. In addition, 577(74.1%) of the participants cleaned their teeth once daily (Table 3). With regard to sugar snacking, almost all the participants ate one type of sugar snack or the other, more than half 507(65.2%) ate these snacks daily (Table 3).

The maximum knowledge score was 11 and mean score was 4.5±1.7 for all participants. Males had a mean knowledge score of 4.5±1.6 and more 421(62.0%) children aged 10-12 years had poor oral health knowledge (*P*=.002). Furthermore, 231(34.0%) participants whose fathers were farmers, had low oral health knowledge scores (*P*=.03), while 378(55.7%) participants whose mothers were traders also had a low oral health knowledge (*P*=.04) (Table 4). Oral health practice scores for the participants showed that 173(22.2%) had good practice, while 605(77.8%) had poor oral health practice. Mean oral health practice score for all participants was 8.0±2.9; difference between scores by sex (males- 7.7±2.9; females- 8.4±2.7) was statistically significant (*P*=<.001). More participants 86(49.7%) whose mothers were traders had higher oral health practice scores (*P*=<.001). A greater

Table 4: Association between socio-demographics and oral health knowledge and practice of the schoolchildren

Socio-demographics	Oral health knowledge Poor n(%)	Fair n(%)	p value	Oral health practice Poor n(%)	Good n(%)	p value
Age (years)						
7-9	147(21.6)	14(14.1)	.002	125(20.7)	36(20.8)	
10-12	421(62.0)	55(55.6)		368(60.8)	108(62.4)	.88
≥13	111(16.3)	30(30.3)		112(18.5)	29(16.8)	
Gender						
Male	364(53.6)	60(60.6)	.19	347(57.4)	77(44.5)	.003
female	315(46.4)	39(39.4)		258(42.6)	96(55.5)	
Mothers' occupation						
Farming	130(19.1)	27(27.3)	.04	128(21.2)	29(16.8)	
Trading	378(55.7)	60(60.3)		352(58.2)	86(49.7)	<.001
Artisans	86(12.7)	7(7.1)		65(10.7)	28(16.2)	
Civil servants	22(3.2)	2(2.0)		1(0.2)	8(4.6)	
Others (housewives, clergy, TBAs, e.t.c.)	63(9.3)	3(3.0)		59(9.7)	22(12.7)	
Mother's educational level						
No formal education	76 (11.2)	12(12.1)	.71	69(11.4)	19(11.0)	.88
Primary	285(42.0)	45(45.5)		259(42.8)	71(41.0)	
Secondary	318 (46.8)	42(42.4)		277(45.8)	83(48.0)	
Father's occupation						
Farming	231(34.0)	45(45.5)	.03	214(35.4)	62(35.8)	
Trading	72(10.6)	15(15.2)		64(10.6)	23(13.3)	.001
Artisans	196(28.9)	15(15.2)		150(24.8)	61(35.3)	
Civil servants	55(8.1)	8(8.1)		51(8.4)	12(6.9)	
Others (Drivers, security men, clergy)	125(18.4)	16(16.2)		126(20.8)	15(8.7)	
Father's educational level						
No formal education	61 (9.0)	7 (7.1)	.21	51(8.4)	17(9.8)	
Primary	264 (38.9)	43(43.4)		244(40.3)	63(36.4)	
Secondary	285 (42.0)	45(45.5)		256(42.3)	74(42.8))	.70
Post secondary	69 (10.2)	4 (4.0)		54(8.9)	19(11.0	

proportion 214(35.4%) of the participants with low oral health practice scores were those whose fathers were farmers (*P*=.001).

Children aged 10-12 years (*P*=.003, 95% CI= 0.2 – 0.70) were 0.4 times more likely to have an oral health knowledge score higher than those in the 7-9 years age group (Table 4). Also, participants whose mothers were traders (*P*= .02, 95% CI= 1.2 - 14.7) were 4 times more likely to have higher oral health knowledge scores compared to those whose mothers were farmers. Participants whose fathers were civil servants were 3 times more likely to have a good oral health practice score compared to those of farmers (*P*=<.001, 95% CI= 1.8-6.1) (Table 5).

Table 5: Oral health knowledge and practice of the schoolchildren and predictor variables

Predictors Oral health knowledge	OR	95% CI	p value	Predictors Oral health practice	OR	95% CI	p value
Age (years)				*Gender*			
7-9		Ref		Male		Ref	
10-12	0.4	0.2-0.7	.003	Female	0.6	0.42-0.8	.003
≥ 13	0.5	0.3-0.8	.004				
Fathers' occupation				*Fathers' occupation*			
Farming		Ref		Farming		Ref	
Trading	1.4	0.7-2.6	.33	Trading	2.7	1.4-5.0	.002
Artisans	1.6	0.7-3.4	2.37	Artisans	3.0	1.4-6.1	.004
Civil servants	0.6	0.3-1.2	.15	Civil servants	3.3	1.8-6.1	<.001
Others (Drivers, security, clergy)	1.2	0.5-2.9	.74	Others (Drivers, security, clergy)	1.6	0.7-3.8	.32
Mothers' occupation				*Mothers' occupation*			
Farming		Ref		Farming		Ref	
Trading	4.2	1.2-14.7	.02	Trading	0.6	0.3-1.2	12
Artisans	3.6	1.1-12.0	.04	Artisans	0.7	0.4-1.1	13
Civil servants	2.3	0.6-9.4	.25	Civil servants	1.2	0.6-2.2	.67
Others (housewives, clergy, TBAs e.t.c)	1.9	0.3-12.3	.51	Others (housewives, clergy, TBAs e.t.c)	21.5	2.6-11.6	.005

Discussion

The socio-economic status of a family which is largely determined by the occupation and level of education of the parents is an important determinant of oral health of children [13]. It also influences oral health knowledge and attitude of parents towards oral health, as well as the level of knowledge of oral health-related measures of children [14].

In this study, participants' knowledge of caries prevention was low; compared to that of rural Zimbabwean schoolchildren [11]. Majority (83.0%) of rural children from Zimbabwe had correct knowledge on the causes of dental caries compared with 29.0% of participants in this study [11]. The knowledge of the Zimbabwean children in relating measures such as tooth brushing, consuming less sugary products, rinsing the mouth after a major meal and use of fluoridated toothpaste to tooth decay was also higher [11]. However, a difference in age may account for this observation as the rural Zimbabwean children studied were 12 year olds unlike this study population which included younger children.

Similar to results obtained from a previous study, males in this study had a slightly higher mean oral health knowledge score compared to females [5]. However, favorable oral health practice is more often reported in girls, and this was consistent with the female participants in this study, suggesting that awareness may not always lead to improved practice [4,15]. Only few (17.9%) participants in this study knew whether fluoride was present in the toothpaste they used, consistent with other studies amongst schoolchildren in some African communities [11,16,17]. This is not limited to Africans, as 78% of Indian schoolchildren

were not aware whether the toothpaste they used was fluoridated or not [5]. This may be attributed to their source of oral health information. For majority of children their source of oral health information is their parents and likewise for the children in this study [5,18]. Parents and caregivers have been seen to have limited knowledge of the causes and prevention of the most common oral diseases [18,19]. In addition, in a previous study it was observed that mothers were unaware of the presence of fluoride in the toothpaste they used and a mother's oral health knowledge was predictive of a child's level of knowledge [18].

Furthermore, it has been reported that parents with higher levels of education had better knowledge of caries prevention and oral health practice [20,21]. This may be the reason why more children whose parents had higher education had better oral health practice in this study. Also, the occupation of a father/ mother influences the oral health knowledge of a child [18]. In this study, a mother's occupation was predictive of the level of knowledge of caries prevention and oral health practice. More children whose mothers were traders had fair oral health knowledge compared to the others. This group of children was also in the majority of those with good oral health practice. This may be due to increased awareness of traders from knowledge obtained from dealing with wares used for oral health care.

The oral health practice of the children in this study was similar to that of other Nigerian rural children, [16,22,23] but differed in some ways from that of children in other parts of Africa and other climes [11,24]. In addition, gender and parents' occupation were predictive factors of oral health practice in this study which was also reported in a study by Castilho *et al* [15].

Therefore, school oral health promotion interventions should be holistic, involving the entire family so as to provide children with better oral health knowledge of caries prevention and oral health practice [25]. This study would have been all encompassing if the knowledge of caries prevention and as well the oral health practice of the parents were assessed along with those of their children.

Conclusion

In summary, the knowledge of caries prevention amongst rural schoolchildren in this study was poor. Similarly, the number of children with good oral health practice was low. A mother's occupation and the age of a child were predictors of knowledge of caries prevention while gender and his/ her parent's occupation predicted oral health practice. Thus, further studies will be necessary to assess these parameters in parents of schoolchildren in rural communities to correlate this with those of their children.

References

1. World Health Organisation, Regional Office for Africa. Oral health in the African region: A regional strategy (1999-2008), Brazzaville, Republic of Congo: World Health Organisation, Regional Office for Africa, 1998.
2. Ab-Murat N and Watt RG. Chief dentists' perceived strengths and weaknesses of oral health promotion activities in Malaysia. Ann Dent 2006; 3: 1-5.
3. Blinkhorn AS. Dental preventive advice for pregnant and nursing mothers–sociological implications. Int Dent J1981; 12: 14–22.
4. Ogola JA. Oral health knowledge, attitudes and practices among 9-12 year old children attending primary schools in Westlands, Nairobi County, Kenya. http://ir library.ku.ac.ke/handle/123456789/10984. Retrieved on the 27th, Dec. 2017.
5. Suprabha BS, Rao A, Shenoy R and Khanal S. Utility of knowledge, attitude, and practice survey, and prevalence of dental caries among 11 to 13 year old children in an urban community in India. Glob Health Action2013; 6: 10.3402/ gha.v6i0.20750. doi: 10.3402/gha.v6i0.20750.
6. Varenne B, Petersen PE and Ouattara S. Oral health behaviour of children and adults in urban and rural Burkina Faso, Africa. Int Dent J 2006; 56:61-70.
7. Tinanoff N, Kanellis MJ and Vargas CM. Current understanding of the epidemiology mechanisms, and prevention of dental caries in preschool children. Pediatr Dent 2002;24(6):543-551.
8. al-Shammery AR, Guile EE and el-Backly M. Prevalence of caries in primary school children in Saudi Arabia. Community Dent and Oral Epidemiol 18: 320–321.
9. Kamil MO, El-Ameen NM, Madkhaly SH, *et al*. Knowledge and attitude of Saudi mothers towards health of primary teeth. JDOH 2015; 7(7): 107-112.
10. Kirkwood BR and Sterne JAC. Essential Medical Statistics. 2nd ed. Goodgame F. (Ed). Massachussetts: Blackwell; 2003. p.420.
11. Mafuvadze BT, Mahachi L. and Mafuvadze B. Dental caries and oral health practice among 12

year old school children from low socio-economic status background in Zimbabwe. Pan Afr Med J 2013; 14: 164. doi:10.11604/pamj.2013.14.2399.

12. Folayan MO, Kolawole KA, Oyedele T, *et al*. Association between knowledge of caries preventive practices, preventive oral health habits of parents and children and caries experience in children resident in sub-urban Nigeria. BMC Oral Health 2015; 15:62, http://doi.org/10.1186/1472-6831-14-156.
13. Petersen PE. Socio-behavioural risk factors in dental caries- International perspectives. Community Dent Oral Epidermoiol 2002; 30: 108-114.
14. Williams NJ, Whittle JG and Gatrell AC. The relationship between socio-demographic characteristics and dental health knowledge and attitudes of parents with young children. Br Dent J 2002; 193: 651-654.
15. Castilho ARF, Mialhe FL, Barbosa TD and Puppin-Rotani RM. Influence of family environment on children's oral health: a systemic review. J Pediatr. (Rio J.) 2013; 89,2: 116-123.
16. Okoye LO and Ekwueme OC. Prevalence of dental caries in a Nigerian rural community: a preliminary local survey. Ann Med Health Sci Res 2011; 1: 187–195.
17. Sofola OO, Shaba OP and Jeboda SO. Oral hygiene and periodontal treatment needs of urban schoolchildren compared with rural school children in Lagos State, Nigeria. Odontostomatol Trop 2003; 101: 25-29.
18. Sehrawat P, Shivlingesh KK, Gupta B, Anand R, S harma A and Chaudhry M. Oral health knowledge , awareness and associated practices of pre-school children's mothers in Greater Noida, India. Niger Postgrad Medical J 2016; 23: 152-157.
19. Al-Samadanil KHM and Ahmad MS. Prevalence of first permanent molar caries in and its relationship to the dental knowledge of 9–12 year olds from Jeddah, Kingdom of Saudi Arabia. ISRN Dent 2012; Article ID 391068, 6pages, doi:10.5402/2012/391068.
20. Abduljalil HS and Abuaffan AH. Knowledge and practice of mothers in relation to dental health of pre-school children. Adv Genet Eng 2016; 5: 153. doi:10.4172/2169-0111.1000153
21. Oredugba F, Agbaje M, Ayedun O and Onajole A. assessment of mothers' oral health knowledge: Towards oral health promotion for infants and children. Health 2014; 6: 908-915.
22. Kolawole KA, Oziegbe EO and Bamise CT. Oral hygiene measures and the periodontal status of schoolchildren. Int J Dent Hygiene 2011; 9: 143-148.
23. Azodo CC and Amenaghawon OP. Oral hygiene status and practices among rural dwellers. Eur J Gen Dent 2013; 2: 42-45.
24. Yabao RN, Duante CA, Velandria FV, *et al*. Prevalence of dental caries and sugar consumption among 6-12-y-old school children in La Trinidad, Benguet, Philippines. Eur J Clin Nutr 2005; 59(12): 1429-1438.
25. Poutanen R, Lahti S, Tolvanen M and Hausen H. Parental influence on children's oral health-related behaviour. Acta Odontol Scand. 2006; 64: 286-292.

Afr. J. Med. Med. Sci. (2020) **49,** 281-286

Fournier's gangrene: management and patient outcomes in Ile-Ife, Nigeria

AA Salako[1,2], TA Badmus[1,2], RN Babalola[2], MC Igbokwe[1,2], A Laoye[2], RA David[2], A Olawamide[2], CI Onyeze[2] and IA Akinbola[2]

Department of Surgery[1], Obafemi Awolowo University and UrologyUnit, Department of Surgery[2], Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. Nigeria

Abstract

Background: Fournier's gangrene (FG) is a rapidly progressive necrotizing fasciitis of the scrotum, perineum and peri-anal regions; and an important cause of morbidity and mortality worldwide. Risk factors range from systemic causes of immunosuppression like diabetes mellitus; to local factors like peri-urethral and anorectal infections. Treatment aims to manage the predisposing factors, debride necrotic tissues, and achieve skin cover. The experience with the management of FG in Ile-Ife, Nigeria is described in this article.

Patients and methods: A review of the records of patients with Fournier's gangrene managed in a tertiary hospital between January 2011 and December, 2017 was performed. Data was analyzed using the Statistical Package for Social Sciences version 20 and statistical significance taken as $p<0.05$.

*Results***:** Thirty one (31) patients were managed for FG during this period. All were males, with a mean age of 46.7 ± 21.1 years. Extent of gangrene was variable, it ranged from the scrotum only in 11 (35%) patients, to as far as gangrene of the abdominal wall in 3 (10%) patients. Diabetes mellitus was the leading predisposing factor, observed in 17 (55%) patients. All patients were managed with intravenous antibiotics; serial debridement, and wound cover as indicated. There were 6 (19%) mortalities. Higher Fournier's Gangrene Severity Index, extent of gangrene, and presence of systemic complications, were significantly associated with mortality.

*Conclusion***:** Fournier's gangrene is a fulminant condition which can result in mortality. Efforts should be directed at treating predisposing factors, health education to encourage early presentation, and aggressive management of the disease.

Keywords: *debridement, fournier, gangrene, mortality, severity*

Correspondence: R.N. Babalola, Urology Unit, Department of Surgery, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria. E-mail:rereloluwa@yahoo.com

Résumé

Contexte: La gangrène de Fournier (GF) est une fasciite nécrosante rapidement progressive du scrotum, du périnée et régions périanales; et une cause importante de morbidité et de mortalité dans le monde. Les facteurs de risque vont des causes systémiques de l'immunosuppression comme le diabète sucré; à des facteurs locaux comme les infections péri-urétrale et anorectale. Le traitement vise à gérer les facteurs prédisposants, à débrider les tissus nécrotiques et à obtenir une couverture cutanée. L'expérience de la gestion de GF à Ile-Ife, Nigeria est décrite dans cet article.

Patients et méthodes: Un examen des dossiers des patients atteints de gangrène de Fournier pris en charge dans un hôpital tertiaire entre janvier 2011 et décembre 2017 a été réalisé. Les données ont été analysées en utilisant le progiciel statistique pour les sciences sociales (SPSS) version 20 et la signification statistique prise comme $p <0,05$.

Résultats **:** Trente et un (31) patients ont été pris en charge pour la GF au cours de cette période. Tous étaient des hommes, avec un âge moyen de 46,7 ± 21,1 ans. L'étendue de la gangrène était variable, elle allait du scrotum seulement chez 11 (35%) patients à la gangrène de la paroi abdominale chez 3 (10%) patients. Le diabète sucré était le principal facteur de prédisposition, observé chez 17 (55%) patients. Tous les patients ont été pris en charge avec des antibiotiques intraveineux; débridement en série et couverture de la plaie comme indiqué. Il y a eu 6 (19%) décès. Un indice de gravité de la gangrène de Fournier plus élevé, l'étendue de la gangrène et la présence de complications systémiques étaient significativement associés à la mortalité.

Conclusion **:** La gangrène de Fournier est une condition fulminante qui peut entraîner la mortalité. Les efforts devraient viser à traiter les facteurs prédisposants, l'éducation sanitaire pour encourager une présentation précoce et une gestion agressive de la maladie.

Mots-clés : *débridement, fournier, gangrène, mortalité, gravité*

Introduction

Fournier's gangrene(FG) is a rapidly progressive necrotizing fasciitis of the scrotum, perineum and peri-anal regions; and an important cause of morbidity and mortality worldwide [1]. This condition is found in all age-groups and sexes, though its far more common in men, with a male to female ratio of 10:1 [2]. The origin of this disease can be traced back to Baurienne in 1764, who described a fatal necrotizing process of the male genitalia [3]. It was however in 1883, after Jean Alfred Fournier published a case-series of FG in five males, that the disease became named after him [4].

Predisposing factors to FG include systemic causes like immunosuppression, as seen in diabetes mellitus, human immunodeficiency virus, cytotoxic drugs, prolonged steroid use and chronic malnutrition [5]. Local factors also have a role, and include poor perianal hygiene, perineal trauma, peri-urethral, scrotal and anorectal infections, urethral stricture, anorectal procedures and urethral instrumentation [5].

FG is poly-microbial and spreads rapidly along the subcutaneous tissue planes [6]. The infection thus spread along fascial planes and could go as high as the torso and as low as the thigh, with spread corresponding to the insertion of the fused Scarpa and Camper's fasciae at the clavicle, and the Colles fascia in the perineum [7]. Patients often present with scrotal pain, swelling and fever, with resultant gangrene of perineal tissues, culminating in extensive skin and subcutaneous tissue loss, septic shock and death [8].

The management of FG requires a high index of suspicion by the physician and prompt treatment by the physician. Treatment is aimed at identifying and controlling the predisposing factors, debridement of all necrotic tissues under antibiotic cover and skin coverage after control of sepsis [9].

Several prognostic scoring indices including the Fournier's Gangrene Severity Index (FGSI), Uludag Fournier's Gangrene Severity Index (UFGSI) and age-adjusted Charlson Comorbidity Index (ACCI), have been used in the last century to grade severity and predict the outcome of patients with FG.[10] Loar *et al* [11] described the FGSI, the most widely studied index, showing it to have a significant correlation with disease-associated mortality. This index was used to ascertain its relationship to outcome in the cohort of patients studied.

The advent of the 21st Century is believed to have led to a change in the presentation and pattern of many infectious diseases in our environment due to improved sanitation, better information dissemination, enlightenment, education, newer antibiotics and better facilities. It is therefore important to document our experience with FG in order to determine whether there has been any change in the morbidity and mortality of FG in our hospital in South-Western Nigeria.

Patients and methods

A retrospective review of the records of all patients with Fournier's gangrene managed in the Urology Unit of the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria, from January 2011 to December 2017 was performed. Ethical approval was obtained from the Ethics and Research Committee of the Hospital. Data retrieved included the socio-demographic characteristics, duration of symptoms before presentation, extent of disease, predisposing factors, clinical features, FGSI and outcome. Data was analyzed using the Statistical Package for Social Sciences version 20 and statistical significance was taken as $p<0.05$.

Results

Thirty one (31) patients were managed for FG during the study period, giving an in-hospital prevalence of 0.6 per 1,000 admissions over this period. All were males, with an age range of 19 to 75 years and a mean age of 46.7±18.9 years. Figure 1 show the age distribution, with 40-49 being the peak age group. Extent of gangrene ranged from involvement of the scrotum only in 11 (35%) patients to involvement of the scrotum with extension to the lower anterior abdominal wall in 3 (10%) patients (Figure 2).

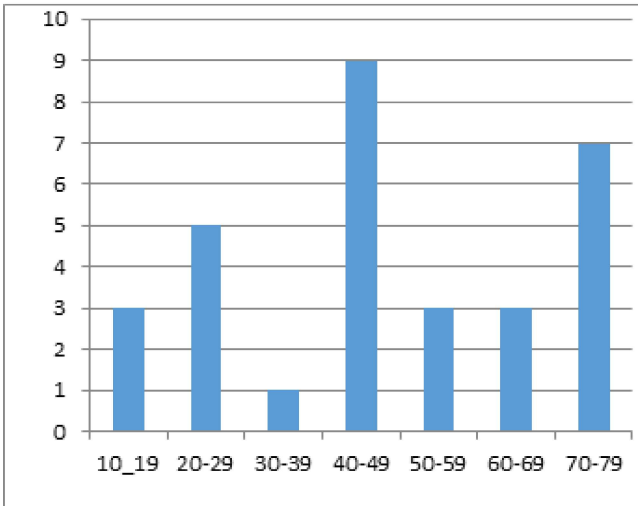


Fig. 1: Age distribution of patients

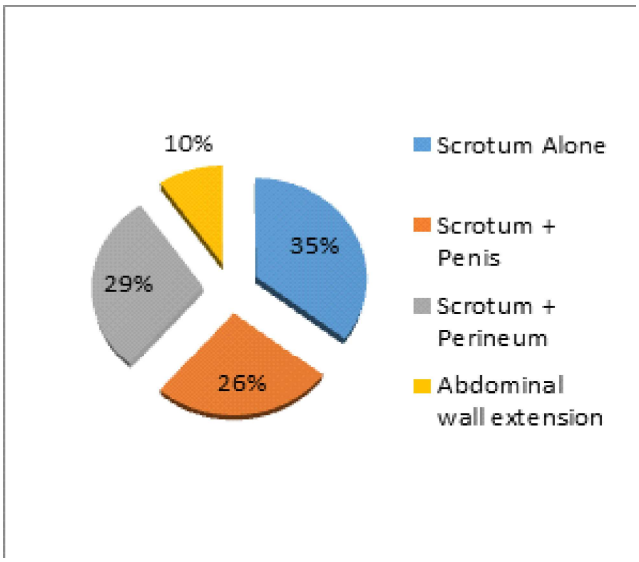


Fig. 2: Extent of gangrene

A predisposing factor was found in 24(77%) patients, whereas, 7(23%) patients, did not have any predisposing factor. Diabetes mellitus was the single leading predisposing factor, observed in 17 (55%) of the patients (Table 1). Wound biopsy microscopy, culture and sensitivity revealed representative organisms in 29 (93.5%) patients. Of these, 15 (51.7%) patients had one organism isolated, whereas 14(48.2%) had confirmed polymicrobial infections. *Escherichia coli* and *Klebsiella spp* were the leading organisms identified (Figure 3).

Table 1: Aetiology of FG in this study.

Aetiology	Number (%)
None	7 (22.6)
Diabetes	17 (54.8)
Other factors	7 (22.6)
Urethral stricture	3
Trauma	2
HIV	1
Ischiorectal abscess	1

All patients were managed with a combination of intravenous fluids and antibiotic resuscitation with an initial debridement within 24 hours of presentation. Subsequently, serial debridement with wound dressings using honey, saline and antibiotic solutions were performed. Complications were observed in 45% of these patients (Figure 4), and FGSI ranged from 3 to 16 (Figure 5).

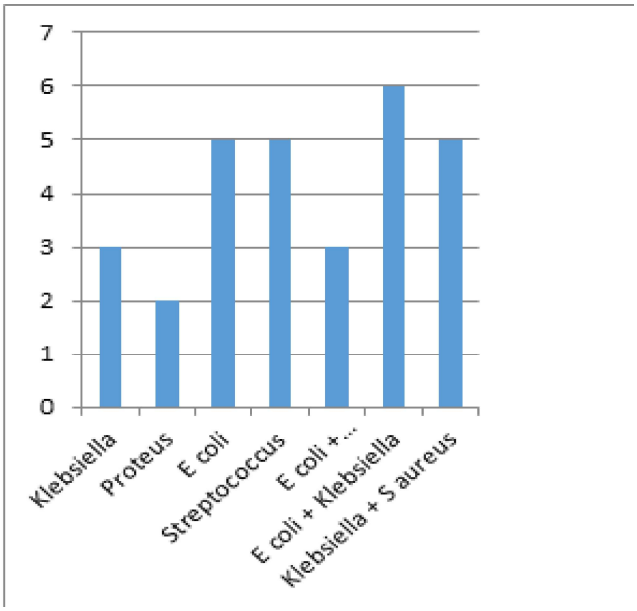


Fig.3: Wound biopsy culture results

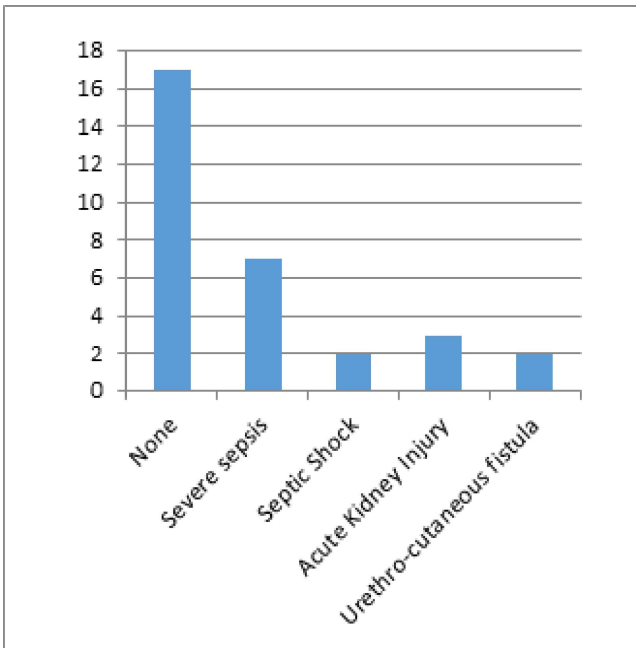


Fig.4: Complications of FG in this study.

Sixteen patients (51.6%) had a secondary closure, 5 (16.1%) had skin grafting while 1 (3.2%) had a flap closure. The mean hospital stay was 23±17 days. Mortality was observed in 6 (19%) patients. The mean FGSI was 6.84 for the survivors and 12.5 for the patients that died. Higher FGSI (p=0.003), extent of gangrene (p=0.02), and presence of systemic

complications (p=0.02), were significantly associated with mortality but diabetes mellitus was not a significant risk factor for mortality (p=0.664).

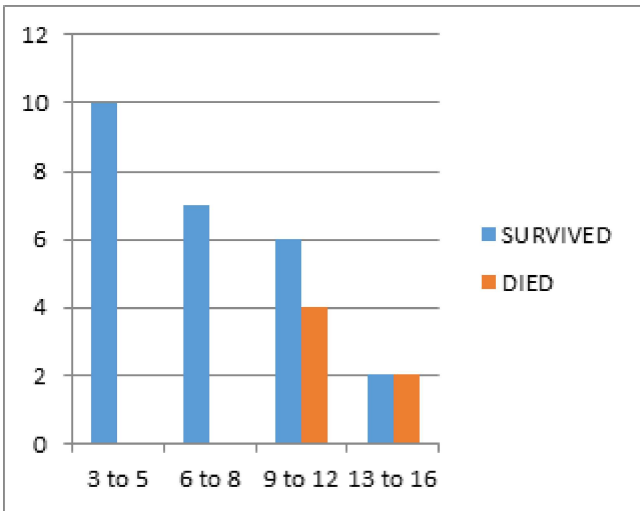


Fig. 5: Fournier gangrene severity index

Fig. 6: Fournier gangrene with extensive scrotal loss and exposed testes

Discussion

This study shows that FG is relatively uncommon in our environment, with only 31 cases managed over a 6-year period. Unfortunately, there is still a high mortality risk, with 1 in 5 deaths among affected cases; and predictors of mortality being high FGSI, extensive gangrene and presence of systemic complications.

This study revealed that FG occurs mostly in adult males, which corroborates the findings of Aji *et al* [9] and Ugwumba *et al* [12]. The mean age at presentation was about the fifth decade of life. This finding is similar to previous reports by Ugwumba *et al* [12] and Omisanjo *et al* [13]. This might coincide with the common age of diagnosis of co-morbidities like diabetes mellitus (DM), in Nigeria, usually about the 5th to 6th decade [14].

Fournier's gangrene often affected people of low socioeconomic status, this might reflect suboptimal nutritional status; poor glycemic control (drug compliance and specialist attention) and inadequate access to quality surgical care [12]. The scrotum is the most common site affected by FG, similar to other studies, where it often occurs alone but may involve other contiguous structures [15] although, abdominal involvement has been reported before [12,13].

Diabetes mellitus is still a leading predisposing factor, corroborating previous reports [12,13,15]. The observation of Human Immunodeficiency Virus (HIV) infection may suggest a strong role for immune compromise in the aetio-pathogenesis of FG. Urethral strictures accounted for less than a fifth of the patients with FG in this series. This was in contrast to findings in Kano, Nigeria, where watering-can perineum was the leading aetiology in an earlier review of FG [9]. The changing trend of post-traumatic strictures equaling, if not surpassing post-infectious urethral strictures, in Nigeria [16] and abroad [17], might explain why lesser strictures are being complicated with FG. Urethro-cutaneous fistulas are described as relatively uncommon complications of FG, as there are only very few case reports describing it in literature [6,18]. Two patients in our review had this complication, and were diabetic patients with penile involvement of an initially scrotal condition.

This study revealed a mortality rate of 19%, although varying outcomes had been reported previously which varied from 11.6% to 41.1% [2,9,19,20]. This might suggest the impact of several factors on the outcome of management, ranging from variable aetiologic factors, presence or absence of co-morbidities, immune status, time of presentation; to development of complications, prevailing institutional factors and facilities for treatment, on the outcome of management. This study further showed that there is an association between extent of gangrene at presentation and the eventual outcome. Other studies have demonstrated similar findings [21,22]. This might be related to delay in presentation and adequate intervention, factors that will need to be improved upon to achieve better outcomes.

The role of the FGSI in predicting mortality has also been shown in this study. This might help to further suggest its widespread use to stratify patients with regards to risk of mortality. As this scoring is done at admission, it might help to promptly identify patients in need of aggressive and effective treatments. Furthermore, the impact of systemic complications; like sepsis, septic shock and renal compromise on mortality, have been highlighted by this study. It is thus important to promptly manage the local infective condition so as to prevent extension of gangrene or development of systemic complications.

Although diabetes was a strong predisposing factor to the development of this condition, it was not an independent risk factor for mortality. This suggests that with adequate local wound care and glycemic control, which might help reduce the development of systemic complications, mortalities from this condition can be largely prevented.

Conclusion

Fournier's gangrene is a fulminant condition which can result in mortality if not promptly and properly managed. Efforts should be directed at appropriately treating predisposing factors, as well as health education to encourage prompt recognition and early presentation. Furthermore, identification of high-risk patients, followed by prompt aggressive management of the condition, will reduce the development of systemic complications and improve overall outcome.

References

1. Chernyadyev SA, Ufimtseva MA, Vishnevskaya IF, *et al.* . Fournier's Gangrene: Literature Review and Clinical Cases. Urol Int. 2018; 101:91-97.
2. Eke N. Fournier's Gangrene: A Review of 1726 Cases. Br J Surg. 2000; 87:718-728.
3. Mallikarjuna MN, Vijayakumar A, Patil VS and Shivswamy BS. Fournier's Gangrene: Current Practices. ISRN Surgery. 2012; 2012:8.
4. Fournier JA. Jean-Alfred Fournier 1832-1914. Gangrene Foudroyante De La Verge (Overwhelming Gangrene). Sem Med 1883. Dis Colon Rectum. 1988; 31:984-988.
5. Ariana S, Kamran A, Abdullatif A, Muhammad SK and Prokar D. Fournier's Gangrene. A Clinical Review. Archiv Ital Urol Androl. 2016; 88:157-164.
6. Katušiæ J, Štimac G, Benko G, *et al.*. Management of Fournier's Gangrene: Case Report and Literature Review. Acta Clin Croat. 2010; 49:453-457.
7. Eke N and Raphael JE. Fournier's Gangrene: IntechOpen; 2011. Available from: https://www.intechopen.com/books/gangrene-current-concepts-and-management- options/fournier-s-gangrene.
8. Mallikarjuna MN, Abhishek V, Vijayraj SP and Shivswamy BS. Fournier's Gangrene: Current Practices. SRN Surgery. 2012; 1:20-28.
9. Aji SA, Alhassan SU and Ujudud MM. Fournier's Gangrene: Experience with Management of 46 Cases in a Tertiary Institution. Open J Urol. 2012; 2:109-112.
10. Tuncel A, Keten T, Aslan Y, *et al*. Comparison of Different Scoring Systems for Outcome Prediction in Patients with Fournier's Gangrene: Experience with 50 Patients. Scand J Urol. 2014; 48:393-399.
11. Laor E, Palmer LS, Tolia BM and Reid RE. Winter HI. Outcome Prediction in Patients with Fournier's Gangrene. J Urol. 1995; 154:89–92.
12. Ugwumba FO, Nnabugwu II and Ozoemena OF. Fournier's Gangrene – Analysis of Management and Outcome in South-Eastern Nigeria. SAJS. 2012; 50: 16-19
13. Omisanjo OA, Bioku MJ, Ikuerowo SO, Sule GA and Esho JO. Clinical Characteristics and Outcome of Management of Fournier's Gangrene at the Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria. Ann Afr Med. 2014; 13:174-178.
14. Fasanmade OA and Dagogo-Jack S. Diabetes Care in Nigeria. Ann Glob Health. 2015; 81:821- 829.
15. Verma S, Sayana A, Kala S and S Rai. Evaluation of the Utility of the Fournier's Gangrene Severity Index in the Management of Fournier's Gangrene in North India: A Multicentre Retrospective Study. J Cutan Aesthet Surg. 2012; 5:273–276.
16. Ekeke ON and Amusan OE. Clinical Presentation and Treatment of Urethral Stricture: Experience from a Tertiary Hospital in Port Harcourt, Nigeria. Afr J Urol. 2017; 23:72-77.
17. Xu YM, Song LJ, Wang KJ, *et al*. Changing Trends in the Causes and Management of Male Urethral Stricture Disease in China: An

Observational Descriptive Study from 13 Centres. BJU Int. 2015; 116:938-944.
18. Chih-Weim H, Guo-Shu H, Wen-Cheng L, *et al.* Urethral Fistula as an Unusual Complication of Fournier's Gangrene: A Case Report and Literature Review. J Med Sci. 2013; 33:365-368.
19. Benjelloun EB, Souiki T, Yakla N, *et al*. Fournier's Gangrene: Our Experience with 50 Patients and Analysis of Factors Affecting Mortality. World J Emerg Surg. 2013; 8:13.
20. Irekpita E, Salami TAT, Dongo AE, *et al*. Fournier's Gangrene: Irrua Teaching Hospital, Nigeria, Experience. Sudan J Dermatol. 2008; 6:34-43.
21. Yong-Kim I. Gangrene: The Prognostic Factors and Validation of Severity Index in Fournier's Gangrene. In: Gangrene - Current Concepts and Management Options. Shanghai, China: InTech; 2011. p. 1-7
22. Saber A and Bajwa TM. A Simplified Prognostic Scoring System for Fournier's Gangrene. Urol Nephrol Open Access J. 2014; 1:79-82.

Afr. J. Med. Med. Sci. (2020) **49,** 233-239

Determinants of non-attendance at scheduled review visits following tooth extraction

OO Gbolahan, TO Aladelusi and AA Ayantunde

*Department of Oral and Maxillofacial Surgery, College of Medicine, University of Ibadan/ UCH, Ibada*n, Nigeria

Abstract

Background: Non-attendance at scheduled review visits remains a challenge that affects all aspects of health care. There is sparse information on prevalence and causes of non-attendance following extraction of teeth in our environment. The aim of this study was to determine the prevalence, patient's characteristic and other determinants of default in follow-up review visit among adult patients following extraction of teeth.

*Methods***:** Descriptive study of 280 consecutive adult patients who presented at the oral surgery clinic for tooth extraction. Clinical and socio-demographic data, phone number, information on whether appointment was kept or missed, if missed, reason for missing the appointment as well as pattern of previous appointment attendance were collected.

Data analysis was done using SPSS version 19.0. Categorical variables were tested using the Pearson's Chi-square test to examine the relationship between non-attendance and specific patients' characteristics. Variables achieving a p value of ≤ 0.05 were considered statistically significant

Results: The study participants consisted of 119 males and 161 females (1:1.35) with a mean (SD) age of 43.3 ($\pm$ 16.8) years. One hundred and eighteen (42.1%) patients failed to attend the follow up appointments; main reasons given for non-attendance included "Being busy (54.9%)", "forgetting appointment (10.8%)". The presence of post-operative complaint (p= 0.0001) and the level of education (0.049) were the statistically significant factors predicting attendance at the review clinic appointments.

Conclusion: Non-attendance at review visit following tooth extraction was high among the study population. Most common reason given for non-attendance was being busy. Presence of symptom was a significant finding among those that attended review appointment.

Keywords: *Post-extraction review, non-attendance, dental, post-operative complaint*

Correspondence: Dr. Olalere O. Gbolahan, Department of Oral and Maxillofacial Surgery, College of Medicine, Unversity of Ibadan, Ibadan, Nigeria. E-mail: gbolahanlere@yahoo.com

Résumé

Contexte : L'absence aux visites d'examen prévues demeure un défi qui touche tous les aspects des soins de santé. Il existe peu d'informations sur la prévalence et les causes d'absence suite à l'extraction de dents dans notre environnement. Le but de cette étude était de déterminer la prévalence, les caractéristiques des patients et d'autres déterminants de l'absence lors de la visite de suivi chez les patients adultes après l'extraction des dents.

Méthodes **:** Une étude descriptive de 280 patients adultes consécutifs qui se sont présentés à la clinique de chirurgie buccale pour l'extraction dentaire. Les données cliniques et sociodémographiques, le numéro de téléphone, les informations sur le maintien ou le manquement du rendez-vous, le cas échéant, la raison du manquement au rendez-vous ainsi que le schéma de la participation aux rendez-vous précédents ont été collectés.

L'analyse des données a été effectuée à l'aide de SPSS version 19.0. Les variables catégorielles ont été testées à l'aide du test Pearson ÷2 pour examiner la relation entre l'absence et les caractéristiques spécifiques des patients. Les variables atteignant une valeur p d" 0,05 ont été considérées comme statistiquement significatives.

Résultats: Les participants à l'étude étaient constitués de 119 hommes et 161 femmes (1:1,35) avec un âge moyen (ET) de 43,3 ($\pm$ 16,8) ans. Cent dix-huit (42,1%) patients ont manqué les rendez-vous de suivi; les principales raisons invoquées pour l'absence étaient "Être occupé (54,9%)", "oublier le rendez-vous (10,8%)". La présence de plaintes postopératoires (p = 0,0001) et le niveau d'éducation (0,049) étaient les facteurs statistiquement significatifs prédisant la présence aux rendez-vous de la clinique d'examen.

Conclusion: L'absence à la visite d'examen après l'extraction dentaire était élevée parmi la population étudiée. La raison la plus souvent invoquée pour l'absence était le fait d'être occupé. La présence de symptômes était une constatation importante parmi ceux qui n'ont pas manqué au rendez-vous d'examen.

Mots - clés : *examen post-extraction, absence, dentaire, plainte postopératoire*

Introduction

Following extraction of teeth, review appointments are usually given to patients which may vary from one to a couple of visits depending on the individual situation and need. The review visit is usually one week after extraction at the first instance with other possible further visits at varying intervals. The visits are meant to assess the progress of healing, ensure there are no post extraction complications, detect and promptly manage any possible complication that might be developing and reinforce oral health education for improved oral health behaviour.

Anecdotally, it's been said that majority of patients who had dental extraction do not show up for the follow up review appointment and as reported by Gambhir, dental patients only visit the dentist when in pain and never bother to return for follow-up in most cases [1]. Non-attendance ('no show') at review appointments in clinics is a global challenge for health services both in developed and even more so in developing countries where ignorance and poverty tends to aggravate the problem [2]. It is believed that for health service provision to have an effective role, we should understand the reasons behind risks associated with and needs of patients who do not engage effectively with healthcare provision, and tailor services better to meet those needs [3].

The rate and causes of non-attendance varies widely between different clinics and between different cultural and socioeconomic environments [4-9]. Non-attendance often has multiple effects on the healthcare system; the effect on the facility includes financial impact, for example, NHS Fylde and Wyre Clinical Commissioning Group reported that the missed 6,893 appointments in December 2017 cost the NHS about £250,000 [10]. This is due to underutilization of facilities and neglect of treatable conditions, which led to an increased expenditure of resources at a later stage. Non-attendance can also severely impact training of students and residents with adverse effect on the accreditation of training health facilities [11]. There is a possibility of missed early signs and delayed treatment of potential complications and overall poorer outcome [12]. No-shows for scheduled appointment reduce patient quality of care and access to services while increasing loss to follow-up and medical costs [13]. Knowing the prevalence and reasons for non-attendance among these patients will aid in designing appropriate intervention strategies to improve attendance as well as oral health attitude and behaviour of the populace. At present, data on prevalence of non-attendance as well as factors responsible for non-attendance at scheduled review appointments following extraction of teeth (especially in developing nations) is scanty. The objectives of this study were therefore to determine the prevalence, patient's characteristic and other determinants of default in follow-up review visit among patients following extraction of teeth.

Material and methods

This descriptive hospital-based study was conducted in a cohort of adult patients who presented for tooth extraction at the University College Hospital (UCH), dental clinic Ibadan between January 2017 and December 2017. The University College Hospital dental clinic is located about 5km northwest of the Ibadan city centre.

Study participants included 280 consecutive adult patients (18 years and above) who had an extraction of one or more permanent teeth at the study center during the study period. Other inclusion criteria were the patients possessing a means of contact; either a functional telephone or address that could be traced. Patients who declined to participate in the study were excluded. The study data was collected using a semi-structured questionnaire after obtaining informed consent for participation in the study and the dental extraction procedure. The data collected included the age, gender, address of residence, mode of transportation to the clinic, distance of residence to the clinic, history of previous hospital or clinic appointments, total household earning, type of employment, highest educational attainment, phone number of patient and that of at least two responsible adult relatives, treatment received, any intra- or post-operative complication, satisfaction at discharge, date of review of extraction site. Data on whether review appointments were kept or missed, if missed, reason for missing the appointment, and pattern of previous dental clinic attendance were also collected.

The ethical approval for the study was obtained from the Oyo state Ethical Review Committee. For the purpose of this study, pattern of dental clinic attendance (visiting status) was grouped into 3: regular attenders, in-trouble attenders, and non-attenders using the criteria adapted from Taiwo and Noah [14].

All the extraction procedures were done aseptically under local anesthesia. Tooth delivery was by intra-alveolar forceps extraction for fully erupted teeth and trans-alveolar extraction (surgical

Table 1: Sociodemographic variables

Variable	Patient attended review visit Yes (%) n = 162	 No (%) n = 118	 Total (%) n = 280	χ^2	p value
Gender					
Male	71 (43.8)	48 (40.7)	119 (42.5)	0.277	0.343
Female	91 (56.2)	70 (59.3)	161 (57.5)		
Level of education					
University	129 (79.6)	94 (79.7)	223 (79.6)	7.867	0.049
Secondary school	19 (11.7)	14 (11.9)	33 (11.8)		
Primary school	13 (8.0)	4 (3.4)	17 (6.1)		
Non formal	1 (0.7)	6 (5.0)	7 (2.5)		
Occupation					
Formal sector	65 (40.1)	51 (43.3)	116 (41.4)	1.750	0.417
Non- formal sector	50 (30.9)	41 (34.7)	91 (32.5)		
Unemployed	47 (29.0)	26 (22.0)	73 (26.1)		
Distance from the hospital					
<20 km	143 (88.3)	105 (88.9)	248 (88.6)	0.941	0.625
>20 km	12 (7.4)	6 (5.2)	18 (6.4)		
Outside Ibadan Metropolis	7 (4.3)	7 (5.9)	14 (5.0)		
Form of transportation					
Trekking distance	7 (4.3)	5 (4.2)	12 (4.3)	0.01	0.999
Private vehicle	63 (38.9)	46 (39.0)	109 (38.9)		
Commercial vehicle	92 (56.8)	67 (56.8)	159 (56.8)		
Number of vehicular transfers					
1	16 (9.9)	15 (12.7)	31 (11.0)	1.087	0.780
2	37 (22.8)	22 (18.6)	59 (21.1)		
>2	40 (24.7)	30 (25.4)	70 (25.0)		
Not applicable	69 (42.6)	51 (43.2)	120 (42.9)		
Total household income					
10,000 – 210,000	98 (60.5)	64 (54.2)	162 (57.9)	6.779	0.148
220,000 – 330,000	12 (7.4)	3 (0.3)	15 (5.3)		
>330,000	2 (1.2)	1 (0.1)	3 (1.1)		
None	23 (14.2)	19 (16.1)	42 (15.0)		
I don't want to tell	27 (16.7)	31 (26.3)	58 (20.7)		
Satisfaction with last treatment					
Yes	150 (92.6)	112 (94.9)	262 (93.6)	3.682	0.152
No	5 (3.1)	0 (0.0)	5 (2.8)		
No response	7 (4.3)	6 (5.1)	13 (4.6)		
Complaint during review visit					
Yes	57 (35.2)	0 (0.0)	57 (20.4)	280.0	0.0001
No	105 (64.8)	0 (0.0)	105 (37.5)		
Not applicable	0 (0.0)	118 (100.0)	118 (42.1)		

disimpaction) for impacted teeth. When the patient was certified fit for discharge, post extraction instructions and medications as per the unit protocol as well as a date for review of the extraction site were given to all patients, no reminders and cancellation system was provided for the appointment. At discharge, date of review was documented in the data form and in a diary in the clinic. The appointment schedule was checked every day to ascertain patients expected for review appointments.

Once a patient didn't turn up for the one week scheduled post extraction review appointment, patient or a responsible relative was contacted via phone call within 12-24hrs and at most one week of the missed

appointment to find out the reason for missing the appointment. If patient or relative could not be contacted by phone and physical visit was not feasible at most by a week after the missed appointment, the patient was excluded from the study.

All the data collected were then transferred to the computer for analysis using Statistical Package for Social Sciences version 19.0 (IBM SPSS Statistics Inc, Chicago, IL, USA). Categorical variables were tested using the Pearson's Chi-square test to examine the relationship between non-attendance and specific patients' characteristics. Variables achieving a p value of ≤ 0.05 were considered statistically significant.

Results

Two hundred and eighty patients comprising 119 males and 161 females (1:1.35) participated in the study. The mean (±SD) age was 43.3 ± 16.8 years with the commonest age group being 31 – 40 years (70, 25.0%). Majority of the participants (141, 52.9%) were below 40 years of age. Two hundred and twenty one (78.9%) participants stayed within Ibadan metropolis with 250 (88.6%) residing less than 20km from the hospital. 12 people were able to access care by trekking to the hospital while 109 (38.9%) came in a private vehicle. One hundred and fifty nine participants (57.1%) commuted in a public transport with 129 (80.69%) of them requiring more than one vehicle (Table 1).

Concerning socioeconomic status, 223 people had university/college degree while only 2.5% had no formal education. Conversely, 73 (26.1%) were unemployed while 116 (41.4%) and 91 (32.5%) work in the formal and non-formal sectors respectively.

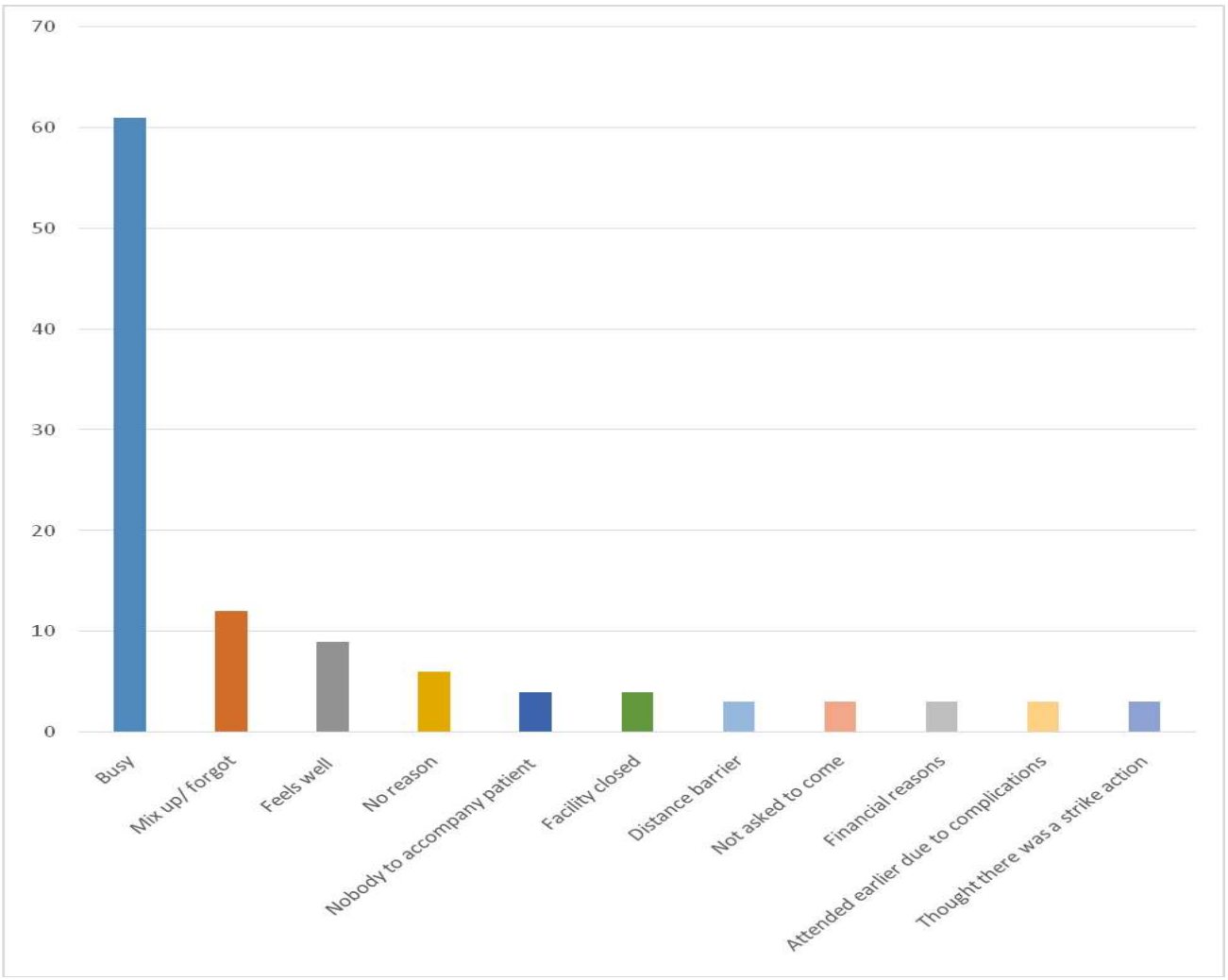


Fig 1. Reasons given for missing the post-operative review appointment

Twenty - five (8.9%) reported a monthly household income of less than ₦15,000 ($50) while only 3.6% earn above ₦300,000 ($800) per month (Table 1).

The commonest reason for attending the exodontia clinic was toothache (251 (89.8%)). Other reasons were broken tooth 16 (5.7%), mobile tooth 8 (2.9%) and prosthetic/orthodontic indications 5 (1.8%). In all, 162 (57.9%) attended the review appointment with 57 (35.2%) of them presenting with secondary complaints. One hundred and eighteen (42.1%) patients failed to attend the follow up appointment; main reasons given for non-attendance included "Being busy and forgetting appointment" (Fig. 1).

The presence of post-operative complaint ($p= 0.0001$) and the level of education ($p=0.049$) were the statistically significant factors predicting attendance at the review clinic appointments.

Discussion

This study showed that non-attendance of post extraction review appointment in our hospital was 42.1%. Various studies had reported non-attendance rates of 3% to 80% at scheduled review visit [15-17]. Previous studies reported a mean no-show prevalence estimation of 23.8%. The highest reported rate was in North America (27.1%) and the lowest in Europe (14.9%), while it was 24.3% in Asia [18,19]. The 42.1% non-attendance rate in this study is higher than the value obtained among dental attendees in the study of Lalloo *et al*. (35%) [20], George *et al*. (34.8%) [21] and Onyejeka *et al*. (27.7%) [22]. The lower rates of default in review attendance in these studies compared to our own figure could be due to differences in indications for clinic attendance, treatment offered and patients' characteristics.

Our study was conducted among patients that presented at oral surgery clinic for extraction mostly occasioned by pain while the other studies were conducted not just among patients visiting dental hospitals for exodontia but also included those attending for various other treatments including preventive, restorative and aesthetic treatments. Generally, it is known that patients attending dental services for cosmetic, restorative and preventive measures are more motivated to attend follow up review than our cohort of patients who are presenting for extraction mainly because of pain symptom. In addition, some patients in the study by Onyejeka received a formal reminder for the review appointment whereas no reminder was used for our patients in the current study. The non-attendance rate in this study is however similar to the figure of 43.8% reported among attendees of a dental training facility in India [21].

The findings of low attendance at the review clinic appointments in the current study and that from India may be an indication of less importance attached to oral healthcare and the oral health awareness level of the two study populations. Published work on the association between patient characteristics and pattern of attendance at scheduled review appointments have shown inconsistent findings [4,23]. Some studies have reported a positive correlation between non-attendance and male gender [11,24], female gender [21], low educational attainment and low socioeconomic factors [25,26], while some reported none [23,27]. With the exception of educational attainment, the present study yielded no statistically significant association between non-attendance and socio-demographic characteristics of patients similar to the findings in the study of Onyejeka *et al*. Transportation mode or distance of residence to the hospital also had no significant association to non-attendance in the present study. This seems to be in conflict with some previous reports who have reported a direct correlation between distance of travel to the dental facility and non-attendance [22,28].

The presence of a post-operative complaint and the educational level were the main factors with significant association in relation to attendance at the review clinic. This study demonstrated that the majority of the patients who attended for review after extraction were in-trouble attenders primarily because of ongoing complaint of post-operative pain. This similar finding was reported in our previous study [29]. Other authors have also reported similar finding that the majority of dental patients only visited the dentist when in pain and never bother to return for follow-up in most cases once the pain has been relieved [1,30]. The positive correlation between educational attainment and attendance at review visit in the present study concurs with the findings in some other studies that reported lower tendency to default among the people with higher educational attainment [5,21,31]. The most common reason given by respondents in the present study for non-attendance was being busy followed by forgetfulness. This has been similarly shown by other previous reports [17,21,22]. Other reasons for missing appointments reported in some studies were financial or transportation issues, feeling that the appointment was unimportant, inability to get time off from work, feeling too ill to attend, administrative errors, and long waiting times [32,33].

It must be noted that although the majority of our patients in this study were satisfied with the initial treatment but this satisfaction level did not translate into better attendance at the review clinic appointments.

Conclusion

Non-attendance at review visit following tooth extraction was high among the study population. Common reasons for non-attendance were being busy and mix-up in the date/forgetfulness. Of note is the fact that majority of the non-attendants contacted apologized that they couldn't attend with most expressing enthusiasm to attend if given another opportunity. Counselling and educating patients during the first visit or before the appointment, use of reminder system, operating evening and weekend dental services as well as giving patient choice of date should be considered as possible strategies for reducing non-attendance at review appointment following tooth extraction.

References

1. Gambhir RS, Brar P, Singh G, Sofat A and Kakar H. Utilization of dental care: An Indian outlook. Journal of Natural Science, Biology, and Medicine. 2013; 4(2): 292-297.
2. Ogunmuyiwa SA, Gbolahan OO, Olaosun AO and Sotannde AI. Orofacial clefts: Our experience in two suburban health facilities. Dentistry. 2013 [cited 2017 Jan 11]; 3: 1[about 4 p]. Available from: www.omicsonline.org
3. Pieper B and DiNardo E. Pearls for practice: reasons for missing appointments in an outpatient clinic for indigent adults. JAANP. 1998; 10: 359 – 364.
4. Ismail IA, Saeed HM and Al-Silwadi MF. Missed dental appointments in the United Arab Emirates.J Int Dent Med Res. 2011; 4: 132-138
5. Deyo RA and Inui TS. Dropouts and broken appointments: A literature review and agenda for future research. Medical Care. 1980; 18(11): 1146-1157.
6. Kendall C and Hailey BJ. The relative effectiveness of three reminder letters on making and keeping mammogram appointments. Behav Med. 1993; 19: 29S-34S.
7. Rust CT, Gallups NH, Clark WS, Jones DS and Wilcox WD. Patient appointment failures in pediatric resident continuity clinics. Arch PediatrAdolesc Med. 1995; 149(6): 693-695.
8. Murdock A, Rodgers C, Lindsay H and Tham TC. Why do patients not keep their appointments? Prospective study in a gastroenterology outpatient clinic. J R Soc Med. 2002; 13(6): 284–286.
9. Chung JW, Wong TK and Teung AC. Non-attendance at an orthopaedic and trauma specialist outpatient department of a regional hospital. J NursManag. 2004; 12: 362-367.
10. Clough D. Missed GP appointments cost up to £250k in just one month! 2018 Feb [cited 2019 Jan 10] Available from: http://www.fyldeandwyreccg.nhs.uk/missed-gp-appointments-cost-250k-just-one-month/.
11. Awartani F: Broken appointment behaviour in a dental school environment. J Contemp Dent Pract. 2003; 4:100-107
12. Van der Meer G, LoockJW.Why Patients Miss Follow-up Appointments: A Prospective Control-Matched Study. East Afr J Publ Health. 2008; 5(3): 154-156.
13. Shabbir A, Alzahrani M and Abu khalid A Why Do Patients Miss Dental Appointments in Eastern Province Military Hospitals, Kingdom of Saudi Arabia?.*Cureus*. 2018 March [cited 2019 Jan 10] 10(3): e2355 [12 pages]. Available from https://www.researchgate.net/publication/323924340_Why_Do_Patients_Miss_Dental_Appointments_in_Eastern_Province_Military_Hospitals_Kingdom_of_Saudi_Arabia
14. Taiwo JO and Noah M. Pattern of dental clinic attendance of registered diabetic patients in Ibadan. J Med Biomed Res. 2006; 5: 36-43.
15. Kheirkhah P, Feng Q, Travis LM, Tavakoli-Tabasi S and Sharafkhaneh A. Prevalence, predictors and economic consequences of no-shows. BMC Health Serv Res. 2016 [cited 2017 Jan 11]; 16: 13 [about 5 p]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4714455/
16. Akande MT and Abdulraheem SI. A study of defaulters in consultant paediatric, Medical and Surgical Outpatient Clinics at the University of Ilorin Teaching Hospital, Ilorin, Nigeria. The Tropical Journal of Health Sciences. 2005; 12: 31-34
17. AlSadhan AS. Frequency of missed and cancelled appointments in King Saud University orthodontic clinic. King Saud University Journal of Dental Sciences. 2013; 4: 77–80
18. Alyahya M, Hijazi HH and Nusairat FT. The Effects of Negative Reinforcement on Increasing Patient

Adherence to Appointments at King Abdullah University Hospital in Jordan. Inquiry. 2016 Jul [cited 2017 Jan 11]; 53 [about 6 p]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5798732/

19. Turkcan A, Nuti L, DeLaurentis PC, *et al*. No-show modeling for adult ambulatory clinics. Handbook of healthcare operations management. Springer; 2013.
20. Lalloo R and McDonald JM. Appointment attendance at a remote rural dental training facility in Australia. BMC Oral Health. 2013 Aug [cited 2017 Jan 11]; 13: 36 [8 p]. Available from: https://bmcoralhealth.biomedcentral.com/articles/10.1186/1472-6831-13-36
21. George AC, Hoshing A and Joshi NV. A study of the reasons for irregular dental attendance in a private dental college in a rural setup. Indian J Dent Res. 2007;18(2):78-81
22. Onyejaka NK, Emele IE and Eboh OF. Appointment Failure among Dental Patients Attending a Government Dental Centre in Enugu, Nigeria. Pesq Bras Odontoped ClinIntegr 2018 April [cited 2019 Feb 12], 18(1): e4004 [7 p] Accessed: Available from: https://www.researchgate.net/publication/324980899_Appointment_Failure_among_Dental_Patients_ Attending_a_Government_Dental_Centre_in_Enugu_Nigeria/citations.
23. Ng T H, How S H, Kuan Y C and Fauzi A R. Defaulters among lung cancer patients in a suburban district in a developing country. Ann Thorac Med. 2012; 7: 12-15
24. Skaret E, Raadal M, Kvale G and Berg E. Missed and cancelled appointments among 12-18-year-olds in the Norwegian Public Dental Service. Eur J Oral Sci. 1998; 106(6): 1006-1012.
25. Nguyen DL, De Jesus RS and Wieland ML. Missed appointments in resident continuity clinic: Patient characteristics and health care outcomes. Journal of Graduate Medical Education. 2011; 3(3): 350-355.
26. Deyo RA and Inui TS. Dropouts and broken appointments: a literature review and agenda for future research. Medical Care. 1980; 18:1146-1157.
27. Giunta D, Briatore A, Baum A, *et al*. Factors associated with nonattendance at clinical medicine scheduled outpatient appointments in a university general hospital. Patient Prefer Adherence. 2013; 7: 1163–1170.
28. Fernandez R, Atassi YSS and Fakiha KZ. Why Patients Miss Their Appointments – A Survey.Donnish Journal of Dentistry and Oral Hygiene. 2018; 4(2): 009-14.
29. Gbolahan OO, Fasola AO and Aladelusi TO. Attitude and Behavior to Oral Health of 456 Patients Who Presented for Tooth Extraction at 2 Health Facilities in Southwestern Nigeria. Journal of Patient Experience: 2018 July [cited 2019 Feb 12] [7 p]. Available from: https://journals.sagepub.com/doi/10.1177/2374373518788851
30. Adegbembo AO. Household utilization of dental services in Ibadan Nigeria. Community Dent Oral Epidemiol. 1994; 22: 338-339.
31. Johnson R, Horne B, Feltbower RG, Butler GE and Glaser AW. Hospital attendance patterns in long term survivors of cancer. Arch Dis Child. 2004;89:374-377
32. Moore CG, Wilson-Witherspoon P, Probst JC. Time and money: effects of no-shows at a family practice residency clinic. Fam Med. 2001; 33: 522–527.
33. Pieper B and DiNardo E. Pearls for practice: reasons for missing appointments in an outpatient clinic for indigent adults. JAANP. 1998; 10: 359–364.

Afr. J. Med. Med. Sci. (2020) **49,** 287-295

Anthropometry parameters in breast cancer patients at the University College Hospital Ibadan: A case-control study

AA Abdus-salam[1]. BO Ogunnorin[1], AA Olabumuyi[2] and AA Orekoya[2]

Departments of Radiation Oncology[1], College of Medicine, University of Ibadan and Radiation Oncology[2], University College Hospital, Ibadan, Nigeria

Abstract

*Background***:** Breast cancer is the commonest female malignancy in the world and in Nigeria. This burden of breast cancer requires preventive efforts directed at an at-risk population. Anthropometry has previously been identified as an important breast cancer risk factor, globally.

*Objective***:** To investigate the association between anthropometry and breast cancer in the University College Hospital (UCH), Ibadan.

Methods: The anthropometric parameters (weight, height, BMI, waist circumference (WC), hip circumference (HC), waist-hip ratio of 70 breast cancer patients and 71 age and gender matched controls were compared.

Results: The cases of breast cancer had statistically significantly lower mean weight, BMI, WC and HC compared to their controls. Low BMI was independently associated with breast cancer on multiple logistic regression with an OR 0.881 ($P < 0.001$)

Conclusion: Due to the advanced stages at which breast cancer patients present to the UCH, Ibadan, the anthropometric indices of the cases were significantly lower than their controls. This further indicates the need for advocacy to encourage patients to present early. In addition, larger cohort or longitudinal studies need to be done in Nigeria to further define the relationship between anthropometry and breast cancer.

Keywords: *Risk Factor, Breast Cancer, Anthropometric Parameters*

Résumé

Contexte **:** Le cancer du sein est la tumeur maligne féminine la plus courante au monde et au Nigéria. Ce fardeau du cancer du sein nécessite des efforts de prévention visant une population à risque. L'anthropométrie a déjà été identifiée comme un facteur de risque de cancer du sein important, à l'échelle mondiale

Objectif **:** Pour étudier l'association entre l'anthropométrie et le cancer du sein au Collège Hospitalier Universitaire (CHU), Ibadan.

Méthodes: Les paramètres anthropométriques (poids, taille, IMC, tour de taille (TT), tour de hanche (TH), rapport taille-hanche de 70 patientes atteintes d'un cancer du sein et 71 témoins appariés selon l'âge et le sexe ont été comparés.

Résultats: Les cas de cancer du sein avaient un poids moyen, un IMC, un TT et un TH significativement plus bas que leurs témoins. Un faible IMC était indépendamment associé au cancer du sein lors d'une régression logistique multiple avec un OR 0,881 ($P <0,001$)

Conclusion: En raison des stades avancés auxquels les patientes atteintes d'un cancer du sein se présentent au CHU, Ibadan, les indices anthropométriques des cas étaient significativement inférieurs à leurs témoins. Cela indique en outre la nécessité de plaidoyer pour encourager les patientes à se présenter tôt. En outre, des études de cohorte ou longitudinales plus amples doivent être effectuées au Nigéria pour définir plus précisément la relation entre l'anthropométrie et le cancer du sein.

Mots - clés : *facteur de risque, cancer du sein, paramètres anthropométriques*

Introduction

Breast cancer is the commonest female malignancy in the world. It accounted for over 600,000 deaths in women in 2018, making breast cancer, the leading cause of female cancer mortalities worldwide [1]. In Nigeria, breast cancer is also the commonest female malignancy. It accounted for close to 30000 cases in 2018 resulting in an age standardized incidence rate of 41.7/100000.[1] Close to half of the incidences in Nigeria result in mortalities, as breast cancer was estimated to be responsible for 11564 deaths in 2018 with an age standardized mortality rate of 18.8/100000 [1].

Unlike the developed countries, the burden of cancer in Nigeria and other developing nations is

Correspondence: Dr. A.A. Olabumuyi, Department of Radiation Oncology, University College Hospital, Ibadan, Nigeria. E-mail: niyi.oogaa@gmail.com

estimated to increase for many years to come [2]. This is mainly due to limited specialist oncology personnel and limited oncology facilities.

This disease burden of cancer in Nigeria requires efforts directed to treat and cure the disease in patients diagnosed with breast cancer, and also, to prevent breast cancer in Nigerians. This is achievable by screening the at-risk populations and identification of modifiable risk factors.

Currently, mammography screening is recommended by the United States' Preventive Services Task Force. We are yet to have a national mammography screening program in the country. Yet, mammography has limitations which include false positives, over diagnosis, undetected cancers and risks associated with exposure to ionizing radiation. Biomarkers such as CA27.29 and CA153 are being investigated for use as a screening method. However, they are not yet in use in Nigeria and they are not recommended for screening for now.

An understanding of the risk factors is key to preventing cancer. The modifiable risk factors which have been investigated and proven to increase one's risk of breast cancer include reproductive factors such as nulliparity, late age at first pregnancy and low duration for breast feeding. Other modifiable risk factors include exposure to ionising radiation, cigarette smoking and alcohol.

Another related group of modifiable risk factors include diet rich in red meat, processed meat and fat; sedentary lifestyle and anthropometric indices such as weight, height, body mass index (BMI), waist circumference, hip circumference and waist-to-hip ratio (WHR). The Cancer Prevention Study II cohort found that women with a higher BMI had a higher risk of dying from breast cancer [3]. A pooled analysis of prospective studies found the risk of breast cancer to be 30% higher in postmenopausal women with a BMI over 31kg/m2 compared with women with a BMI of 20kg/m2 or less [4]. Conversely, studies show that in premenopausal women elevated BMI and indices of adiposity are associated with a reduced risk of breast cancer [5-7].

WHR and waist circumference are indices of central obesity. Literature shows that higher WHR and waist circumference (WC) increased the risk of breast cancer in both premenopausal and postmenopausal women [8,9]. In a meta-analysis by Connolly *et al*, the summarized risk for the highest partition of WHR compared to the lowest for all studies analysed was 1.62 (95% CI = 1.28-2.04) [9]. In spite of these general trends, there are ethnic variations and studies from Nigeria tend to differ a bit. In the study by Ogundiran *et al*, an inverse relationship was found between breast cancer risk and BMI. However the study noted a positive association between height and breast cancer risk [10]. Another case-control study by Adebamowo *et al* revealed cases were most likely to be tall and obese than controls. But, after adjusting for confounders, BMI was not significantly associated with breast cancer risk [11]. Regarding WHR, a study by Adebamowo *et al* reported a statistically significant increased risk of postmenopausal breast cancer in women with WHR > 0.85 compared to those with WHR < 0.77. However, the likelihood ratio test for trend was insignificant (P=0.07) [12]. These variations in previous studies merit additional studies to confirm the relationship between anthropometry and the risk of breast cancer in Nigeria.

This study was thus undertaken to investigate the effect of anthropometry on breast cancer risk among patients in the University College Hospital, Ibadan.

Materials and methods

The study was conducted at the University College Hospital (UCH), Ibadan. The case group comprised of 70 patients with newly diagnosed breast cancer recruited at the Radiation Oncology and Surgical Oncology clinics, UCH between August 2016 and January 2017. The control group consisted of 71 age-matched non-breast cancer patients recruited at the Family Medicine Clinic and Chief Tony Anenih Geriatric Centre Outpatient Clinic, UCH between February 2017 and May 2017.

The inclusion criteria for the cases were patient with histological diagnosed breast cancer who had no previous cancer treatment (mastectomy, chemotherapy, radiation therapy, hormonal therapy). Patients with uncontrolled chronic comorbidities such as hypertension and diabetes mellitus, hypo/hyperthyroidism; patients on drugs known to affect lipid metabolism (HMG CoA reductase inhibitors (statins), bile acid sequestrants, nicotinic acid, fibric acids, hormone replacement therapy and other hormonal agents); patients with poor performance status (ECOG $\geq$ 3); patients with obvious nutritional impairment (severe mucositis, naso-gastric tube feeding, or parenteral feeding) were all excluded. The inclusion criterion for controls was the patient's gender and age (±1year) matches a case. The exclusion criteria

applied to controls were: Patients with breast disease; patients with uncontrolled chronic comorbidities such as hypertension and diabetes mellitus, hypo/hyperthyroidism, patients on drugs known to affect lipid metabolism (HMG CoA reductase inhibitors (statins), bile acid sequestrants, nicotinic acid, fibric acids, hormone replacement therapy and other hormonal agents), patients with poor performance status (ECOG $\geq$ 3), patients with obvious nutritional impairment (severe mucositis, naso-gastric tube feeding, or parenteral feeding).

The study design was (cross-sectional) case-control. Anthropometric indices of body fat distribution (height, weight, BMI, waist circumference, hip circumference, and waist-to-hip ratio) were measured in the cases and controls.

A questionnaire was used to retrieve information including sociodemographic data, clinical data and the anthropometric indices. Waist circumference was measured at the midpoint between the iliac crest and the lower ribs while the hip circumferences were measured at the largest circumference at the hip. The waist-to-hip ratio (WHR) was calculated by dividing the circumferences at the waist by the circumferences at the hip.

The study was approved by the joint ethical review committee of the University of Ibadan/University College Hospital, Ibadan (approval number: UI/EC/15/0460).

Table 1: Cross tabulation of Demographic parameters with disease status of study population

Variable	Disease Status				P Value
	Case		Control		
	N	%‘	N	%	
Marital status (N)	70		71		0.126
Not currently married	25	35.7	17	23.9	
Currently married	45	64.3	54	76.1	
Religion (N)	70		71		0.670
Christianity	49	70.0	52	73.2	
Islam	21	30.0	19	26.8	
Level of Education (N)	69		71		0.204
< Secondary	22	31.9	30	42.3	
$\geq$ Secondary	47	68.1	41	57.7	
Occupation (N)	70		66		0.676
Professional/Civil servant	21	30.0	22	33.3	
Artisan/Trader/Others**	49	70.0	44	66.7	
Employment status (N)	70		71		0.047^
Employed	48	68.6	59	83.1	
Unemployed	15	21.4	5	7.0	
Retired	7	10.0	7	9.9	
Ethnicity (N)	70		71		0.786
Yoruba	59	84.3	61	85.9	
Others*	11	15.7	10	14.1	

^ *Statistically significant at 0.05*
** *others include: Peace Corps officer, Librarian, Farmer and House-wife*
* *other includes: Igbo, Hausa, Urhobo, Igala and Mandingo*

Statistical analysis

The IBM SPSS v21 was used to analyse the data. Descriptive statistics (means and standard deviation for quantitative variables and frequencies and percentages for qualitative) were presented and appropriate tables and charts were used. The t-test was used to compare the mean levels of the quantitative outcomes between cases and controls.

Multiple logistic regression analysis was done on the significant variables to further adjust for confounding variables in the comparison of outcomes

between cases and controls. Level of significance was set at 5%.

Results

All the cases were women with age-range of 23 to 82years and with a mean age of 52.1±12.0years. While the age-range and mean age of the age-matched apparently healthy controls was 24 to 83years and 52.5±12.6years respectively. The difference between the cases and controls with regards to ethnicity, marital status, religion, education and occupation was not statistically significant. Over 83% of the controls were employed as opposed to 68.6% of cases, this difference was statistically significant (P = 0.047) (table 1).

was not statistically significant. None of the participants in the study had a history of smoking. The cases had significantly higher systolic and diastolic blood pressures (table 3).

The weights of the cases were statistically significantly lower (P = 0.002). This was also the relationship among the postmenopausal women among whom the mean weight was 66.7Kg compared to 77.1Kg in the controls (P = 0.003). The premenopausal cases also had lower mean weights. However, the difference was not statistically significant (P = 0.160) (table 4). The average height in the two groups was the same. Therefore, the cases had a lower mean BMI compared to controls (P =

Table 2: Reproductive factors associated with the disease status of study population

Variable	Disease status				P Value
	Case		Control		
	N	%	N	%	
Menarche (N)	70		71		0.795
≤13y	13	18.6	12	16.9	
>13y	57	81.4	59	83.1	
Age at 1st confinement (N)	60		62		0.817
≤30y	54	90.0	55	88.7	
>30y	6	10.0	7	11.3	
Duration of Breastfeeding (N)	62		58		0.186
≤1y	23	37.1	15	25.9	
>1y	39	62.9	43	74.1	
Menopause (N)	42		34		1.000*
≤55y	38	90.5	31	91.2	
>55y	4	9.5	3	8.8	
Parity (N)	70		69		0.713
0-2	19	27.2	16	23.2	
3-5	36	51.4	40	58.0	
Greater or Equals 6	15	21.4	13	18.8	

** Fisher's exact value reported*

A higher proportion of cases had earlier menarche and later menopause. But these differences were not statistically significant. Similarly, a non-significant higher proportion of cases breastfed for a shorter duration compared to controls (table 2).

There was no significant difference between the cases and controls with regards to family history of breast cancer and presence or absence of comorbidities. A higher proportion of the cases were either currently taking alcohol or had taken in the past (14.5%) compared to 5.6% of controls. This difference

0.001). There was no significant difference in the BMI among the premenopausal women. The postmenopausal cases also had lower mean BMIs (25.0Kg/m^2) compared to postmenopausal controls (29.5Kg/m^2), this difference was statistically significant (P = 0.05) (table 4). The pattern with weight and BMI was also expressed in waist circumference with cases having lower mean values but only in the entire sample and in the postmenopausal women were the differences statistically significant (P = 0.001). The hip

Table 3: Medical and social factors associated with disease status of the study population

Variable	Disease status		P Value
	Case (%)	Control (%)	
Family History (N)	70	71	0.275*
No	92.9	97.2	
Yes	7.1	2.8	
Comorbidities (N)	70	71	0.178
Present	18.6	28.2	
Absent	81.4	71.8	
Systolic BP (mmHg)*	137.1±25.0	129.7±16.4	0.044^
Diastolic BP (mmHg)*	85.4±13.0	79.1±10.6	0.002^
Alcohol history (N)	62	71	0.141*
Never used	85.5	94.4	
Current/Past users	14.5	5.6	
Tobacco history (N)	70	71	NA
No	100.0	100.0	
Yes	0.0	0.0	

** Fisher's exact value reported*
^ statistically significant at 0.05
NA Not applicable

Table 4: Comparing mean values of anthropometric indices in cases and controls

Variable	Menopausal status	Case		Control		P
		N	$\bar{X}$±SD	N	±SD	
Weight (Kg)	Premenopausal	28	68.2±17.0	37	74.9±20.0	0.160
	Postmenopausal	42	66.7±14.8	34	77.1±13.9	0.003^
	Both	70	67.3±15.6	71	76.0±17.3	0.002^
Height (m)	Premenopausal	28	1.6±0.1	37	1.6±0.1	0.309
	Postmenopausal	42	1.6±0.1	34	1.6±0.1	0.376
	Both	70	1.6±0.1	71	1.6±0.1	0.218
BMI (Kg/m^2)	Premenopausal	28	25.3±6.2	37	28.0±6.5	0.102
	Postmenopausal	42	25.0±5.2	34	29.5±6.2	0.001^
	Both	70	25.1±5.6	71	28.7±6.4	0.001^
WC (cm)	Premenopausal	28	85.3±13.0	37	91.8±16.0	0.083
	Postmenopausal	42	88.5±11.8	34	97.8±12.8	0.001^
	Both	70	87.2±12.3	71	94.6±14.7	0.001^
HC (cm)	Premenopausal	28	98.4±11.3	37	106.3±11.5	0.007^
	Postmenopausal	42	100.8±10.3	34	1.08.9±22.5	0.039^
	Both	70	99.8±10.7	71	107.6±17.5	0.002^
WHR	Premenopausal	28	0.9±0.1	37	0.9±0.1	0.833
	Postmenopausal	42	0.9±0.1	34	0.9±0.3	0.191
	Both	70	0.9±0.2	71	0.9±0.2	0.369

^ Statistically significant at 0.05

circumferences of the entire participants, the postmenopausal and the premenopausal women were significantly lower among the cases ($P < 0.005$). However, the cases and controls in the entire sample

Table 5: Logistic Regress of employment status, systolic BP, diastolic BP and BMI

Variable	Model1				Model2				Model3			
	P Value	OR	Confidence level of OR		P Value	OR	Confidence level of OR		P Value	OR	Confidence level of OR	
			Lower	Higher			Lower	Higher			Lower	Higher
Employment status (N)												
Employed		1.000				1.000				1.000		
Unemployed	0.021^	3.609	1.210	10.764	0.049^	3.086	1.007	9.464	0.097	2.740	0.835	8.994
Retired	0.656	1.289	0.422	3.941	0.926	1.058	0.321	3.493	0.711	1.264	0.367	4.354
Systolic BP					0.653	0.994	0.969	1.020	0.926	0.999	0.971	1.027
Diastolic BP					0.029^	1.054	1.005	1.104	0.036^	1.054	1.004	1.108
BMI									<0.001^	0.881	0.822	0.944
Model X^2		5.966, df 2, 0.051				14.157, df 4, 0.007				28.932, df 5, <0.001		
Nagelkerke R^2		0.057				0.132				0.256		

^ *Statistically significant at 0.05*

and in both the postmenopausal and premenopausal divisions had fairly similar mean WHR's (table 4).

Table 5 shows the results of stepwise logistic regression models used to analyse the risk/association of variables which were hitherto significant on bivariate analysis (employment status, systolic blood pressure, diastolic blood pressure and BMI [representing anthropometry]). This was to confirm the independence of the association between anthropometry (BMI) and breast cancer. Model 3 indicates that elevated diastolic blood pressure was an independent associated factor for breast cancer (P = 0.036). With an odds ratio (OR) of 1.054, every 1mmHg increased the likelihood of breast cancer by 5.4%. In the model, we used BMI to represent anthropometry as they all had similar trend on bivariate analysis. Low BMI was independently associated with breast cancer (P < 0.001). The OR of 0.881 indicates every 1Kg/m2 increase in BMI reduced the likelihood of breast cancer by 11.9%. The model also hinted at the fact that the association between unemployment and breast cancer was confounded by low BMI as it lost its statistical significance in the model.

Discussion

This study was primarily conducted to observe the correlation of anthropometric parameters with breast cancer. This study demonstrated that breast cancer remains a disease of middle and old age. The mean age in the study was about 52years. There was a significantly higher proportion of unemployment among the cases of breast cancer compared to the controls. This could be dismissed as a coincidence. However, literature shows that a diagnosis of cancer and/or the toll of cancer have a negative impact on employment. A study by Park et al noted that cancer patients in Korea were more likely to lose their jobs and less likely to get re-employed compared to those who are not afflicted with the disease.[13] However, the association between breast cancer and unemployment merits further investigation, as it did not remain an independent risk factor upon logistic regression indicating that there may be relevant confounders such as BMI.

The mean systolic and diastolic blood pressure values were found to be statistically significantly higher among the cases. Yet, the values were within the normal limits for both cases and controls. The implication of a diagnosis of cancer among the newly diagnosed patients may have led to anxieties featured by this relatively higher blood pressure among the cases.

This study showed an inverse relationship between most of the anthropometric indices and breast cancer, which might be explained by the late stage at which the patients present in the University College Hospital, Ibadan, and other centres in Nigeria. This is an interesting departure from several studies which had shown a direct association between anthropometric indices and breast cancer risk [7,14]. However, the findings are in keeping with some similar studies conducted in this environment [10].

The cases and controls had the same mean height. Previous studies, including the ones done in Nigeria such as reported by Ogundiran et al and Adebamowo et al indicate tall height to be a risk factor for breast cancer [10,11].

This study revealed a statistically significant higher weight and BMI in controls compared to cases. This pattern is particularly significant among the postmenopausal women in this study (P value = 0.001). Among the premenopausal women, there was a non-significant higher mean BMI in the controls. Low BMI was also proven to be an independent associated factor of breast cancer with logistic regression. Cases with low BMI compared to controls are not in keeping with findings in literature, globally. Only in premenopausal breast cancer was this noted. This is explained by the fact that premenopausal obesity is associated with anovulatory menstrual cycles that result in low serum oestrogen levels [4,14]. However, previous studies in our environment, particularly the studies done in our centre are at variance with global findings. The study by Adebamowo *et al* showed no significant association [11]. The study by Ogundiran *et al* revealed an inverse association between BMI and breast cancer indicating low BMI to be associated with breast cancer (P-trend 0.009) [10].

The controls in this study had significantly higher mean waist and hip circumferences than cases. This finding persisted significantly among the postmenopausal women. In the premenopausal women, controls also had higher mean waist and hip circumferences, but only the hip circumference was significant. Amadou et al conducted a detailed meta-analysis which found a significant positive association between WHR and breast cancer. Their study however showed significant heterogeneity between the different studies, also the relationship exists more among Asians than other ethnic groups [7]. Other studies have also shown an association between waist circumferences and WHR with breast cancer among Asians [7,15,16].

However, another study by Amadou *et al* among Mexican women revealed a significantly inverse association between waist circumference and WHR with breast cancer [17]. Another study from the Iowa Women's Health Study reported no association between waist circumference and WHR with breast cancer [18]. The fact that literature has shown a varying relationship based on ethnicity warrants a look into African studies. A study by Adebamowo showed a significant positive association between higher WHR and postmenopausal breast cancer but no association in premenopausal women.[12] In another study among African Americans by Hall *et al*, a positive association was found between WHR and premenopausal breast cancer (RR = 2.50; 95% CI: 1.1- 5.67; Ptrend < 0.005) [19].

Even though there was an inverse relationship between BMI and premenopausal breast cancer in this study, it is unlikely that the same reason for the relationship in global studies (anovulatory menstrual cycles) obtains in this study. For one, the inverse association between BMI and breast cancer among the premenopausal women in this study was not significant. Furthermore, if it were the anovulatory theory that was responsible for the premenopausal inverse risk, the association in the postmenopausal women should have flipped into a direct risk.

The likely hypothesis for this inverse relationship between anthropometry and breast cancer would be an explanation peculiar to our environment. In this study the cases of breast cancer were more likely to be unemployed, and would more likely present in advanced stages. This implies that patients with breast cancer in our environment present at stages where the wasting effect of breast cancer sets in or is already in play. Additionally, the socioeconomic status of patients with breast cancer is relatively lower, as they are usually unemployed. In Nigeria, the ratio of oncological centres to citizen is abysmally low, as alluded to in the introduction. As such, patients need to travel from distant regions of the country to seek oncological care. The living conditions of most of the patients that travel from distant regions are usually suboptimal. The inverse relationship between BMI, WC and HC and breast cancer is thus likely due to the socioeconomic status (impacted by unemployment) and the advanced stage of presentation.

Limitations

This study was designed with objectives to investigate the relationship between (mean values of) anthropometry and breast cancer. With this study, categorical analyses based on WHO cut-off points for BMI were not done.

This study is cross-sectional by design. As such, findings noted were those seen in the participants of the study on the day they were recruited. With this type of study, a lot of assumptions have to be made.

The controls used were apparently healthy patients of the family medicine department and Chief Tony Anenih Geriatric Centre clinics. It was ascertained that the controls recruited had no clinical evidence of breast cancer or complaints of any other breast pathology. However, mammography studies were not done in them. This implies a remote possibility of a control having a yet to be discovered early breast cancer.

Recommendations

This study raises scientific questions that need to be investigated. The inverse relationship between anthropometry and breast cancer in our environment needs to be further investigated. To achieve this, larger, better funded and more carefully conducted studies need to be done. It is not just enough to have a larger sample size. Though this would help to analyse by categories such as group staging, T-stage and other cut-off points. It would be desirable to have cohort studies, longitudinal studies and prospective studies to investigate these possible associations. It is only with such studies that risk factors can be definitively deduced. The more centres across the nation or West African region involved with these proposed studies, the more elaborate the conclusions that can be drawn.

The significant association between cases of breast cancer and unemployment is worrisome. It further justifies breast cancer awareness programs, routine mammography and even risk factor studies such as this. The aim is to identify the cancer early and for prompt and adequate treatment. This would enable the patients to get rehabilitated readily and keep their jobs. A national intervention to ensure cancer patients can keep their jobs for as long as their health allows, and are not discriminated against for employment would be welcome.

The elevated systolic and diastolic blood pressures in the cases of breast cancer could be a sign of anxiety. Counselling sessions/clinics with attending clinical psycho-oncologists are helpful in addressing the anxieties cancer patients have.

References

1. Cancer today, http://gco.iarc.fr/today/home (accessed 25 November 2018).
2. Vineis P and Wild CP. Global cancer patterns: causes and prevention. The Lancet 2014; 383: 549–557.
3. Calle EE, Rodriguez C, Walker-Thurmond K, *et al.* Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. New England Journal of Medicine 2003; 348: 1625–1638.
4. Van den Brandt PA, Spiegelman D, Yaun S-S, *et al*. Pooled analysis of prospective cohort studies on height, weight, and breast cancer risk. American journal of epidemiology 2000; 152: 514–527.
5. Baer HJ, Tworoger SS, Hankinson SE, *et al.* Body fatness at young ages and risk of breast cancer throughout life. American journal of epidemiology 2010; 171: 1183–1194.
6. Feigelson HS, Jonas CR, Teras LR, *et al*. Weight gain, body mass index, hormone replacement therapy, and postmenopausal breast cancer in a large prospective study. Cancer Epidemiology Biomarkers & Prevention 2004; 13: 220–224.
7. Amadou A, Hainaut P and Romieu I. Role of Obesity in the Risk of Breast Cancer: Lessons from Anthropometry. Journal of Oncology 2013; 2013: 1–19.
8. Harvie M, Hooper L and Howell AH. Central obesity and breast cancer risk: a systematic review. Obesity reviews 2003; 4: 157–173.
9. Connolly BS, Barnett C, Vogt KN, *et al*. A Meta-Analysis of Published Literature on Waist-to-Hip Ratio and Risk of Breast Cancer. Nutrition and Cancer 2002; 44: 127–138.
10. Ogundiran TO, Huo D, Adenipekun A, *et al*. Case-control study of body size and breast cancer risk in Nigerian women. American journal of epidemiology 2010; 172: 682–690.
11. Adebamowo CA, Ogundiran TO, Adenipekun AA, *et al*. Obesity and height in urban Nigerian women with breast cancer. Annals of epidemiology 2003; 13: 455–461.
12. Adebamowo CA, Ogundiran TO, Adenipekun AA, *et al*. Waist-hip ratio and breast cancer risk in urbanized Nigerian women. Breast Cancer *Res* 2003; 5: R18–R24.
13. Park J-H, Park J-H and Kim S-G. Effect of cancer diagnosis on patient employment status: a nationwide longitudinal study in Korea. Psychooncology 2009; 18: 691–699.
14. Renehan AG, Tyson M, Egger M, *et al.* Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. The Lancet 2008; 371: 569–578.
15. Shin A, Matthews CE, Shu X, *et al.* Joint effects of body size, energy intake, and physical activity on breast cancer risk. Breast Cancer Research and Treatment 2009; 113: 153–61.
16. Ng E-H, Gao F, Ji C-Y, *et al.* Risk factors for breast carcinoma in Singaporean Chinese women. Cancer 1997; 80: 725–731.
17. Amadou A, Torres Mejia G, Fagherazzi G, *et al.* Anthropometry, Silhouette Trajectory, and Risk of Breast Cancer in Mexican Women. American Journal of Preventive Medicine 2014; 46: S52–S64.
18. Sellers TA, Davis J, Cerhan JR, *et al*. Interaction of Waist/Hip Ratio and Family History on the Risk of Hormone Receptor-defined Breast Cancer in a Prospective Study of Postmenopausal Women. Am J Epidemiol 2002; 155: 225–233.
19. Hall IJ, Newman B, Millikan RC, *et al*. Body Size and Breast Cancer Risk in Black Women and White Women The Carolina Breast Cancer Study. Am J Epidemiol 2000; 151: 754–764.

Afr. J. Med. Med. Sci. (2020) **49,** 189-200

Controlling behaviour: Experience of women in Ibadan, Southwest Nigeria

MO Balogun[1], FI Fawole[2] and ET Owoaje[1]

Departments of Community Medicine[1] and Epidemiology and Medical Statistics[2], College of Medicine, University of Ibadan, Ibadan, Nigeria

Abstract

Background: The traditional Nigerian society is patriarchal and men use control tactics such as isolation and intimidation to maintain power over women. Controlling behaviour is a prevalent type of Intimate Partner Violence (IPV) among women. Little is known about the prevalence of controlling behavior in Nigeria. Studies on women's experiences of IPV in Nigeria have focused mainly on physical and sexual forms of violence, while experience of controlling behaviours has remained largely un-researched. The purpose of the study was to determine prevalence of the different forms of controlling behaviour and identify associated factors among women in Ibadan, Southwest Nigeria.

Methods: Using a cross-sectional community-based study design, a multistage sampling method was used to select 600 women aged between 15 and 49 years. A pretested semi-structured questionnaire was then used to obtain information on sociodemographic characteristics of respondents and their partners and experience of controlling behaviour

Results: The prevalence of controlling behaviour was 49.5% and the most common form was partner insisting on knowing where respondents were at all times (34.8%). Respondents in relationships for more than 10years (OR: 2.9; 95% CI: 1.6-5.2), who experienced psychological (OR: 1.8; 95% CI: 1.04-3.0) and physical violence (OR: 1.9; 95% CI: 1.1-3.4) were more likely to have partners who perpetrated controlling behaviour. Partners who had been involved in physical fights were more likely to experience all forms of controlling behaviour.

Conclusion: The prevalence of experience of controlling behaviour is high among women in Ibadan, Southwest Nigeria and the most common form of controlling behaviour experienced was partner insisting on knowing where respondents were at all times. Controlling behavior was also associated with all forms of violence including physical, psychological and sexual violence by male partners.

Correspondence: Dr. M.O. Balogun, Department of Community Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: mobalogun2004@yahoo.com

Keywords: *Controlling behaviour, prevalence psychological violence, southwest Nigeria*

Résumé

Contexte : La société nigériane traditionnelle est patriarcale et les hommes utilisent des tactiques de contrôle telles que l'isolement et l'intimidation pour maintenir le pouvoir sur les femmes. Le contrôle du comportement est un type répandu de violence entre partenaires intimes (VPI) chez les femmes. On sait peu de choses sur la prévalence du contrôle des comportements au Nigéria. Les études sur les expériences des femmes en matière de VPI au Nigéria se sont principalement concentrées sur les formes de violence physique et sexuelle, tandis que l'expérience des comportements de contrôle est restée largement non documentée. Le but de l'étude était de déterminer la prévalence des différentes formes de contrôle du comportement et d'identifier les facteurs associés chez les femmes à Ibadan, au sud-ouest du Nigéria.

Méthodes: En utilisant un plan d'étude transversal à base communautaire, une méthode d'échantillonnage à plusieurs degrés a été utilisée pour sélectionner 600 femmes âgées de 15 à 49 ans. Un questionnaire semi-structuré prétesté a ensuite été utilisé pour obtenir des informations sur les caractéristiques sociodémographiques des répondants et de leurs partenaires et sur l'expérience de contrôle de comportement.

Résultats: La prévalence du contrôle de comportement était de 49,5% et la forme la plus courante était le partenaire insistant pour savoir où se trouvaient les répondantes à tout moment (34,8%). Les répondantes en relation depuis plus de 10 ans (OR: 2,9; IC 95%: 1,6-5,2), qui ont subi des violences psychologiques (OR: 1,8; IC 95%: 1,04-3,0) et des violences physiques (OR: 1,9; IC 95%: 1,1 -3,4) étaient plus susceptibles d'avoir des partenaires qui avaient adopté un contrôle de comportement. Les partenaires qui avaient été impliqués dans des combats physiques étaient plus susceptibles d'éprouver toutes les formes de contrôle de comportement.

Conclusion: La prévalence de l'expérience du contrôle de comportement est élevée chez les femmes à Ibadan, dans le sud-ouest du Nigéria et la forme la plus courante de contrôle du comportement était le partenaire insistant pour savoir où se trouvaient les répondantes à tout moment. Le contrôle du comportement était également associé à toutes les formes de violence, y

compris la violence physique, psychologique et sexuelle exercée par des partenaires masculins.

Mots-clés: *Contrôle de comportement, prévalence de la violence psychologique, sud-ouest du Nigéria*

Introduction

Violence against women, particularly intimate partner violence and sexual violence against women, are major public health problems and violations of women's human rights [1]. Intimate partner violence (IPV) can result in physical, mental, sexual, reproductive health and other health problems such as HIV, STIs, depression and alcohol use disorders [2]. Women exposed to IPV are 1.5 times more likely to acquire HIV and contract sexually transmitted infections (STIs) and twice as likely to experience depression and alcohol use disorders [2]. Globally, 42% of women who experienced physical or sexual violence were injured and 38% of all murders of women were committed by their intimate partners [2].

The WHO reported that the global prevalence of physical and/or sexual IPV among all ever-partnered women was 30.0% [2]. The prevalence was highest in the WHO African, Eastern Mediterranean and South-E ast Asia Regions, where approximately 37% of ever-partnered women reported having experienced physical and/or sexual IPV at some point in their lives [2].

Physical and sexual violence is usually accompanied by controlling behaviours, and studies have shown that controlling behavior is significantly associated with higher likelihood of physical violence and sexual violence [3,4].

Globally, researchers have reported women's experience of controlling behavior as being a major health problem [3]. Barkho *et al* reported that 93% of Iraqi immigrant women in Metro Detroit experienced controlling behaviors [5]. Women in Sweden [6], rural Vietnam [7] and Sri Lanka [8] reported prevalences of 41%, 32.1% and 30% respectively. Kapiga *et al*. reported that controlling behaviour was the most prevalent type of IPV among women in Mwanza, Tanzania with 82% experiencing it in their lifetime [9].

Little is known about the prevalence of controlling behavior in Nigeria. Studies on women's experiences IPV in Nigeria have focused mainly on physical and sexual forms of violence and not on experience of controlling behaviours. The traditional Nigerian society is patriarchal; this male-dominated family structure and social order encourages men to dominate and control their partners [10]. In Nigeria very few studies have reported the prevalence and risk factors of experience of controlling behaviours [11,10]. The few available studies found that controlling behaviour was the most common form of IPV experienced by women in Southwestern Nigeria [12]. Hence there is need for empirical data on this form of IPV to guide the development of evidence based prevention strategies. In view of this, this study aims to determine prevalence of the different forms of controlling behaviour and identify factors that make women vulnerable to this form of IPV.

Methodology

Study Area

The study was a community-based cross-sectional study conducted in selected urban and rural communities in Akinyele Government Area (LGA) in Ibadan, Oyo State. Oyo State is one of the 36 states of Nigeria and is located in the Southwestern region of the country. Akinyele Local Government Area (LGA) is a semi-urban LGA, with an estimated 342,626 residents [13]. The majority of the residents are of Yoruba ethnicity. The residents in the urban areas are traders and artisans, while residents of the larger and many rural settlements are farmers [13]. The study population consisted of women aged 15 - 49 years residing in Akinyele LGA.

Study design

The study was a community-based cross-sectional study

Sample size determination

The minimum number of women necessary to study was determined to be 596 using an estimate of the prevalence of IPV obtained from a Nigerian study which reported a prevalence of 31% [14] and adjusting for non-response of 5% and design effect of 1.5.

Sampling technique

A multistage sampling technique was used. The four levels of selection were: ward, community, enumeration area and household. In stage 1 the LGA which has 12 wards was stratified into two groups based on their development into ten rural and two urban wards. In stage 2, one rural and urban ward each were randomly sampled from the list of rural and urban wards of the LGA. In stage 3, six communities each were selected by simple random sampling from 29 communities in

the rural ward and 24 communities in the urban ward. In stage 4, in the rural communities, two enumeration areas were selected by the ballot method while in the urban communities, because of the high population density, only one enumeration area was selected, to give a total of 18 enumeration areas. In stage 5, all households in the selected enumeration areas were visited, and an adult woman aged between 15-49 years was interviewed in every household; in households with more than one adult woman, one respondent was randomly selected using the ballot method. There were about 30-50 households in each enumeration area. Among selected women in each household, no woman refused to participate in the survey. A total of 600 respondents (300 rural and 300 urban women) were interviewed.

Data collection instrument

A semi-structured 84-item questionnaire was adapted from the standardized questionnaire used in the WHO Multi-country Study on Women's Health and Domestic Violence. [15] The questionnaire was pre-tested in a community in Ojoo ward that was not involved in the study and then revised to correct any ambiguity.

Data collection

The questionnaire was prepared in English but was translated to Yoruba, the local language, and back translated to English to ensure that its original meaning was retained. The English questionnaire was administered to respondents who could communicate in English in the urban area, while the Yoruba questionnaire was administered to respondents who could only communicate in Yoruba in both the rural and urban communities. Data collection was done by four research assistants who were aged between 26-32 years and had at least secondary education. The research assistants were trained on issues related to IPV and oriented to the concepts of gender equality and gender discrimination. During their training, interviewers received strict instructions about the importance of maintaining confidentiality, being non-judgmental and respecting respondents' decisions. The interview took about 30 minutes to complete.

Study variables

Dependent variables

The dependent variables are lifetime and current prevalence of the experience of controlling behaviour. The WHO Multi-country Study definitions were adopted for defining controlling behaviours [15]. Controlling behaviors by an intimate partner was defined as acts including keeping her from seeing friends, restricting contact with her family of birth, insisting on knowing where she was at all times, ignoring and treating her indifferently, getting angry if she spoke with another man, being suspicious that she was unfaithful, and expecting her to ask permission before seeking health care for herself [15]. Occurrence of controlling behavior by partner at any point in their lives was classified as lifetime prevalence of controlling behavior**,** while current prevalence was occurrence of controlling behavior by partner in the last 12 months prior to the interview.

Independent Variables

The independent variables included socio-demographic characteristics, such as age of respondent; partners' age; marital status; tribe (Yoruba or others; a merger of Hausa, Ibo and other minor ethnic groups); and religious affiliation. Level of education classified as no education, primary, secondary and tertiary; average monthly income [$<$ N10,000 (\$67) and $\geq$ N10,000(\$67)]; number of children ($\leq$2children, $\geq$ 3 children); length of the relationship ($\leq$ 2 years, 3 to 9 years, 10 years and above); partners' characteristics included his sociodemographic characteristics, alcohol and drug (e.g cannabis, marijuana) use; and past involvements in physical fights which were all classified as "yes" or "no".

Other independent variables included emotional or psychological violence which was said to occur when a woman was insulted or made to feel bad about herself, belittled or humiliated in front of other people, was scared or intimidated on purpose, such as by the way he looked at her, by yelling or smashing things, or threatening to hurt someone she cared about [15]. A woman was classified to have experienced physical violence in an intimate partner relationship when she was slapped or had something thrown at her that could hurt her; if she was pushed or shoved, hit with a fist or something else that could cause injury; kicked, dragged or beaten up; choked or burnt on purpose; or when the perpetrator threatened to use or actually used a gun, knife or other weapon against her [15]. Sexual violence by an intimate partner occurred when a woman was physically forced to have sexual intercourse when she did not want to, or had sexual intercourse because she was afraid of what her partner might do if she did not, or if she was forced to

do something else of a sexual nature that she found degrading or humiliating [15]. These same definitions were adopted in this study.

Data analysis

The data were analyzed using SPSS (Statistical Package for Social Sciences software programme) version 15 [16]. Univariate analysis was done by generating frequencies and proportions for the variables. The associations between current or lifetime experience of IPV and the different socio-demographic variables were done using the Chi square test. The variables which were significantly related to dependent variables at the 5% level in univariate logistic regression analysis were entered into a multiple logistic regression model. Multiple logistic regression was used to identify independent factors associated with the current experience of IPV; and odds ratios (ORs) and their 95% confidence intervals (CIs) were reported. The independent variables were examined for co-linearity before entry into the multiple logistic regression model, but none was excluded because they were not related to each other Confounding was deemed to be present if the odds ratios from the bivariate and multiple regression analysis differed by more than 10%. Level of significance for all tests was at 5%.

Ethical Considerations

The WHO Guidelines on Ethics and Gender Based Violence was used as a guide [17]. Ethical approval was obtained from the Joint University of Ibadan and University College Hospital Institutional Review

Table 1: Socio-demographic Characteristics of Respondents and Partners

Socio-demographic Characteristics of respondents	Total N=600 n (%)	Socio-demographic Characteristics of partners	Total N=600 n (%)
Age group (years)		*Age group (years)*	
15-24	181 (30.2)	≤34	244 (40.7)
25-34	234 (39.0)	35-44	197 (32.8)
≥35	185 (30.8)	≥45	159 (26.5)
Mean Age (±S.D) years	29.7(± 8.5)	Mean Age (±S.D) years	37.9 (± 11.9)
Marital Status		*Consumes alcohol*	
Never married	84 (14.0)	Yes	100 (16.7)
Ever married/cohabiting	516 (86.0)	No	500 (83.3)
Level of Education		*Level of Education*	
None	89 (14.9)	None	86 (14.3)
Primary	289 (48.4)	Primary	184 (30.7)
Secondary	187 (31.3)	Secondary and above	330(55.0)
Tertiary	32 (5.4)		
*Occupation**		*Occupation*	
Professional & Skilled	87 (14.5)	Professional & Skilled	254 (42.3)
Partly Skilled	405 (67.5)	Partly Skilled & unskilled	346 (57.7)
Unskilled	108 (18.0)		
Religion		*Used psychoactive drugs*	
Christianity	314 (52.3)	Yes	28 (4.7)
Islam	286 (47.7)	No	572 (95.3)
Average Monthly Income		*History of involvement in physical fight*	
< N10000 (67 dollars)	462 (77.0)	Yes	40 (6.7)
≥N10000 (67 dollars)	138 (23.0)	No	560 (90.3)
Location		*Location*	
Rural	300 (50.0)	Rural	300 (50.0)
Urban	300 (50.0)	Urban	300 (50.0)

* *Professional & Skilled e.g. doctors, plumbers*
Partly Skilled e.g. petty traders, farmers
Unskilled e.g. housewives, students

Committee (UI/IRC/07/0042). Verbal informed consent was obtained after explaining the purpose of the study to the respondents. Respondents' anonymity and confidentiality were maintained by using identification numbers only. All interviews were conducted in a private and quiet place in the homes of respondents. Before asking the sensitive questions in the interview, women were informed that they were free to terminate the interview or to skip any questions they did not wish to answer. If the interview was interrupted in anyway by a visitor, the interviewers were trained either to terminate the interview or to stop asking about violence and to move on to the less sensitive topic of hypertension until privacy was guaranteed. Women whose husbands were at home at the time of interview were revisited at a different time. The safety of the respondents was paramount and in situations where an interview would jeopardize respondent's safety, the interview was not conducted. Respondents with adverse health consequences were referred to the Ijaiye Health centre and General Hospital, Moniya in the rural and urban sites respectively.

Results

Table 1 shows the sociodemographic characteristics of the respondents and their partners. The mean age of respondents was 29.7 ± 8.5 years with 39% aged between 25-34years. A large proportion of respondents (86.0%) have ever married and 52.3% were Christians. About half of respondents (47.5%) had attained primary school education, two-thirds (67.5%) were partly skilled, while 77.0% earned less than N10,000($67) a month. Generally, partners were older with a mean age 37.9±11.9 years and 30.7% had attained primary school education. One-fifth (16.7%) of partners consumed alcohol, 4.7% used psychoactive drugs, and 6.7% had history of involvement in physical fights.

Prevalence of lifetime, current and forms of controlling behavior experienced

Both lifetime and current prevalence of controlling behaviour were 49.5% (Table 2).

The most common form of controlling behaviour experienced by the respondents was "partner insisting on knowing where they were at all times (34.8%)" Other forms experienced were, "partner expects you to ask his permission before seeking health care for yourself" (21.7%), "partner gets angry if you speak with another man" (16.5%), "partner tries to keep you from seeing your friends" (12.7%), "partner often suspicious that you are unfaithful" (5.4%), "partner ignores you and treats you indifferently" (4.6%), "partner tries to restrict contact with your family of birth" (4.3%).

Factors associated with experience of controlling behavior

Table 3 shows bivariate analysis of respondents and partners characteristics and experience of controlling behavior. Controlling behavior was significantly higher

Table 2: Prevalence of controlling behavior

Description	N=600 N	%
Lifetime prevalence of controlling behavior		
Yes	297	49.5
No	303	50.5
Prevalence of current controlling behavior		
Yes	297	49.5
No	303	50.5
*Forms of controlling behavior**		
Partner insists on knowing where you are at all times	219	34.8
Partner expects you to ask his permission before seeking healthcare for yourself	137	21.7
Partner gets angry if you speak with another man	104	16.5
Partner tries to keep you from seeing your friends	80	12.7
Partner is often suspicious that you are unfaithful	34	5.4
Partner ignores you and treats you indifferently	29	4.6
Partner tries to restrict contact with your family of birth	27	4.3

**Multiple response*

Table 3: Respondents" and partners" characteristics associated with controlling behaviour

Socio-demographic Characteristics of respondents	Controlling behaviour Yes (%)	Controlling behaviour No (%)	p-value	Socio-demographic Characteristics of partners	Controlling behaviour Yes (%)	Controlling behaviour No (%)
Age group (Years)n=600				*Age group (years)n=600*		
15-24	102 (56.4)	79 (43.6)		≤34	139(57.0)	105 (43.0)
25-34	128 (54.7)	106 (45.3)	0.001	35-44	107 (54.3)	90 (45.7)
≥35	67 (36.2)	118 (63.8)		≥45	51 (32.1)	108 (67.9)
Marital Status				*Level of Education 599*		
Never married	251 (48.6)	265 (51.4)		None	31 (39.7)	47 (60.3)
Ever married	46 (54.8)	38(45.2)	0.30	Primary	81 (44.5)	101(55.5)
				Secondary	142 (53.6)	123 (46.4)
				Tertiary	43 (58.1)	31 (41.9)
Level of Education 597				*Occupation 594*		
None	31(34.8)	58(65.2)		Professional & Skilled	134(53.4)	117(46.6)
Primary	143(49.5)	146(50.5)	0.015	Partly Skilled	134 (45.4)	161 (54.6)
Secondary	101(54.0)	86(46.0)		Unskilled	25(52.1)	23 (47.9)
Tertiary	19 (59.4)	13(40.6)				
Religion				*Consumes alcohol*		
Christianity	149(52.1)	137 (47.9)		Yes	50 (50.5)	49 (49.5)
Islam	148(47.1)	166 (52.9)	0.22	No	247 (49.3)	254 (50.7)
Tribe				*Used psychoactive drugs*		
Yoruba	238 (47.6)	262 (52.4)		Yes	12(46.2)	14(53.8)
Others	59 (59.0)	41 (41.0)	0.037	No	285(49.7)	289 (50.3)
Occupation				*History of involvement*		
Professional & Skilled	49 (58.3)	35 (41.7)		*in physical fight*		
Partly Skilled	84(45.5)	220 (54.5)	0.021	Yes	21 (70.0)	9 (30.0)
Unskilled	164(57.1)	48(42.9)		No	276(48.4)	294 (51.6)
Average Monthly Income				*Relationship*		
< 10000	110 (53.7)	95 (46.3)		*characteristics Length*		
≥ 10000	187 (47.3)	208(52.7)	0.14	*of relationship*		
				≤2	201(56.6)	154 (43.4)
				≥3	96 (39.2)	149 (60.8)
Number of children alive 483				*Psychological violence*		
1-2	109 (57.1)	82(42.9)		Yes	126(63.6)	72 (36.4)
3-4	81 (46.8)	92 (53.2)	0.004	No	171 (42.5)	231 (57.5)
≥5	45 (37.8)	74 (62.2)				
Location				*Physical violence*		
Rural	126 (42.0)	174(58.0)		Yes	78 (63.9)	259 (54.2)
Urban	171 (57.0)	129 (43.0)	<0.001	No	219 (45.8)	44 (36.1)
				Sexual violence		
				Yes	40(40.6)	26 (39.4)
				No	257(48.1)	277 (51.9)

among urban women, younger women aged 15-24 years, and women with higher level of education ($p < 0.05$ respectively).

Partners' characteristics including younger age of partner (≤34 years); higher educational level, prior involvement in physical fights, relationship of short duration (≤2 years) and quarrelling often in the relationship were positively associated with controlling behavior ($p < 0.05$).

Experience of controlling behavior was also significantly associated with experience of psychological and physical violence ($p < 0.001$ respectively).

Predictors of experience of controlling behaviour

Table 4 shows the logistic regression analysis of predictors of experience of controlling behavior. These are younger age (15-24 years) of respondents (OR: 2.2; 95% CI: 1.1-4.3), residing in urban areas (OR: 1.5; 95% CI: 1.2-3.3), being in a relationship with a partner aged below 45years (OR: 2.4; 95%CI: 1.5-4.1); and being in relationship where they quarreled often with

Table 4: Predictors of controlling behaviour

Respondents' characteristics	Controlling behaviour OR (CI)	p-value	Partners' characteristics	Controlling behaviour OR (CI)	p-value
Age group (Years)			*Partners' age group (yrs)*		
15-24	2.2(1.1-4.3)	0.03	≤34	2.0(1.1-3.7)	
25-34	1.7 (1.1-2.8)	0.03	35-44	2.4(1.5-4.1)	0.001
≥35	1		≥45	1	
Level of Education			*Partners' level of Education*		
None	1		None	1	
Primary	1.3(0.7-2.2)	0.4	Primary	0.7(0.4-1.4)	0.3
Secondary	1.3(0.7-2.6)	0.4	Secondary	1.0(0.5-1.8)	0.96
Tertiary	1.3 (0.5-3.8)	0.6	Tertiary	1.4(0.6-3.0)	0.39
Tribe			*Involved in physical fight*		
Yoruba	1	0.03	Yes	2.3 (0.9-5.7)	0.07
Others	1.9 (1.0-3.3)		No	1	
Occupation					
Professional &			*Length of relationship**		
Skilled	1.1 (0.5-2.4)	0.8	≥ 2	1	0.13
Partly Skilled	0.8 (0.4-1.5)	0.5	≥3	0.7(0.4-1.1)	
Unskilled	1				
Number of children alive			*Frequency of quarrel**		
1-2	1.0 (0.6-1.9)	0.9	Rarely	1	
3-4	1.1 (0.6-1.8)	0.8	Sometimes	1.0 (0.7-1.4)	0.83
≥5	1		Often	2.6(1.1-5.9)	0.03
Location			*Psychological violence*		
Rural	1	0.046	Yes	2.1(1.4-3.0)	0.000
Urban	1.5(1.01-2.34)		No	1	

partner (OR:2.6; 95% CI: 1.1-5.9), and where partner perpetuates psychological violence (OR: 2.1; 95% CI: 1.4-3.0).

Predictors of forms of controlling behavior

Table 5 presents the logistic regression analysis of factors significantly related with forms of controlling behavior. Respondents in relationships for more than 10years (OR: 2.6; 95% CI: 1.18-5.75), who reported experience of psychological violence (OR: 1.9; 95% CI: 1.08-3.32) and physical violence (OR: 1.9; 95% CI: 1.1-3.7) were more likely to have partners who tried to keep them from seeing friends.

Similarly, women in relationship with partners who had history of involvement in physical fight (OR: 4.2; 95% CI: 1.2-14.8) and who experienced physical violence from partners (OR: 7.0; 95% CI: 2.5-19.4) were more likely to have partners who tried to restrict contact with family members.

Women with partners who had history of involvement in physical (OR: 2.5; 95%CI: 1.1-5.8 and women who experienced psychosocial violence from partners (OR: 2.1; 95% CI: 1.4-3.3), were more likely to have partners who insisted on knowing their whereabouts at all times.

Respondents' with partners that consumes\d alcohol (OR: 0.5; 95% CI: 0.2-0.9), partners prior involvement in physical fights (OR: 2.5; 95% CI: 1.1-5.8), experience of psychological violence (OR: 2.2; 95% CI: 1.4-3.5) and experience of physical violence (OR: 2.1; 95%CI: 1.2 - 3.7) were predictors of "having a partner who expects you to ask permission before seeking healthcare.

Discussion

This study examined factors associated with different forms of controlling behavior among women in South West Nigeria. The lifetime and current prevalence of

Table 5: Predictors of forms of controlling behaviour

Socio-demographic Characteristics Partners	Partner tries to keep you from seeing friends	p-value	Partner tries to restrict contact with your family	p-value	Partner insists on knowing where you are at all times	p-value	Partner expects you to ask permission before seeking healthcare	p-value
Age of respondent								
15-24	0.837 (0.273 – 2.568)	0.756	2.152 (0.300 – 15.42)	0.446	0.892 (0.406 – 1.959)	0.775	1.424(0.575 – 3.521)	0.445
25-34	0.845 (0.335 – 2.132)	0.721	3.255 (0.651 – 16.28)	0.151	0.821 (0.437 – 1.540)	0.538	0.919 (0.442 – 1.910)	0.821
35 and above	Ref		Ref		Ref		Ref	
Location								
Urban	1.317 (0.769 – 2.255)	0.316	2.456 (0.965 – 6.248)	0.059	1.222 (0.837 – 1.783)	0.299	0.910 (0.589 – 1.407)	0.672
Rural	Ref		Ref		Ref		Ref	
Length of relationship								
10 years and above	2.604 (1.18 – 5.747)	0.018	3.64 (0.952 – 13.888)	0.059	1.620 (0.938 – 2.793)	0.084	1.395 (0.739 – 2.632)	0.304
Less than 10 years	Ref		Ref		Ref		Ref	
Partners Age								
<34	1.155 (0.395 – 3.376)	0.793	0.163 (0.032 – 0.887)	0.036	2.016 (0.959 – 4.235)	0.064	1.521 (0.631 – 3.669)	0.350
35-44	1.073 (0.434 – 2.651)	0.878	0.164 (0.036 – 0.746)	0.019	1.777 (0.974 – 3.241)	0.061	1.662 (0.813 – 3.401)	0.164
≥45	Ref		Ref		Ref		Ref	
Partner's alcohol consumption								
Yes	1.622 (0.858 – 3.064)	0.136	1.185 (0.424 – 3.309)	0.746	0.970 (0.586 – 1.604)	0.906	0.508 (0.270 – 0.956)	0.036
No	Ref		Ref		Ref		Ref	
Partner's involvement in physical fight								
Yes	1.291 (0.467 – 3.571)	0.623	4.212 (1.198 – 14.805)	0.025	2.589 (1.148 – 5.841)	0.022	.544 (1.101 – 5.880)	0.029
No	Ref		Ref		Ref		2Ref	
Experience of Psychological violence								
Yes	1.900 (1.088 – 3.321)	0.024	2.439 (0.890 – 6.682)	0.083	2.190 (1.457 – 3.291)	<0.001	2.222 (1.403 – 3.520)	0.001
No	Ref		Ref		Ref		Ref	
Experience of physical violence								
Yes	1.962 (1.045 – 3.685)	0.036	7.029 (2.548 – 19.390)	<0.001	1.355 (0.828 – 2.218)	0.227	2.188 (1.276 – 3.753)	0.004
No	Ref		Ref		Ref		Ref	
Experience of sexual violence								
Yes	1.175 (0.571 – 2.417)	0.661	2.411 (0.887 – 6.554)	0.084	0.815 (0.452 – 1.470)	0.497	0.808 (0.416 – 1.568)	0.528
No	Ref		Ref		Ref		Ref	

controlling behavior, reported in this study was 49.5%. This was lower than the 63% previously reported by Antai (2011) in a nationally representative survey conducted among reproductive aged women in Nigeria; although this estimate was higher than studies conducted in Sweden (41%),[6] Malawi (33%),[18] rural Vietnam (32.1%),[8] and Sri Lanka (30%).[7] This is probably due to the patriarchal system which is predominant in most parts of sub-Saharan Africa where men exercise more authority and control over their spouses and families [14]

Moreover, Olayanju *et al* (2013) asserted that though Nigeria is highly multi-ethnic, with very rich customs and traditions, the cultural context across most parts of the nation is marked by patriarchy where men's show of authority, dominion and control over women is considered acceptable [19]. In many of these traditional settings, men are perceived as 'owners' of their wives and the subordinate status of women are entrenched; with most men insisting on knowing their wives' friends and whereabouts; and wives are generally required to ask for permission before seeking healthcare.

The commonest controlling behaviours experienced by women were; partner insisting on knowing where she was at all times, expecting her to ask for his permission before seeking healthcare, getting angry when she speaks with another man, and trying to keep her from seeing her friends, were all consistent with previous literature on the common forms of controlling behavior in Africa [10,18].

This suggests that controlling behaviour is prevalent in Africa, thus further reflecting the prevailing patriarchal system existing in these countries. The relatively high proportion of women in this study who are expected to obtain permission from their partners before seeking healthcare may pose a significant danger to their lives and those of their children, since women are the main caregivers of their children. Timing in accessing healthcare services is critical when making health care decisions, and women could be at increased risk of adverse health outcome, both morbidity and mortality, when there is delay in making timely decisions to seek health care for themselves or their children [20].

Younger aged women in relationship with older partners, were more likely to experience controlling behavior as well as other forms of IPV when compared with older women.[6],[8] Young women often lack the experience in asserting themselves, and are thus more vulnerable to controlling behaviours compared to their much older counterparts. Additionally, the higher prevalence of controlling behavior observed among couples whose relationship was less than 10 years, compared to women who have been in a relationship with spouse for much longer duration may be attributed to the fact that young couples require time to gradually build trust in their relationships.

Similar to reports by Krantz and Nguyen women with younger aged partners were also more likely to experience controlling behaviours, This is probably due to partners' youthful exuberance, lack of maturity and patience in managing relationship dynamics [7] In addition, adolescence and young adulthood is a period during which violence, as well as other types of behaviors are exhibited and this is mainly inflamed by peer pressure, coupled with the need to exhibit dominance of the opposite sex [21]

Contrary to beliefs from other reports,that better education reduces experience of controlling behavior place of residence and level of education of respondents did not influence experience of controlling behavior in this study as experience of controlling behaviour was higher among women with tertiary education, and women living in urban areas.[18],[22],[23] This may be explained by the fact that traditional norms seem to have a greater influence on human behavior in a patriarchal society such as Nigeria rather than other factors including educational level or urbanization [24]

The quality of relationship such as frequent quarrels was associated with the experience of controlling behavior. Previous studies have shown that frequent quarrels in relationships are associated with the experience of IPV. [21, 25] Frequent quarrels were associated with all forms of controlling behavior. Selic, Svab & Gucek reported that a history of frequent disputes in intimate relationship was the most powerful risk factor for psychological violence.[26] Quarrels could be as a result of the controlling behavior being perpetuated by the partner, and quarrels may also arise when the woman resists control. Further qualitative studies will be useful to determine the triggers of quarrels and explore other forms of verbal abuse [24]. Consistent with previous studies on IPV in Nigeria, findings from this study suggests that women who report being controlled are more likely to experience all forms of violence including physical, psychological and sexual violence [10] the explanations for this is not far-fetched as controlling behaviors are not only

precursors, but also significantly increase the likelihood of all forms of violence against women [10].

The findings that controlling behaviour is more common than physical/sexual violence and also most consistently associated with most health symptoms reported by women who experienced IPV are also consistent with literature [27].

Finally, consistent with previous studies,[28-30] the link between exhibiting controlling behaviors as well as engaging in IPV, with the male spouses' involvement in aggressive or delinquent behavior has been further reinforced by our study findings. There is therefore need to commence gender-based violence education early, starting at childhood and reinforcing this message during adolescence and even to early adulthood that all forms of gender-based violence is unacceptable, while also debunking the traditional norms which are inimical to the general well-being of both genders.

Limitations

Our study has some limitations. First, there may have been underestimation of prevalence rates of controlling bahaviours and other forms of IPV experienced because of the stigma associated with disclosure however, safety, privacy and confidentiality were ensured during the interviews.

The study is cross-sectional and could not determine if women experienced controlling behavior before experiencing the other types of IPV. Some studies have suggested that controlling behavior could be a precursor of experiencing the other forms of violence [18].

Questions about partners' violent behaviors were based on respondents' knowledge rather than partners-report. Thus increasing the chances of either underreporting or overestimating the true situation. Future research is needed to investigate factors associated with perpetration of violence from the male perspective. The history of financial autonomy of the women and family history of violence in respondents' or partners' parents was not ascertained and thus could have confounded the observations, both factors have been reported to be associated with experiencing violence [20,28]. Lastly, this study did not inquire about health consequences of controlling behavior. Health care providers should, therefore, consider incorporating questions on controlling behavior when asking patients about their IPV experiences.

Despite these limitations, this study has clearly explored the various forms of controlling behaviours experienced by women of reproductive age in a low income setting and how these controlling behaviours are linked with their spouse's involvement in physically aggressive activities., thus reinforcing the need for commencement of education on gender-based violence as early as possible for both male and female children and young adolescents.

Conclusion

Prevalence of controlling behavior was high among women in southwestern Nigeria. The most common form of controlling behavior was partner insisting on knowing where respondents were at all times. Younger women and younger aged partners, frequent quarrels in relationship and history of partner's involvement in physical fights were associated with forms of controlling behavior.

Long-term strategies including early education in gender-based violence, promotion of peaceful coexistence and debunking some traditional norms through enlightenments, advocacy and policy change are needed to put an end to cultural and societal norms reinforcing IPV

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. WHO. Global and regional estimates of violence against women: prevalence and health effects of intimate partner violence and non-partner sexual violence. WHO (2013).https://www.who.int/reproductivehealth/publications/violence/9789241564625/en/ (Accessed October 23rd, 2013).
2. WHO. Violence against women. Intimate partner and sexual violence against women. Fact sheet (2013). http://www.who.int/mediacentre/factsheets/fs239/en/index.html (Accessed October 23rd, 2013).
3. Heise LL, Ellsberg M and Gottemoeller M. Ending violence against women. In Population Reports, (1999).Series L, No.11,Volume XXVII Centre for Communications Programs Baltimore, MD, Johns Hopkins University School of Public Health.
4. Gage S and Hutchinson P. Power, control and intimate partner sexual violence in Haiti. Arch Sex Behav, (2006).35, 11–26. doi: 10.1007/s10508-006-8991-0

5. Barkho E, Fakhouri M and Arnetz JE. Intimate partner violence among Iraqi immigrant women in Metro Detroit: a pilot study J Immigr Minor Health, (2011). 13(4):725-731.
6. Lövestad S and Krantz G. Men's and women's exposure and perpetration of partner violence: an epidemiological study from Sweden. BMC Public Health Nov (2012). 2, 12, 945.
7. Krantz G and Nguyen DV. The role of controlling behaviour in intimate partner violence and its health effects: a population based study from rural Vietnam. BMC Public Health, May (2009).14, 9, 143.
8. Jayasuriya V, Wijewardena K and Axemo P. Intimate partner violence against women in the capital province of Sri Lanka: prevalence, risk factors, and help seeking. Violence Against Women; (2011).17(8), 1086-102.
9. Kapiga S, Harvey S, Muhammad AK, *et al*. Prevalence of intimate partner violence and abuse and associated factors among women enrolled into a cluster randomized trial in northwestern Tanzania. BMC Public Health. (2017). 17(1), 190.
10. Antai D. Controlling behavior, power relations within intimate relationships and intimate partner physical and sexual violence against women in Nigeria. BMC Public Health, (2011).29, 11, 511.
11. National Population Commission (NPC) [Nigeria] and ICF Macro. Nigeria Demographic and Health Survey 2008. Abuja, Nigeria: National Population Commission and ICF Macro. (2009).
12. Balogun MO and John-Akinola YO. A Qualitative Study of Intimate Partner Violence Among Women in Nigeria. J Interpers Violence, (2015). 30(14), 2410-2427.
13. National Population Commission (NPC). Final results of 2006 population census of Nigeria. NPC, (2006) Abuja, Nigeria
14. Fawole OI, Aderonmu AL and Fawole AO. Intimate Partner Abuse: wife beating among civil servants in Ibadan, Nigeria. Afr J Reprod Health, (2005).9, 54-64.
15. Garcia-Moreno C, Jansen HA, Ellsberg M, Heise L and Watts CH. WHO Multi country Study on Women's Health and Domestic Violence against Women: Initial results on prevalence, health outcomes and women's responses. World Health Organization, Geneva. (2005).
16. SPSS 15.0 Command Syntax Reference 2006.
17. WHO. Putting women first: ethical and safety recommendations for research on domestic violence against women. (WHO/FCH/GWH/ 01.1). World Health Organization, (2001) Geneva
18. Mandal M and Hindin MJ. Men's controlling behaviors and women's experiences of physical violence in Malawi. Matern Child Health J, Sep (2013), 17(7), 1332-8. doi: 10.1007/s10995-012-1137-1.
19. Olayanju L, Naguib RN, Nguyen QT, Bali RK and Vung ND. Combating intimate partner violence in Africa: Opportunities and challenges in five African countries. Aggressive and Violent behaviour, (2013).18, 101-112.
20. UNFPA. Setting standards for emergency obstetric and newborn care (2014). http://www.unfpa.org/ resources/setting-standards-emergency-obstetric-and-newborn-care (Accessed 19th October, 2015).
21. Krug EG, Dahlberg LL, Mercy JA, Zwi AB and Lozano R. World report on violence and health. Geneva, World Health Organization, (2002).114-146,159.
22. Walton-Moss BJ, Manganello J, Frye V and Campbell JC. Risk factors for intimate partner violence and associated injury among urban women. J Community Health, Oct (2005). 30(5), 377-89.
23. Abramsky T, Watts C, Garcia-Moreno C, *et al.* What factors are associated with recent intimate partner violence? Findings from the WHO multi-country study on women's health and domestic violence. BMC Public Health, (2011).11(1), 109. doi: 10.1186/1471-2458-11-109.
24. Balogun MO, Owoaje ET and Fawole OI. Intimate Partner Violence in Southwestern Nigeria: Are there rural-urban differences? Women and Health, (2012).52(7), 627-45.
25. Stöckl H, March L, Pallitto C, Garcia-Moreno C. WHO Multi-country Study Team. Intimate partner violence among adolescents and young women: prevalence and associated factors in nine countries: a cross-sectional study. BMC Public Health, (2014). 25, 14, 751. doi: 10.1186/1471-2458-14-751.
26. Selic P, Svab I, Gucek NK. A cross-sectional study identifying the pattern of factors related to psychological intimate partner violence exposure in Slovenian family practice attendees: what hurt them the most. BMC Public Health, (2014). 14,223. doi: 10.1186/1471-2458-14-223.

27. Stöckl H and Penhale B. Intimate Partner Violence and Its Association with Physical and Mental Health Symptoms Among Older Women in Germany. J Interpers Violence, (2015). 30(17), 3089-111.
28. El-Zanaty F and Ann W. Cairo, Egypt: Ministry of Health and Population, National Population Council, El-Zanaty and Associates, and ORC Macro. Egypt Demographic and Health Survey 2005.
29. Djikanovic B, Jansen HA and Otasevic S. Factors associated with intimate partner violence against women in Serbia: a cross-sectional study. J Epidemiol Community Health, (2010).64(8), 728-35.
30. Abeya SG, Afework MF, and Yalew AW. Intimate partner violence against women in western Ethiopia: prevalence, patterns, and associated factors. BMC Public Health, (2011). 9, 11, 913.

Afr. J. Med. Med. Sci. (2020) **49,** 297-306

Evaluation of pattern of presentation and a group of possible predictors of restoration failure in NCCLs

MO Imemesi[1], AO Arigbede[2] and C Udoye[1]
Department of Restorative Dentistry[1], University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu and Department of Restorative Dentistry[2], University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria

Abstract
Background: Early failure of restorations placed on teeth with NCCLs is well known despite the improvement in resin and adhesive technology.
*Objective***:** This study was designed to evaluate the pattern of presentation of NCCLs and a group of possible predictors of failure of restorations in NCCLs.
*Methodology***:** A double-blind randomized clinical study was conducted among patients who presented at the restorative clinic of a Nigerian Teaching Hospital with at least two adjacent NCCLs on vital teeth excluding molars. Ethical approval was obtained for the study. From the calculated sample size, 83 resin composite and 83 RMGIC restorations were done for 29 patients following standard procedure. Tooth for restoration and the material involved were selected by simple random sampling. Review evaluations were done 1 week, 4 months, 8 months and 12 months post operatively. Two independent calibrated examiners evaluated the restorations. Relevant FDI criteria for clinical evaluation of restoration were employed. Log-rank analysis was used to compare the survival times of the two materials while the Cox regression analysis was performed to determine the predictors of failure. The level of significance was $p \leq 0.05$.
*Results***:** Most of the patients, 17 (58.6%) were more than 50 years in age and the majority, 21(72.4%) were males. The premolars were the most treated teeth (41.0%). Most of the restorations were done in the maxillary arch (120, 72.3%) and left side of the mouth (85, 51.2%). At the 12th month review appointment, seven (5.8%) out of the 120 upper restorations and 9 (19.6%) out of the 46 lower restorations had failed. The mean survival time for restorations in the maxillary arch (46.49±0.74 weeks) was higher than that of the lower (40.95±2.15 weeks). The highest failure rate was recorded on the premolars. Log rank statistical test showed a statistically significant difference between the rates of failure in relation to the arch (X^2=6.948, df=1, p=0.008) and the survival times in relation to the material (X^2=7.005, df=1, p=.008). Cox regression analysis revealed that the type of material was the only significant predictor of survival of the restorations (p=0.028).
*Conclusion***:** More NCCLs were found in the older individuals, males, premolars, upper and left side of the arch. The type of material used for restoration was the only predictor of failure or survival.

Keywords: *Cervical abrasion, Composite resins, non-carious cervical lesion, resin modified glass ionomer cement.*

Résumé
Contexte: L'échec précoce des restaurations placées sur les dents avec des NCCL est bien connu malgré l'amélioration de la technologie des résines et des adhésifs.
Objectif **:** Cette étude a été conçue pour évaluer le modèle de présentation des NCCL et un groupe de prédicteurs possibles d'échec des restaurations dans les NCCL.
Méthodologie **:** Une étude clinique randomisée en double-aveugle a été menée auprès de patients qui se sont présentés à la clinique de restauration d'un hôpital d'enseignement nigérian avec au moins deux NCCL adjacents sur les dents vitales, à l'exception des molaires. Une approbation éthique a été obtenue pour l'étude. À partir de la taille d'échantillon calculée, 83 restaurations en composite de résine et 83 restaurations RMGIC ont été effectuées pour 29 patients suivant une procédure standard. La dent à restaurer et le matériau impliqué ont été sélectionnés par simple échantillonnage aléatoire. Les évaluations des examens ont été effectuées 1 semaine, 4 mois, 8 mois et 12 mois après l'opération. Deux indépendants examinateurs calibrés ont évalué les restaurations. Les critères FDI pertinents pour l'évaluation clinique de la restauration ont été utilisés. L'analyse log-rang a été utilisée pour comparer les temps de survie des deux matériaux tandis que l'analyse de régression de Cox a été effectuée pour déterminer les prédicteurs d'échec. Le niveau de signification était $p \leq 0,05$.

Correspondence: Prof. A.O. Arigbede, Department of Restorative Dentistry, Univrsity of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria. E-mail: abiodun.arigbede@uniport.edu.ng

Résultats **:** La plupart des patients, 17 (58,6%) étaient âgés de plus de 50 ans et la majorité, 21 (72,4%) étaient des hommes. Les prémolaires étaient les dents les plus traitées (41,0%). La plupart des restaurations ont été réalisées dans l'arche maxillaire (120, 72,3%) et le côté gauche de la bouche (85, 51,2%).
Lors du rendez-vous d'examen du 12e mois, sept (5,8%) des 120 restaurations supérieures et 9 (19,6%) des 46 restaurations inférieures avaient échoué. Le temps de survie moyen pour les restaurations de l'arche maxillaire (46,49 ± 0,74 semaines) était supérieur à celui du bas (40,95 ± 2,15 semaines). Le taux d'échec le plus élevé a été enregistré sur les prémolaires. Le test statistique log-rang a montré une différence statistiquement significative entre les taux d'échec par rapport à l'arche ($X^2 = 6,948$, df = 1, p = 0,008) et les temps de survie par rapport au matériau ($X^2 = 7,005$, df = 1, p = 0,008). L'analyse de régression de Cox a révélé que le type de matériau était le seul prédicteur significatif de la survie des restaurations (p = 0,028).
Conclusion **:** Plus de NCCL ont été trouvés chez les individus plus âgés, les hommes, les prémolaires, le côté supérieur et gauche de l'arche. Le type de matériau utilisé pour la restauration était le seul prédicteur d'échec ou de survie.

Mots-clés: *abrasion cervicale, résines composites, lésion cervicale non carieuse, ciment ionomère de verre modifié à la résine.*
non-carious cervical lesion, resin modified glass ionomer cement.

Introduction

One of the major reasons why multiple restorations are inserted in adult patients is non-carious cervical lesions (NCCLs) [1-3]. The lesions are among the non-carious tooth defects [4] and some of the implicated aetio-pathologic factors include abrasion, attrition, erosion and abfraction [1,2]. Complex interaction among a plethora of factors including improper brushing technique, acidic diets and bad oral habits like bruxism, nail biting and pipe smoking give rise to NCCLs [3]. The defects are common in the cervical areas because of the relatively thin enamel around the enamel-cemental junction [1]. It is a generally preventable oral health condition even though the causes are multifactorial. Previous reports suggest that the lesions are particularly common among the elderly and multiple contiguous teeth are usually involved [1-4]. The lesion is asymptomatic initially [5], but as the loss of tooth structure encroaches into the dentinal layer and beyond, the patient may present with one or more of the following: tooth sensitivity, pain, accumulation of plaque, tooth fracture, poor aesthetics and tooth loss [1-4].

The buccal surface appears to be the most frequent location, though the lingual and interproximal surfaces may also be affected [2,3,6]. This group of lesions were found to be more common on premolars, first molars and canines [3,4,5]. It is also believed to be common in the upper arch. The defects may be flattened, irregular in shape, circular or wedge shaped and depending on the severity, it may be shallow or deep, narrow or broad [3,4] and the margins may be sub gingival [7]. A prevalence of between 5 and 85% had been reported. [4] In other studies, a prevalence of 39%-77% was reported in the middle age group and 57%-81% among the elderly [4,8,9]. High prevalence of the lesions had been attributed to the decline in the rate and number of tooth loss as well as increased number of elderly population in the society [10,11].

Management of the lesion varies from preventive option to preventive and restorative options. The preventive option may include instructions on proper brushing technique, diet modification and occlusal adjustment [1,11]. Resin Modified Glass Ionomer Cement (RMGIC) and other tooth coloured restorative materials are used for its restoration [1,11]. Early restoration failure is closely associated with this condition on account of their peculiar histological and structural features [7]. This is why care must be taken to identify and manage the causative factors and to place the restorations. This study was designed to evaluate the pattern of presentation and identify the predictors of restoration failure.

Materials and method

This was a double-blind randomized clinical study conducted to identify the determinants of restoration failure in NCCLs restored with light cure microhybrid composite (DMP Ltd Kalyvion Markolond Zone Greece) and resin-modified glass ionomer cement (VITRO FIL LC Glass ionomer, DFLIndustria e Comercio S.A. Estrada do Guerengue, 2059 Rio de Janeiro-RJ- Brasil-CEP: 22713-002). Patients with NCCLs attending the restorative clinic of a Nigerian Teaching Hospital, Ituku-Ozalla, Enugu who met the inclusion criteria and were willing to sign the inform consent form were invited to participate in the study. The Health Research Ethics Committee (HREC) of the Teaching Hospital approved the study.

The sample size was determined using the formula for comparison of equal proportions [12].

$$n = \frac{(\{ Z_\alpha + Z_\beta \}^2 \{ P_1 q_{1+} p_{2q2} \})}{(P_1 - P2_)^2}$$ where

n = minimum sample size for each group; P = Prevalence or proportion of the attribute present in the population. P_1 represents the percentage success of resin modified glass ionomer cement and P_2 the percentage success of composite restoration while q= 1- P. Z_α= standard normal deviate corresponding to the level of significance at 95% confident interval = 1.96. Z_β = standard normal deviate corresponding with 1 minus power at 80% = 0.84. Based on the percentage success of RMGIC and composite resin done in Ile-lfe, Nigeria [13], a value of 91.1 % for RMGIC and 74.1% for composite resin was obtained. Thus: P_1 = 91.1% and P_2 = 74.1%. From the calculation, n = 74.0. To compensate for attrition and to ensure validity, a 10% drop-out rate was used, giving a minimum sample size of 81 restorations per group.

Adult patients between 20 and 65 years of age who presented with good oral hygiene, adequate mouth opening, sound periodontal health, low caries risk, , at least two adjacent vital teeth with unrestored NCCLs with supra gingival apical limit and patients who were ready to sign the inform consent form were recruited. Patients who grind their teeth, smoke, had reduced salivary flow and who did not meet the other inclusion requirements were excluded from the study.

Scaling and polishing, oral hygiene instructions, radiographic and pulp vitality investigations were carried out where indicated and not more than 3 pairs of restorations were placed on a subject as prescribed in the FDI guidelines [13,14]. Standard procedure was followed in shade selection and restoration techniques. Simple random sampling by balloting was employed to select the teeth and the materials for restoration. This sampling technique conformed with the requirements of the American Dental Association guidelines for testing a new material [14]. Intra oral clinical photographs were taken for reference purposes. During the composite resin and RMGIC restorations' procedures, cotton wool rolls and suction tip attached to a complete dental chair unit (Unijet 75 suction system - Cefla dentale Imola (BO) Italy. S.N. LE841911) were employed for teeth isolation.

For resin composites restoration, etching was done with 37% orthophosphoric acid gel (DMP etching gel DMP Ltd Kalyvion Markolond Zone Greece) for 15 - 20 seconds over enamel surface roughened superficially for 15 seconds on dentine surface. Afterwards, the tooth surface was rinsed and dried with oil free air, giving a chalky white appearance. Using a light brushing motion for 15-20 seconds, the bonding agent (bonding, DMP Ltd Kalyvion Markolond Zone Greece) was applied evenly and cured with LED light for 15 seconds (SOEDENT 7A LED). The resin composite was applied and cured incrementally, using agate spatula. The applied composite was cured with a visible blue light (LED dental curing light - SOEDENT 7A LED) in the following order: 40 seconds (for lighter shade – A1, A2, A3) and 60 seconds (for darker shades – A3.5, B3), according to the manufacturer's specification. Primer (VITRO FIL PRIMER) was applied and cured for 20 seconds. The RMGIC (VITRO FIL LC powder) was mixed with the liquid (VITRO FIL LC liquid) according to the manufacturer's instructions. The resin was then applied, contoured and cured with LED light (SOEDENT 7A LED) for 20 seconds. After polymerisation, the finishing was accomplished with a thin finishing diamond tip (Dia bur, made by Mani, Inc. 8-3 kiyohara industrial park UT SunomiYa Tochigi Japan), under water jet. The restoration was coated with natural glaze provided (Natural Glaze) to allow for a full jellification of the cement in contact with saliva.

The criteria employed for evaluation of the restorations were those described by the World Dental Federation (FDI) and those that were relevant for this study included: Aesthetic criteria: 1-4, Functional criteria: 5, 6, 9 and 10 and Biological criteria: 11, 12 and 13 were employed (Appendix 1). Two calibrated independent examiners excluding the clinician who single-handedly inserted the fillings assessed the restorations. Kappa statistics was used to test inter-examiner agreement (the Kappa value was 0.9). Only the lead investigator was aware of the type of restoration on each tooth. The review appointments were fixed at: one (1) week, four (4) months, eight (8) months and twelve (12) months after placement of restoration. Independent assessments were made by the examiners, after which they compared notes and resolved differences.

Data management

The Statistical Package for Social Sciences (SPSS), version 17.0. Chicago: SPSS Inc. was used for the analysis. Summary statistics was generated and Chi square was used to compare the distribution of restoration in terms of tooth and arch types as well as the side of the mouth concerned. The Kaplan-Meier

estimates were used to calculate the survival of the restorations while the Log-rank test was used for testing the difference between the Kaplan-Meier curves. Cox regression analysis was performed to identify the predictors of failure/retention. The level of significance was set at $p \leq 0.05$.

Results

Twenty-nine patients most of whom were males, 21(72.4%) participated in the study. Most of the patients, 17 (58.6%) were more than 50years in age, 8 (27.6%) belongs to the 41-50 years age group, 3 (10.4%) were in the 31-40years age group while only 1 (3.4%) was less than 30 years. One hundred and sixty-six restorations were placed, in all half of this number was composite restoration while the remaining half was RMGIC restoration. The premolars were the most treated teeth (41.0%) followed closely by incisors (36.7%). The canines had the lowest number of restorations (22.3%) in this study. The majority of the restorations were done in the maxillary arch (120, 72.3%) and left side of the mouth (85, 51.2%). Chi sq. showed no statistical significant difference in the distribution of restorations in relation to type of tooth (χ^2= 0.102, P= 0.950), arch type (χ^2=1.083, P= 0.298) and side of the mouth involved (χ^2=0.603, P= 0.438).

in the upper arch failed while 9(19.6%) out of the 46 restorations done in the lower arch failed. The mean survival time for restorations in the maxillary arch was 46.49±0.74 weeks while that of mandibular arch was 40.95±2.15weeks. Log rank statistical test showed a statistically significant difference between the rates of failure in relation to the arch (X^2=6.948, df=1, p=0.008).

Eight (9.9%) out of the 81 restorations done on the right side of the arch failed, while 8(9.4%) out of the 85 restorations done on the left side also failed. The mean survival time for restorations on the right side of the mouth was 44.77±0.1.28 weeks and 44.99±1.19 weeks for the left side. Log rank statistical test showed no statistically significant difference between the rates of failure in relation to the side of the arch (X^2=0.008, df=1, p=0.927).

In terms of failure in relation to the type of tooth restored, 5(8.3%) out of the 61 restorations done on the incisors failed, 2(5.4%) out of the 37 restorations placed on the canines failed while 9(13,2%) out of the 68 restorations placed on premolars failed. Highest failure rate was recorded on the premolars. The mean survival time for restorations on incisors was 45.19±1.25weeks, on canines was 46.62±1.00 weeks and that of the premolars was 43.51±1.69. The canines had the highest survival time followed by the incisors.

Table 1: Determinants of survival time using Cox regression analysis

Variable	B	SE	Wald	Df	Hazard ratio	95.0% CI	p-value
Maxillary arch(REF)							
Mandibular arch	-.947	.547	2.993	1	.388	0.133-1.134	0.084
Right side of mouth(REF)							
Left side of mouth	.189	.502	.142	1	1.208	0.452-3.232	0.706
Incisor(REF)							
Canine	-.332	.601	.305	1	.718	0.221-2.331	0.581
Premolar	-.978	.793	1.522	1	.376	0.079-1.778	0.217
RMGIC(REF)							
Composite	-1.426	.649	4.830	1	.240	0.067-0.857	0.028

REF=Reference, C.I=Confidence interval.

In terms of retention, at the 12th month review appointment, a total number of eleven resin composite restorations were found to be clinically poor while 2 were found to be clinically unsatisfactory (13failures) as against RMGIC where 1 restoration was clinically poor and two were clinically unsatisfactory (3failures). On the whole, 16 restorations had unacceptable outcome. Seven (5.8%) out of the 120 restorations done

Log Rank analysis showed no statistically significant difference in survival time among the three types of teeth evaluated (X^2=3.049, df=2, p=0.218).

As regard the type of material used for restoration, 3(3.6%) out of the 83 RMGIC restorations failed unlike in resin composite restoration cases where 13(15.7%) failures were recorded. The mean survival time for RMGIC restorations was 47.10±0.77 weeks

while that of resin composite restorations was 42.90±1.48 weeks. Log Rank analysis showed that the difference in survival time was statistically significant (X^2=7.005, df=1, p=.008).

Cox regression analysis was done to identify the predictor of failure/survival (Table 1). The type of material emerged as the only significant determinant of survival of the restorations (p=0.028). Resin-modified glass ionomer cement restorations had 0.240 hazard to survival compared to resin composite restorations at 95% confidence interval of 0.067 to 0.857.

Discussion

Information on predictors of failure or survival of restoration done on teeth with NCCLs is very important for prevention purposes and patient management. Most of the patients who participated in this study were more than 50 years in age. This corroborates the reports that the lesion is more common among the elderly [4,7,11]. Positive correlation between age and presence of NCCLs had been reported [7]. The prevalence of the condition among the middle aged and elderly is a function of years of service and cumulative stresses received by the retained teeth of the older individuals [1,3,5,15]. Non carious cervical tooth defects are not acute lesions; they arise from a chronic and complex interactions of chemical, physical and mechanical processes that involve usage of improper brushing technique, engagement in bad oral habits like bruxism and ingestion of acidic foods and drinks over a long period of time [1-3]. Most of the participants in this study were males in line with the existing literatures on this subject which suggest that the lesions tend to occur more in males [1,3,15-17]. It had been postulated that the higher occurrence of the lesions among males may be due to higher bite force or different dietary patterns [18]. It could also be that males indulged more on oral habits that induced destructive occlusal stress on their teeth.

Most of the restorations in this study were done in the maxillary arch (72.3%). This was consistent with the findings of Mujeeb *et al* [3], Yan and Yang [16], and Adeleke and Oginni [13]. In contrast, Kolak *et al* [1]. reported more cases in the lower arch. It is not clear at the moment why the prevalence of NCCLs in relation to dental arch varies from one study to the other, the role of oral habits and occlusal irregularities in this regard need to be investigated. The reason why more lesions are located in the upper jaw may be due to the fact that the upper teeth are larger and more accessible.

More NCCLs were found on the left side of the arch in this study in agreement with the report of Kolat *et al* [1]. It has been suggested that right handed brushers tend to have more lesions on the left side of the mouth and vice versa [5]. Mujeed *et al* [3] found a statistically significant relationship in this regard but Oginni *et al* [19] did not. The reason for this trend is because more brushing force tends to be generated on the side opposite to the brush holding hand.

The most treated teeth in this study were the premolars (41.0%). This further lends credence to the existing large report on this finding [1,4,5,18,20,21]. Reports on distribution of NCCLs according to types of tooth are variable[1,3] but it is not common to have more NCCLs on incisors than canines, but literature review showed that incisors, canines, and premolars are the most commonly affected teeth [3]. It is believed that NCCLs are particularly common on the premolars because of their centric anatomic position [3] where maximum tooth brushing force is generated [18]; and perhaps because of frequent presence of premature occlusal contacts on premolars and limited protective effect by saliva [1].

Restoring and maintaining restoration on teeth with NCCLs is challenging [22]. The causes of the premature failure are not yet fully understood[10] even though remarkable advancement had been achieved [22,23]. This study showed that there were statistically significant differences between survival times in relation to the arch and type of material used for restoration. Cox regression analysis revealed that only the type of material used for restoration is a predictor of failure /retention. This finding is in agreement with the report of Pecie *et al* [10] that suggests product-dependent good clinical outcome as it relates to longevity of restoration on teeth with NCCLs exist. It had also been revealed that the type of adhesive system employed is a function of whether long lasting restorations would be obtained or not [24,25] RMGIC performed better than resin composites in this study as reported by Adeleke and Oginni [13]. The problems with resin composites in NCCLs restorations had been linked to higher microleakage and reduced marginal adaptation as a result of stress on tooth-restoration interface which emanates from polymerization shrinkage as well as tensile stress caused by oblique occlusal loading [10,26,27]. Studies on longevity of NCCLs restoration should be interpreted with caution because it has been stated that a particular product may give varying results on account of the technique applied

[10] and skills of the clinician.[18] More prospective long time studies are needed in order to identify products that give consistent and long lasting restoration.

Conclusion

More NCCLs were found in the older individuals, males, premolars, upper and left side of the arch. The type of material used for restoration was the only predictor of failure or survival.

References

1. Kolak V, Pešic D, Melih I, *et al*. Epidemiological investigation of non-carious cervical lesions and possible etiological factors.. J Clin Exp Dent. 2018;10 (7):e648-e656.
2. Nguyen C, Ranjitkar S, Kaidonis JA and Townsend GC. A qualitative assessment of non-carious cervical lesion in extracted human teeth. Aust Dent J. 2008;53(1):46-51.
3. Mujeeb F, Soomro ZA, Rashid S and Hosein T. Risk factors associated with non-carious cervical lesions at a teaching hospital. J Pak Dent Assoc. 2015,24(4): 188-193.
4. Nascimento MM, Gordan VV, Qvist V, *et al*. Dental Practice-Based Research Network Collaborative Group.Restoration of noncarious tooth defects by dentists in The Dental Practice-Based Research Network. J Am Dent Assoc. 2011;142 (12):1368-75.
5. Selma J, Amra V, Samra K, Irmina T and Anita B. Faculty of Dental Medicine, University of Sarajevo, Bosnia and Hercegovina. The Prevalence, Distribution and Expression of Noncarious Cervical Lesions (NCCL) in Permanent Dentition. Materia Socio Medica. 2010 ;22:200-204.
6. Sneed WD. Non-carious cervical lesions: why on the facial? A theory J Esthet Restor Dent. 2011;23(4):197-200.
7. Kampanas NS and Antoniadou M. Glass Ionomer Cements for the Restoration of Non-Carious Cervical Lesions in the Geriatric Patient. J. Funct Biomater. 2018; 9(3). pii: E42. doi: 10.3390/ jfb9030042.
8. Duangthip D, Man A, Poon PH, *et al*. Occlusal stress is involved in the formation of non-carious cervical lesions. A systematic review of abfraction. Am J Dent.2017;30(4):212-220.
9. Ceruti P, Menicucci G, Mariani GD, Pittoni D and Gassino G. Non carious cervical lesions. A review. Minerva Stomatol. 2006;55(1-2):43-57.
10. Pecie R, Krejci I, Bortolotto T.Garcia-Godoy F, Noncarious cervical lesions (NCCL) – A clinical concept based on the literature review. Part 2: Restoration. Am J Dent. 2011;24(3):183-192
11. Perez CdosR, Gonzalez MR, Prado NAS, *et a*l. Restoration of Noncarious Cervical Lesions: When, Why, and How. Int J Dent 2012;2012:687058.doi:10.1155/2012/687058.
12. Varkevisser CM, Pathmanathan I and Brownlee A. Module 11: Sampling (IDRC). In designing and conducting health systems research projects: volume 1 Proposal Development and Fieldwork. Canada: International Development Research Center. 2003. Available at: http://web.idrc.ca/en/ ev-33011-201-1-DOTOPIC.html. [Accessed on May 21, 2019].
13. Adeleke , Oginni AO. Clinical evaluation of resin composite and resin-modified glass-ionomer cement in non-carious cervical lesions. J West Afr Coll Surg. 2012;2(4):21–37.
14. Hickel R, Peschke A, Tyas M, *et al*. FDI World Dental Federation- clinical criteria for the evaluation of direct and indirect restorations. Update and clinical examples. J Adhes Dent. 2010;12(4):259-272.
15. Teixeira DNR, Zeola LF, Machado AC, Gomes RR, Souza PG, Mendes DC, Soares PV. Relationship between noncarious cervical lesions, cervical study.lesions, cervical dentin hypersensitivity, gingival recession, and associated risk factors: A cross-sectional study. J Dent. 2018;76:93-97.doi:10.1016/j.dent.2018.06.017.
16. Yan W and Yang D. The Prevalence, characteristics and risk factors in non-carious cervical lesion: A survey on 295 people in Guangzhou area. Oral Hyg Health. 2014;2:125. doi:10.4172/2332-0702.1000125
17. Ibrahim KG and Abu-bakr NH, Ibrahim YE. Prevalence of dental ab-fraction among a sample of Sudanese patients. Arch Orofac Sci. 2012;7(2):50-55.
18. Sunny OA, Philip OU and Amaechi UA. Risk factors for tooth wear lesions among patients attending the dental clinic of a Nigerian Teaching Hospital, Benin City: A pilot study. Sahel Med J.2015;18:188-191
19. Oginni A.O., Olusile AO and Udoye CI. Non-carious cervical lesions in a Nigerian population: abrasion or abfraction? Int Dent J. 2003;53(5):275-279.

20. Borcic J, Anic I, Urek MM and Ferreri S. The prevalence of non-carious cervical lesions in permanent dentition. J Oral Rehabil. 2004;31(2):117-123.
21. Aw TC, Lepe X, Johnson GH and Mancl L. Characteristics of noncarious cervical lesions: a clinical investigation. J Am Dent Assoc. 2002;133 (6):725-733.
22. Santiago SL, Passos VF, Vieira AHM, *et al.* Two-year clinical evaluation of resinous restorative systems in non-carious cervical lesions. Braz Dent J. 2010;21(3):229-234.
23. Franco EB, Benetti AR, Ishikiriama SK, *et al*. Five-year clinical performance of resin composite versus resin modified glass ionomer restorative system in non-carious cervical lesions. Oper Dent. 2006;31 (4):403-408.
24. Kubo S, Kawasaki K, Yokota H and Hayashi Y. Five-year clinical evaluation of two adhesive systems in non-carious cervical lesions. J Dent. 2006;34(2):97-105.
25. Burrow MF and Tyas MJ. Clinical evaluation of three adhesive systems for the restoration of non-carious cervical lesions. Oper Dent. 2007;32(1):11-15.
26. Terry DA, McGuire MK, McLaren E, Fulton R and Swift EJ Jr. Perioesthetic approach to the diagnosis and treatment of carious and noncarious cervical lesions: Part II. J Esthet Restor Dent. 2003;15(5):284-296.
27. Ichim I, Li Q, Loughran J, Swain MV and Kieser J. Restoration of non-carious cervical lesions. Part I. Modelling of restorative fracture. Dent Mater. 2007;23(12):1553-1561.

Appendix 1.

Allocation of criteria to clinical observations

A. Esthetic properties	1. Surface luster	2. Surface staining	3. Color stability and translucency	4. Anatomic form
1. Clinically excellent/ very good	1.1 Luster comparable to enamel	2.1 No surface Staining	3.1 Good color match. No difference in shade	4.1 Form is ideal
2. Clinically good (after polishing very good)	1.2 Slightly dull, not noticeable from speaking distance	2.2 Minor staining, easily Removable	3.2 Minor deviations	4.2 Form is only affected
3. Clinically sufficient/ satisfactory (minor shortcomings, no unacceptable effects but not adjustable w/o damage to the tooth)	1.3 Dull surface but acceptable if covered with film of saliva	2.3 Moderate surface staining, also present on other teeth, not Esthetically Unacceptable	3.3 Clear deviation but acceptable. Does not affect esthetics: 3.3.1 more opaque 3.3.2 more translucent 3.3.3 darker 3.3.4 brighter	4.3 Form differs but is not esthetically displeasing
4. Clinically unsatisfactory (but reparable)	1.4 Rough surface, cannot be masked by saliva firm, simple polishing is not sufficient. Further intervention Necessary	2.4 Surface staining present on the restoration and is unacceptable; major intervention necessary for improvement	3.4 (Localized) clinically unsatisfactory but can be corrected by repair; 3.4.1 too opaque 3.4.2 too translucent 3.4.3 too dark 3.4.4 too bright	4.4 Form is affected and unacceptable esthetically. Intervention (correction) necessary
5. Clinically poor (replacement necessary)	1.5 Quite rough, unacceptable plaque retentive surface	2.5 Severe staining and/ or subsurface staining (generalized or localized); not accessible for intervention)	3.5 Unacceptable. Replacement necessary	4.5 Form is completely unsatisfactory and/or lost. Repair not feasible/ reasonable, replacement needed
Overall esthetic score	Acceptable esthetically (n and %):		Not acceptable (n % and reasons):	

Allocation of criteria to clinical observations (continued)

B. Functional properties	5. fractures and retention	6. marginal adaptation	7. wear	8. contact point/ food impact	9. radiographic examination (when applicable)	10. patient's view
1. Clinically excellent/very good	5.1 Restoration retained, no fractures/cracks	6.1 Harmonious outline, no gaps, no discoloration	7.1 Physiological wear equivalent to enamel (80-129% of corresponding enamel)	8.1 Normal contact point (floss or 25µm metal blade of can be inserted but not 50µm blade)	9.1 No pathology, harmonious transition between restoration and tooth	10.1 Entirely satisfied
2. Clinically good (after polishing very good)	5.2 Small hairline crack	6.2.1 Marginal gap (<150µm) 6.2.2 Small marginal fracture removable by polishing	7.2 Normal wear with only slight difference to Enamel (50-80% or 120-150% of corresponding enamel)	8.2 Slightly too strong but no disadvantage	9.2.1 Acceptable material excess present 9.2.2 Positive/ negative step present at margin <150µm	10.2 Satisfied
3. Clinically sufficient/ satisfactory (minor shortcomings, no unacceptable effects but not adjustable w/o tooth)	5.3 Two or more or larger hairline cracks and/or chipping (not affecting the marginal integrity or proximal contact)	6.3.1 Gap <250µm not Removable 6.3.2 Several small enamel or dentin fractures	7.3 Differing wear rate to enamel but within biological variation (<50% of 150-300% of corresponding enamel)	8.3 Slightly too weakm no indication of danage to tooth, gingivae or periodontal structures (50µm metal blade can pass easily but not 100µm)	9.3.1 Marginal gap <250µm 9.3.2 Negative steps visible <250µm no adverse effects noticed 9.3.3 Poor radiopacity of filling material	10.3 Minor criticism of esthetics 10.3.1 Esthetic shortcomings 10.3.2 Some lack of chewing comfort 10.3.3 Time consuming procedure and/or similar; no adverse clinical effects
4. Clinically unsatisfactory (but reparable)	5.4 Chipping fractures which damage marginal quality or proximal contacts; bulk fractures with or without partial loss (less than half of the restoration)	6.4.1 Gap >250µm or dentin/ base Exposed 6.4.2 Chip fracture damaging margins 6.4.3 Notable enamel or dentin wall fracture	7.4 Wear considerably exceeds normal enamel wear; or occlusal contact points are lost (restoration >300% of enamel wear or antagonist >300%)	8.4 Too weak (100 µm metal blade can pass) and possible damage (food impacion) Repair possible	9.4.1 Marginal gap >250µm 9.4.2 Material excess accessible but not removable 9.4.3 Negative steps >250µm and reparable	10.4 Desire for improvement (reshaping of anatomic form or refurbishing etc.)
5. Clinically poor (replacement necessary	5.5 (Partial or complete) loss of restoration	6.5 Filling loose but in situ	7.5 Waer is excessive (restoration or antagonist >500% of corresponding enamel)	8.5 Too weak and.or clear demage (food impaction) and/or pain/gingivitis. Requires repalcement	9.5.1 Secondary caries, large gaps 9.5.2 Apical pathology 9.5.3 Fracture/loss of restoration or tooth	10.5 Completely dissatisfied and/or adverse effects incl. pain
Overall functional score	Acceptable function (n and %):			Not acceptable (n % and reasons):		

Allocation of criteria to clinical observations (continued)

C. Biological properties	11. Postoperative (hyper-sentivity and tooth vitality)	12. Recurrence of caries, erosion, abtraction	13. Tooth integrity (enamel cracks)	14. Periodontal response (always compared to a reference tooth)	15. Adjacent mucosa	16. oral and general health
1. Clinically very good	11.1 No hypersensitivity normal vitality	12.1 No secondary or primary caries	13.1 Complete integrity	14.1 No plaque, no inflammation, no pockets	15.1 Healthy mucosa adjacent to restoration	16.1 No oral or general symptoms
2. Clinically good (after correction very good)	11.2 Low hypersensitivity for a limited period of time, normal vitality	12.2 Very small and localized 1. demineralization 2. erosion or 3. abrasion/abfraction. No operative treatment required	13.2.1 Small marginal enamel split (<150mm) 13.2.2 Hairline crack in enamel (<150mm not probable)	14.2 Little plaque no inflammation (gingivitis). no pocket development	15.2 Healthy after minor removal of mechanical irritations (sharp edges etc.)	16.2 Minor transient symptoms of short duration (of known or unknown origin) local or generalized.
3. Clinically sufficient/ satisfactory (minor shortcomings, no unacceptable effects but not adjustable w/o tooth)	11.3.1 Premature/ slightly more intense 11.3.2 Delayed/ weak sensitivity; no subjective complaints, no treatment needed.	12.3 Larger areas of 1. demineralization 2. erosion or 3. abrasion/ abfraction but only preventive measures necessary (dentin not eposed)	13.3.1 Enamel split <250mm 13.3.2 Crack <250mm; no adverse effects	14.3.1 Plaque accumulation at acceptable level 14.3.2 Gingival bleeding acceptable 14.3.3 Pocket formation acceptable	15.3 Alteration of mucosa but no suspicion of causal relationship with filling material	16.3 Transient symptoms, local and/or general
4. Clinically unsatisfactory (repair for prophylactic reasons)	11.4.1 Premature/ very intense 11.4.2 Extremely delayed/weak with subjective complaints 11.4.3 Negative sentivity intervention necessary but no replacement	12.4.1 Caries with cavitation 12.4.2 Erosion in dentin 12.4.3 Abrasion/ abfraction in dentin. Localized and accessible and can be repaired	13.4.1 Major enamel split (gap >250mm or dentin or base exposed) 13.4.2 Crack >250mm (probe penetrates)	14.4.1 Plaque accumulation not acceptable 14.4.2 Gingival bleeding not acceptable 14.4.3 Pocket depth increase >1mm compared to reference tooth	15.4 Suspected mild allergic, lichenoid or toxicological reation	16.4 Persisting local or general symptoms of oral contact stomatitis or lichen planus or allergic reactions (or remitting). Intervention necessary but no replacement
5. Clinically poor (replacement necessary	11.5 Very intense, acute pulpits or nonvital. Endodontic treatment is necessary and restoration has to be replaced	12.5 Deep secondary caries or exposed dentin that is not accessible for repair of restoration	13.5 Cusp or tooth fracture	14.5 Severe/acute gingivitis or periodonititis	15.5 Suspected severe allergic, lichenoid or toxicological reation	16.5 Acute/severe local and/or general symptoms
Overall biological score	Acceptable biologically (n and %):			Not acceptable (n % and reasons):		
TOTAL SCORE	Acceptable biologically (n and %):			Not acceptable, reasons		

Afr. J. Med. Med. Sci. (2020) **49,** 307-314

Cardiovascular and anti-infective drugs utilization and expenditure from a community pharmacy in South-western Nigeria

ADA Adedapo[1], M Osiyemi[1] and IA Adedapo[2]
Department of Pharmacology and Therapeutics[1], University of Ibadan, College of Medicine, University College Hospital, Ibadan, Nigeria

Abstract
Background: Study of drug utilization and expenditure patterns is an important tool of the health system. A void exists in such research in sub-Saharan Africa. This is a pilot study on the drug expenditure and utilization patterns in an ideal community pharmacy in south-western Nigeria.
Methods: Data on drug expenditure (NGN) and drug quantity (mg) for cardiovascular and anti-infective drugs were obtained from the electronic database of the pharmacy over a period of twenty-two months. Data analysed within the period included 63,157 items.
Results: The total drug utilization, 50.82 kg and expenditure, NGN 30,908,084.10 ($190,790.64) for cardiovascular and anti-infective drugs within the study period comprised NGN 22,761,195.88 ($140,501.21) for anti-infectives (73.64%) and the remaining ¦ 8,146,888.22 ($50,289.43) for cardiovascular drugs (26.36%). Anti-infective drugs utilization was more, 48.14 kg (94.73%) compared to cardiovascular drugs, 2.68kg (5.27%) p<0.05. Antimalarial drugs utilization 2,253,000 mg at NGN 2,276, 255 ($14,050.96), accounted for about 10.0% of the total expenditure on anti-infective agents and 7.36% of the total expenditure for the study. Anti-tuberculosis drugs (isoniazid, ethambutol, pyrazinamide and rifampicin) a subclass of anti-infective agents had an aggregate expenditure of NGN 92,345.00 ($570.03). This accounted for about 0.41% of total expenditure on anti-infective agents. The total quantity of anti-tuberculosis drugs used within the study period was 504,950 mg.
Conclusion: The study showed huge expenditure and utilization on cardiovascular and anti-infective drugs within the study area. However, anti-infective drugs were more utilized suggesting that infection is more public goodS.

Keywords: *Drug utilization, cardiovascular, anti-infective, community pharmacy, pharmacoepidemiology.*

Correspondence: Dr. Aduragbenro D.A. Adedapo, Department of Pharmacology and Therapeutics, College of Medicine, University of Ibadan, Ibadan Nigeria. E-mail: debyee1965@yahoo.co.uk

Résumé
Contexte : L'étude de l'utilisation des médicaments et des modes de dépenses est un outil important du système de santé. Un vide existe dans de telles recherches en Afrique subsaharienne. Ceci s'agit d'une étude pilote sur les dépenses et les modes d'utilisation des médicaments dans une pharmacie communautaire idéale dans le sud-ouest du Nigéria.
Méthodes : Les données sur les dépenses en médicament (¦) et la quantité de médicament (mg) pour les médicaments cardiovasculaires et anti-infectieux ont été obtenues à partir de la base de données électronique de la pharmacie sur une période de vingt-deux mois. Les données analysées au cours de la période comprenaient 63.157 éléments.
Résultats : L'utilisation totale des médicaments, 50,82 kg et les dépenses, ¦ 30.908.084,10 ($190.790,64) pour les médicaments cardiovasculaires et anti-infectieux au cours de la période d'étude comprenaient ¦ 22.761.195,88 ($140.501,21) pour les anti-infectieux (73,64%) et les ¦ 8.146.688,22 ($50.289,43) restants pour les médicaments cardiovasculaires (26,36%). L'utilisation des médicaments anti-infectieux était plus élevée, 48,14 kg (94,73%) par rapport aux médicaments cardiovasculaires, 2,68 kg (5,27%) p <0,05. L'utilisation de médicaments antipaludiques 2.253.000 mg à ¦ 2.276.255 ($14.050,96) représentait environ 10,0% des dépenses totales en agents anti-infectieux et 7,36% des dépenses totales pour l'étude. Les médicaments antituberculeux (isoniazide, éthambutol, pyrazinamide et rifampicine), une sous-classe d'agents anti-infectieux ont eu une dépense globale de ¦ 92.345,00 ($570,03). Cela représentait environ 0,41% des dépenses totales en agents anti-infectieux. La quantité totale de médicaments antituberculeux utilisés au cours de la période d'étude était de 504.950 mg.
Conclusion : L'étude a montré d'énormes dépenses et utilisation de médicaments cardiovasculaires et anti-infectieux dans l'endroit d'étude. Cependant, les médicaments anti-infectieux étaient plus utilisés, ce qui suggère que l'infection est plus de bien public.

Mots-clés: *utilisation de médicament, cardiovasculaire, anti-infectieux, pharmacie communautaire, pharmaco-épidémiologie* .

Introduction

Humans seek ways of maintaining or improving health conditions. One of the most important ways of meeting health needs is the use of medicines. Analyses of drug utilization and expenditure need to be entrenched in health systems. Many new drugs have been introduced and are widely used in the treatment of various disease conditions [1]. These new drugs made up about 15% of the total new chemical and biological entities in the US in the year 2010 [1, 2]. How much of these are in use in Nigeria is yet to be ascertained. It has been observed that healthcare spending promises to remain relevant, with the government embarking on a continuous pursuit of a reduction in the expenditure. This goes to show how vital and important this area is and will remain to any country [3].

The increasing expenditures on drugs as a result of the introduction of the new drugs mount pressure, not only on the government, but also on the healthcare systems in their efforts to continue to provide comprehensive care. It has been advocated that there is a need for models for introducing newer and expensive medicines into the market [2] which include forecasting of drug utilization and expenditure patterns. Drug utilization study as defined by the World Health Organization in 1977 is the study of marketing, distribution, prescription, and use of drugs in a society, with special emphases on the resulting medical, social and economic consequences [4]. Sources of data on drug utilization include aggregated and patient level data such as sales, purchase, dispensing, and procurement data [5].

Drug utilization studies help our understanding of how drugs are being used in so many ways. At the patient level, it gives an idea of the number of patients exposed to a drug within a given period of time, either regarding the period of commencement of use (incidence), or over a period of time (prevalence) [4,5]. It can also explain the extent of use of such drug in a certain area, and this could form a component of a continuous evaluation system if the same patterns and trends are followed over time. The need to establish dedicated unit for analyses of medicine use as well as having expert committee in advisory capacity to drug utilization is germane [5]. Health care practitioners should be encouraged and empowered to undertake drug utilization studies in clinical practice.

Furthermore, drug utilization studies can be used to determine the pattern of drug use and the extent to which alternative medicines are being used to treat the same disease or health conditions. It affords comparisons of drug use with recommended guidelines. The ultimate aim of drug utilization studies is to aid the rational use of drugs in populations [4]. It as well gives a clearer understanding about the efficiency of drug use in real life, a phenomenon of real-world data for real-world evidence. The results obtained are useful in introducing or modifying drug policies at different levels of government. The metrics of drug utilization include costs and cost figures are needed for a complete analysis of drug expenditure.

Drug expenditure can then be said to be the monetary cost of acquiring drug items within a population [5]. Drug expenditure forms a major part of the total health care expenditure of countries all over the world, Nigeria inclusive. To this end, proper study of drug utilization and expenditure patterns is an important tool towards a better understanding and planning of the health system aimed at universal health coverage and access to medicine globally including Nigeria.

This work is a pilot study on the drug expenditure and utilization patterns in one of the biggest community pharmacy outlets in Ibadan, south-western Nigeria. The study focuses on trend in utilization and expenditure of cardiovascular and anti-infective drugs by a reference population. The selection of these few classes for this pilot study was based on a previous epidemiological report of cardiovascular and infective diseases ranking topmost of disease prevalence in a study on morbidity and mortality pattern [6]. Information gathered from hospital admissions in Adeoyo State Hospital, south-western Nigeria in 2012 showed that cardiovascular diseases especially hypertension and hypertension related diseases such as heart failure, cerebrovascular accident were the most frequent cause of admissions accounting for 36.8%, while infectious diseases followed with about 25% of all medical admissions in the hospital [6].

The study attempts to explicate the relationship between the cost of a drug product and its utilization or purchase by patients at community pharmacies. Deductions and results from such studies are of immense value to the health sector of the country as well as the entire economy of the nation. Aggregate data research on drug utilization and expenditure are few in sub-Saharan Africa, hence this study.

Materials and methods

Study site

This was a pilot study carried out at a community pharmacy located in Ibadan, a city in Oyo State, South west of Nigeria. It is one of the largest community pharmacies in the state. It sub-serves the major population of the Ibadan South West Local Government, made up of about 283,098 people [7].

Study design

This is a descriptive study. The data covering a period of twenty-two months (October 2011 and July 2013) from a community pharmacy was extracted from the database of the Pharmacy. The names (generic and brand names) of each drug studied were used to identify its location in the database. Thereafter, all the various formulations and strengths available for the drug were as well extracted.

Inclusion criteria

All drugs that belonged to the classes C (drugs acting on the cardiovascular system), J (anti-infectives for systemic use) and P (antimalarial drugs) [8] of the Essential Medicines List of the Federal Republic of Nigeria and World Health Organization [9, 10, 11], that were available at the Pharmacy for sale and recorded within the time frame of the study were included in the study.

Data extraction/collection

Each drug purchased, as proxy for drug utilization, analysed was made up of 6 rows, each providing information on the posting date (date of sale), drug description (brand name), selling price, generic name, strength and anatomical chemical classification (ATC) code up to at least the third level of classification. In all, annual expenditures for two pharmacological groups (cardiovascular and anti-infectives) at the third ATC level were included in the analysis. Expenditure was measured in Nigerian Naira (¦) (1U.S dollar= ¦ 162.00 as at March 2014).

The drug description row specified the unit of sales, whether per sachet of 10 or per sachet of fourteen while some drugs were sold and recorded per tablet. All the injectable formulations recorded were inputed as sales per ampoule or vial as the case may be. The drugs with different brand names but of the same generic origin were then merged for analysis as a single entity.

Data analysis

The data entry was with Microsoft Office Excel 2010. Manual, SAS 9.4 and SPSS analysis were done and then summarized in percentages and proportions appropriately. Cardiovascular and anti-infective drugs were analysed for differences with respect to quantity,

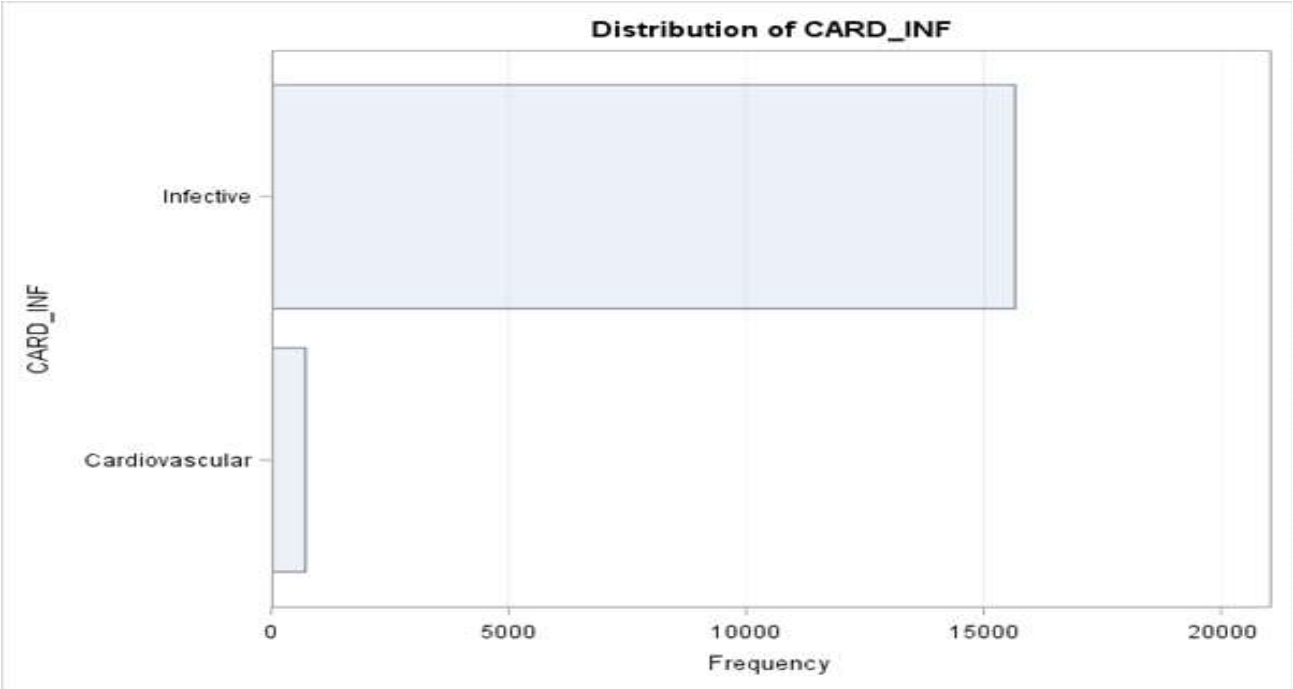


Fig. 1: Frequency of prescriptions of cardiovascular and anti-infective drugs in a community pharmacy between October 2011 to July 2013

cost/expenditure and total volume using analysis of variance and level of significance was set at $p < 0.05$.

Results

Overall, data for 63,034 items were extracted and analysed for the purpose of this study. The frequency of prescriptions of anti-infective drugs was far in excess of cardiovascular drugs (Figure 1).

Cardiovascular stimulants (C01C), cardiac glycosides (C01A) and vasodilators (C01D) had low expenditure while calcium channels blockers C08A, angiotensin converting enzyme inhibitors C09A and centrally acting antihypertensive drugs C02A constituted highest expenditure of the cardiovascular drug (Table 1).

Expenditure for anti-infective drugs was highest for beta-lactam J01C antibiotics NGN 5,660,135.00 (USD 34,939.10), followed by fluoroquinolines J01M NGN 2,659,105.00 (USD 16,377.19) and cephalosporins J01D USD 9.171.05 (NGN 1,585,710) in 2012. Clindamycin had the least volume and expenditure of the anti-infective drugs purchased from the community pharmacy (Table 2).

Antimalarial drugs constituted 5-7.3% and 8.2-12% of the volume and expenditure of the anti-infective drugs respectively. These included artemisinin combination therapies (ACTs) comprising the highest volume (68.26%) and expenditure (73.84%), quinine the lowest (3.13% volume, 0.49% expenditure) and halofantrine and chloroquine (Table 3).

Table 1: Aggregate Sales of Cardiovascular Drugs in a Community Pharmacy between October 2011 and July 2013

Name	ATC CODE	Utilization (mg)			Expenditure (NGN)			
		Oct-Dec 2011	Jan-Dec 2012	Jan-July 2013	Total	Oct-Dec 2011	Jan-Dec 2012	Jan-July 2013	Total
Cardiac glycosides	C01 A	115	357.50	268.75	741.25	5,060	18,695	11,900	35,655
Cardiac stimulants	C01 C	8	57	0	65	280	2,565	0	2,845
Vasodilators	C01 D	2,665	12,890	6,745	22,300	6,895	33,875	13,895	54,665
Centrally acting agents	C02 A	198,250	1,115,250	775,000	2,088,500	167,465	745,430	383,160	1,296,055
Diuretics	C03 D	14,245	55,665	35,530	105,440	115,745	514,790	314,330	944,865
Frusemide	C03 C	5,620	7,650	920	14,190	1,027.60	3,384.33	1,131.73	5,543.66
Beta blockers	C07 A	17,676.25	39,475	10,518.75	67,670	13,384.56	46,325	30,485	90,195
CCB	C08 C	42,620	166,225	77,515	286,360	588,275	2,090,050	934,180	3,612,505
ACEIs	C09 A	3,890	26,935	18,905	49,730	134,510	840,520	460,380	1,435,410
ACEI combination	C09 B	752.5	5,192.50	2,467.50	8,412.50	22,870	178,785	76,820	278,475
ARBs	C09 C	1,600	7,520	4,240	13,360	35,820	187,920	102,710	326,450
ARB combination	C09 D	1,695	4,375	170	6,240	25,660	37,155	1,410	64,225
Total		289,13675	1,441,592	932,280	2,663,008.75	1,116,992.16	4,699,494.33	2,330,401.73	8,146,888.32
Grand total			2,663,008.75				8,146,888.22		

CCBs calcium channel blockers; ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers.

Table 2: Aggregate Sales for Anti-infectives in a Community Pharmacy between October 2011 and July 2013

Class	ATC Code	Utilization (mg)				Expenditure NGN)			
		Oct-Dec 2011	Jan-Dec 2012	Jan-July 2013	Total	Oct-Dec 2011	Jan-Dec 2012	Jan-July 2013	Total
Tetracyclines	J01A	289,900	827,100	443,650	1,560,650	58,010	184,400	103,330	345,740
Penicillins	J01C	2,029,914	6,407,392	3,558,033.50	11,995,339.50	1,353,780	5,660,135	3,155,495	10,169,410
Cephalosporins	J01D	144,450	572,050	283,800	1,000,300	463,445	1,485,710	669,170	2,618,325
Sulphonamides	J01E	642,098	2,827,676	1,300,760	4,770,534	95,657.40	561,404.22	245,243.36	902,304.98
Aminoglycosides	J01G	154,000	668,000	386,000	1,208,000	13,565	55,755	30,480	99,800
Fluoroquinolones	J01M	551,230	1,821,906	731,970	3,105,106	776,895	2,653,105	969,385	4,399,385
Secnidazole	P01A	1,000	70,500	30,500	102,000	600	43,965	18,300	62,865
Nitroimidazole	J01X	844,700	3,516,200	1,973,100	6,334,000	97,015	508,365	265,270	870,650
Clindamycin	J01F	0	0	600	600	0	0	1,200	1,200
Nitrofurantoin	J01X	42,100	229,950	113,000	385,050	3,444	30,049.70	8,932.20	42,425
Antifungals	J02A	26,750	89,150	51,000	166,900	155,580	447,785	244,130	847,495
Antihelminths	PO2B	1,500	5,400	3,600	10,500	3,400	18,555	11,040	32,995
Antituberculosis	JO4A	71,945	287,305	145,700	504,950.00	19,150	48,110	25,085	92,345
Antimalarials	POIB	255,230	1,286,770	711,000	2,253,000	271,845	1,217,730	786,680	2,276,255
Total		5,054,817	18,609,399	9,732,713.5	33,396,929.50	3,312386.40	12,915,068.92	6,533,740.56	22,761,195.88
Grand Total			33,396,929.50					22,761,195.88	

Table 3: Aggregate sales for antimalarial drugs between October 2011 and July 2013 including percentage of the total anti-infective drug utilisation and expenditure

Name	ATC Code	Utilization (mg)				Expenditure (NGN)			
		Oct – Dec 2011	Jan – Dec 2012	Jan – July 2013	Total	Oct – Dec 2011	Jan – Dec 2012	Jan – July 2013	Total
Artemisinin combination	P01B	17,4030	835,570	528,400	1,538,000	194,755	903,295	582,625	1,680,675
Halofantrine	P01B	27,500	99,500	68,000	195,000	70,020	278,645	184,610	533,275
Chloroquine	P01B	48,600	310,300	90,600	449,500	6,390	29,580	15,240	51,210
Quinine	PO1B	5,100	41,400	24,000	70,500	680	6,210	4,205	11,095
Total (%)		255,230 (5.05)	1,286,770 (6.91)	711,000 (7.31)	2,253,000	271,845 (8.21)	1,217,730 (9.43)	786,680 (12.04)	2,276,255
Grand total			2,253,000				2,276,255		

Rifampicin J04A recorded the highest expenditure of the anti-tuberculosis drugs, while ethambutol had the lowest (Table 4).

Looking at the data obtained for chloroquine accounted for 2.25% (NGN 51,210; $316.11) of the total expenditure on antimalarial drugs for the twenty-

Table 4: Aggeregate Sales for Anti-tuberculosis Drugs in a Community Pharmacy between October 2011 to July 2013

Name	ATC Code	Utilization (mg)				Expenditure (NGB)			
		Oct–Dec 2011	Jan–Dec 2012	Jan–July 2013	Total	Oct–Dec 2011	Jan–Dec 2012	Jan-July 2013	Total
Isoniazid	J04A	2,145	3,355	1,150	6,650	4,290	13,220	4,600	22,110
Ethambutol	J04A	0	12,000	8,800	20,800	0	3,150	2,310	5,460
Pyrazinamide	J04A	50,000	237,000	112,500	399,500	1,000	5,510	1,125	7,635
Rifampicin	JO4A	19,800	34,950	23,250	78,000	13,860	26,230	17,050	57,140
Total		71,945	287,305	145,700	504,950	19,150	48,110	25,085	92,345
(% of total anti-infective		(1.42)	(1.54)	(1.50)		(0.58)	(0.37)	(0.38)	
Grand total			504,950				92,345		

Anti-infective drugs significantly were more than cardiovascular drugs in quantity and cost/expenditure $p<0.05$ (Table 5).

two months study period. This shows it is still used, despite the withdrawal for *P. falciparum* malaria treatment, however, when combined with primaquine,

Table 5: Comparative analysis of quantity, cost and total volume of cardiovascular and anti-infective drug prescriptions from a community pharmacy between October 2011 to July 2013

		Sum of Squares	df	Mean Square	F	Sig.
Quantity	Between Groups	3020.299	1	3020.299	275.535	.000
	Within Groups	692279.099	63155	10.962		
	Total	695299.398	63156			
Cost/expenditure	Between Groups	3599623.776	1	3599623.776	7.303	.007
	Within Groups	31129254852.593	63155	492902.460		
	Total	31132854476.368	63156			
strength (mg)	Between Groups	1618499743.472	1	1618499743.472	50336.563	.000
	Within Groups	2030658130.610	63155	32153.561		
	Total	3649157874.082	63156			
Total utilization (mg)	Between Groups	3467075112.227	1	3467075112.227	2848.590	.000
	Within Groups	76867204529.530	63155	1217119.856		
	Total	80334279641.757	63156			

Discussion

Considering the fact that these above figures were obtained from one of the community pharmacies in Oyo state, Nigeria, it is evident that drug expenditure makes up a huge part of the national healthcare budget of Nigeria. As at 15th of March, 2012, about 130 community pharmacies were registered in Oyo state. If just one of these pharmacies had drug expenditure and utilization values as high as those obtained in this pharmacy, then it can be categorically said that community pharmacies also a play a big role in the health care system of the country.

it is the treatment of choice for sensitive *P. vivax* malaria [12]. Its use may be due to its perceived safety and efficacy by some individuals or due to its indication in other condition [13-15]. Albeit, when compared to other antimalarial drugs, its use is considerably lower. This is understandable considering the fact that chloroquine is no longer an essential drug and has been effectively substituted with fixed dose Artemisinin Combination Therapies (ACTs), which form the heart of the WHO strategy to control malaria. ACTs had an outstanding proportion of over 76% of the total antimalarial drug expenditure. This is not surprising because it is the

efficacious and the recommended drugs for malaria treatment which has led to remarkable awareness campaign on the safety and efficacy of the drug regimens.

From Table 2, Beta lactam antibiotics had the highest drug expenditure. Examples of such antibiotic include amoxicillin, ampicillin, cloxacillin, flucloxacillin etc. Some contributing factors to this high expenditure include high cost of some brands (such as Beecham Amoxil, GSK Augmentin etc).

Anti-tuberculosis drugs (e.g pyrazinamide, rifampicin, ethambutol, and isoniazid) made up just about 0.41% of total expenditure for anti-infective agents. This may give a false pointer to the reduction in the incidence of tuberculosis in the country. However, there are various Donor Agencies who give the drugs free to patients in the hospitals with a view to ensure direct observed therapy (DOT) for enhanced adherence to medication. Rifampicin had the highest demand (NGN 57,140; $352.72), followed distantly by isoniazid. This is apparent, knowing that rifampicin has a wide variety of uses apart from tuberculosis, namely: leprosy, serious staphylococcal infections, and prophylaxis of meningococcal meningitis and *Haemophilus influenza* (type B) infection as well as in combination with vancomycin for the treatment of suspected or known penicillin resistant strains of pneumococcus [13,14,16-18].

Future studies to give an insight into the factors affecting drug utilization and expenditure within community pharmacies are suggested. These will attempt to explicate the relationship between the cost of a drug product and its utilization or purchase by patients at community pharmacies. Other potential data sources include the National Health Insurance Scheme (NHIS) for further work on such drug utilization and expenditure studies. A minireview of the NHIS claims database in Ghana muted among other things lack of access to databases as a hindrance to drug utilization research [19].

From the pilot study carried out, drug expenditure seems to be a more accurate method of evaluating drug utilization than drug volume. This is because a standard unit of cost can be used for all the items in a study. In this case, the unit of cost was the Nigerian currency, which is the Nigerian naira (NGN). Comparisons can be made with drug expenditure values of other countries by merely using appropriate conversion rates. Therefore, the amount spent on all drug items, whether tablets, syrups, suspensions or injections, was measured in naira (NGN). However, the standard method of expressing drug utilization to afford comparison with other countries is the defined daily dose (DDD) [4].

Whereas in the case of evaluation of drug volume, the unit mostly used in the study was the milligram (mg). This is not uniform for all drugs. For instance, crystal penicillin is produced in International Units (I.U) and this could lead to an unnecessary increase in the measurement of anti-infective drug volume if not converted to milligram. Injections are also produced in milligrams per milliliter (mg/ml) necessitating appropriate conversion. These variations need to be put into consideration in achieving accurate evaluation of drug volumes. Comparison of drug utilization within drug group while feasible becomes rather challenging across drug group. Further work can be done on the Defined Daily Dose (DDD) which presents a better and standard way of quantifying drug volume.

Drug expenditure makes up an important part of the total healthcare expenditure of Nigeria [20]. There is a positive relationship between health care expenditure and economic growth [21].

Limitations

Data for three years was originally intended, but due to challenges with the database of the pharmacy, the electronic database only provided the data that was available in the pharmacy for October 2011 to July 2013. D ata on antiviral drugs (J05) were not available.

Conclusion

The evaluation of drug expenditure and utilization in this study has shown the higher use and more expenditure for anti-infective drugs which may suggest that infective conditions are public goods.

Acknowledgements

Professor Lars Gustafsson, Sweden is appreciated for suggesting the study and providing the first reference. Professor Adedoyin Soyibo is appreciated for his prompt review of the manuscript and provision of necessary reference. The cooperation of the Management and Staff of the Pharmacy is profound. We acknowledged MIM for providing the platform to present the abstract at 7th African MIM Conference held in Dakar, Senegal on April 16 -20, 2018.

References

1. Li P, Zheng Y and Chen X. Drugs for Autoimmune Inflammatory Diseases: From Small Molecule Compounds to Anti-TNF Biologics. Front. Pharmacol. 2017; 8:460. doi: 10.3389/ fphar.2017.00460 (Accessed January 6, 2020)

2. Wettermark B, Persson ME, Wilking N, *et al*. Forecasting drug expenditure and utilisation patterns in a metropolitan health region. BMC Heal Serv Res. 2010;10(128):4–17.
3. Hoffman JM, Li E, Doloresco F, *et al*. Projecting future drug expenditures in U.S. nonfederal hospitals and clinics—2013. Am J Heal Pharm, 2013; 70(6):525–539. doi:102146/ajh120759.
4. World Health Organisation / WHO International Working Group for Drug Statistics Methodology; WHO Collaborating Centre for Drug Statistics Methodology; WHO Collaborating Centre for Drug Utilisation Research and Clinical Pharmacological Services. Introduction to drug utilisation research. 2003. 6-10 p.
5. World Health Organization. Methods to analyse medicines in utilisation and expenditure to support pharmaceutical implemetation. Geneva: 2018. Licence CC BY-NC-SA 3.0 IGO
6. Adedapo ADA, Fawole O, Bamgboye A, *et al*. Morbidity and mortality patterns of medical admissions in a Nigerian secondary health care hospital. Afr J Med Sci. 2012;41(1):13–20.
7. National Bureau of Statistics Federal Republic of Nigeria. Annual Abstract of Statistics, 2011. 2011.
8. WHO Collaborating Centre for Drug Statistics Methodology, ATC classification index with DDDs 2020. Oslo 2009.
9. The Federal Ministry of Health Abuja Nigeria in collaboration with World Health Organization and European Commission. Essential Medicines List [Internet]. 5th ed. 2010 [cited 2019 Mar 8]. Available from: http://apps.who.int/medicinedocs/documents/s19018en/s19018en.pdf
10. World Health Organization. WHO Department of Essential Drugs and Medicines., 2014
11. Sowunmi A. University College Hospital, Ibadan Essential Drugs List and Formulary. 4th revisi. Daybis limited, Ibadan, Nigeria; 2011.
12. World Health Organisation. Guidelines for the treatment of malaria. 2nd edition. Geneva: 2010.
13. British National Formulary. 62nd ed. BMJ Group Tavistock Square, London WCIH 9JP,UK; 2011.
14. British National Formulary. 76th ed. BMJ Group Tavistock Square, London WCIH 9JP,UK; 2019.
15. Taherian, E., Rao, A., Malemud, C. J., and Askari, A. D. The biological and clinical activity of anti-malarial drugs in autoimmune disorders. Curr. Rheumatol. Rev. 2013; 9, 45–62. doi: 10.2174/1573397111309010010
16. Mandell GL and Petri WA. Antimicrobial agents (continued) Drugs used in the chemotherapy of tuberculosis, Mycobacterial avium complex disease, and leprosy. In: Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, editors. Goodman's and Gilman's The pharmacological basis of Therapeutics. 9th ed. Mc Graw Hill USA; 1996. p. 1155–74. 10.
17. Beauduy CE, Winston LG. Beta-Lactam & other cell wall-& membrane-active antibiotics. In: Katzung BG, editor. Basic and clinical pharmacology. 14th ed. USA: McGraw-Hill 2018; pg 795-814.
18. Beauduy CE and Winston LG. Antimycobacterial drugs. In: Katzung BG, editor. Basic and clinical pharmacology. 14th ed. USA: McGraw-Hill 2018 pgs 842-852.
19. Ankrak D, Hallas J, Odei J *et al*., A review of the Ghana National health insurance scheme claims database: possibilities and limits of drug utilization research. Basic and Clinical Pharmacology and Therapeutics 2019;124(1): 18-27 https://onlinelbrary,wiley.com/doi/full/10.1111/bcpt.13136
20. Soyibo A, Olaniyan O and Lawanson AO. National health accounts: Structure, trends and sustainability of health expenditure in Nigeria. African J Econ policy. 2007;14(1):83–109.
21. OECD. "Health expenditure and financing: Health expenditure indicators", OECD Health Statistics, 2019 (database), https://doi.org/10.1787/data-00349-en (Accessed on 31 December 2019).

Afr. J. Med. Med. Sci. (2020) **49,** 163-171 *Review Article*

The use of herbal medicine for treatment of HIV infection

AA Onifade

Immunology Department, College of Medicine, University of Ibadan, Ibadan, Nigeria, School of Laboratory Medicine and Medical Sciences, University of KwaZulu Natal, South Africa

Abstract

*Background***:** It was documented by the World Health Organization that the use of herbal medicines for treatment of illnesses is common. Human immunodeficiency (HIV) infection is a chronic illness which catalyses the interest of infected patient to source for herbal therapy.

Aim: This review aimed at reporting efficacy and safety of herbal medicines used for treatment of HIV infection. The search engine of herbal medicine, products, medicinal plants, alternative therapy, complementary therapy used for HIV infection in Pub med, Science direct, Google scholar and Scopus were used.

*Result***:** The widely reported availability and potency of products, belief and culture of people are useful aids to herbal medicine practice. Some of these documented potent herbal medicines were used as complementary therapy especially for the symptoms and signs associated with HIV infection. With advent of free and accessible highly active antiretroviral therapy (HAART) there are some documented beneficial or deleterious effects when some herbal medicines are used as complementary therapy. Some documented herbs have been identified to be effective against the dreadful organism, HIV and may be used as complementary or alternative therapy

Conclusion: This review show that many herbal medicines have potential for treatment of HIV infections however, documented efficacy and safety especially with possible drug interactions with orthodox drugs need further exploration.

Keywords: *Herbal medicines; chronic illness; safety; efficacy; drug interaction*

Résumé

Contexte: Il a été documenté par l'Organisation Mondiale de la Santé que l'utilisation de plantes médicinales pour le traitement des maladies est courante. L'infection immunodéficience humaine (VIH) est une maladie chronique qui catalyse l'intérêt du patient infecté à se procurer de phytothérapie.

Objectif **:** Cette revue visait à signaler l'efficacité et l'innocuité des plantes médicinales utilisées pour le traitement de l'infection par le VIH. L'engin de recherche de la phytothérapie, des produits, des plantes médicinales, des thérapies alternatives, des thérapies complémentaires utilisées pour l'infection à VIH dans Pub med, Science direct, Google scholar et Scopus ont été utilisés.

*Résultat***:** La grande disponibilité et la puissance des produits, la croyance et la culture des gens sont des aides utiles à la pratique de la phytothérapie. Certains de ces médicaments à base de plantes puissants documentés ont été utilisés comme thérapie complémentaire, en particulier pour les symptômes et les signes associés à l'infection par le VIH. Avec l'avènement de la thérapie antirétrovirale hautement active gratuite et accessible (HAART), il existe des effets bénéfiques ou délétères documentés lorsque certains médicaments à base de plantes sont utilisés comme thérapie complémentaire. Certaines herbes documentées ont été identifiées comme étant efficaces contre l'horrible organisme, VIH et peuvent être utilisées comme thérapie complémentaire ou alternative

Conclusion **:** Cette revue montre que de nombreux médicaments à base de plantes ont un potentiel pour le traitement des infections VIH, cependant, l'efficacité et l'innocuité documentées, en particulier avec les interactions médicamenteuses possibles avec les médicaments orthodoxes, nécessitent une exploration plus approfondie.

Mots-clés : *plantes médicinales ; maladie chronique ; sécurité ; efficacité ; interaction médicamenteuse*

Introduction

The burden of HIV infection cannot be over-estimated. Human immunodeficiency virus infection is a great burden to individual patients, families and friends, communities and nations at large. The United Nations reported that HIV infection gulped over 20 billion

Correspondence: Dr. A.A. Onifade, Department of Immunology, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: abdulfattahkunle@gmail.com

dollars in 2017 alone and there is increasing pressure on nations to commit more funds for subsequent years [1]. Despite this huge amount of fund committed by nations, almost one million people lost their lives to HIV - related diseases in 2017 [1]. The fact that HIV is not curable and its association with immune deficiency resulting in opportunistic infections that may not respond to antimicrobial agents prompted many infected patients to find solace in herbal medication [2, 3]. With advent of HIV infection, the use of herbal medicine is becoming popular as documented by the World Health Organization [4, 5].

Herbal medicine is heavily used worldwide. In the rural and poor socio-economic areas in developing countries, herbal medicine is usually the option before or immediately after failed self medication [2, 4, 5]. In many of these countries, popularity of herbal medicine is increasing because there is freedom of publicity of the potential drug by the herbal therapist which is not enjoyed by orthodox medical practitioners because of regulation. This is complicated by inability of orthodox health practitioners to satisfactorily explain with scientific evidence the roles and limitations of herbal medicines due to paucity of documented facts about the therapy [6, 7]. It is worthy to note that many orthodox medical schools do not have curriculum for herbal medicines thus their graduates would out rightly condemn their use even if some are beneficial [5-8]. However, in developed countries, the use of scientific methods with technology has made herbal medicine more popular and acceptable to many people when compared with sophisticated theories that usually transferred from one groups, societies, communities or generation to another in developing world [6, 8]. In fact in these countries, the safety of many herbal medicines and their possible interactions with orthodox drugs are now in public domain thus causing fewer problems within medical circle [5]. In this review, factors that encourage use of herbal medicine to treat HIV infection are enumerated below.

Human immunodeficiency (HIV) infection as a chronic or terminal illness

As of now, no proven and acceptable scientific curable agent has been approved for HIV infection. Because HIV infects immune cells and destroys them gradually, there will be reduction in these immune cells leading to poor performance in specific immune response until it reaches elastic limit where opportunistic infections and related diseases start their manifestations [9]. Continuous weight loss and/or fever that are not responding to conventional orthodox medication are blanket approval to herbal medicine exploration [10]. Because of poor quality of life associated with progressive advanced HIV infection, any potential therapeutic option would be welcome and herbal medicine is the first or second choice to spiritualism. The orthodox therapeutic agents termed highly active antiretroviral therapy (HAART) is associated with some side-effects that could make some HIV patients to source for alternative or complementary solutions [2, 4, 5].

Herbal medicine as blood cleanser

Herbal medicines are usually associated with multiple functions [11-15]. It is generally believed that herbal medicines taking orally clean blood from all infectious agents. The claim that herbal medicine can be used for multipurposes cannot be overestimated [14, 15]. It is not uncommon to read the claims of some herbal therapists that their herbal medicines flush all kinds of diseases in the body [3]. Because advanced HIV infection or AIDS is associated with many diseases, the blood cleanser option may be considered by HIV patients [3, 10, 12]. Therefore many HIV patients would have tried to explore herbal medicines that could treat multiple symptoms of HIV infection before presentation in orthodox health care centres [3, 10].

Poverty

The use of herbal medicines had been associated with financial capability in low economic countries [16, 17]. It is generally believed in rural areas that herbal medicines are cheap because of their abundance in the community. In urban areas, because of poverty or need for monetary gains, demand for herbal medicines for HIV infection was increasing thus herbal therapists' businesses are proliferating [16]. Average HIV patient is desperate to get the virus completely out of the body therefore he/she may be ready to spend affordable amount on potential beneficial herbal medicine [17].

Belief and culture

There is no doubt that belief is very important in African and Asian communities. Many Africans, Asians and other ethnics have high inclination towards the use of herbal medicines for treatment of illnesses [4, 5]. It is generally believed that herbal medicines are natural and gift of God therefore will perform wonders [18].

Herbal therapists are usually respected in their communities because of their previous services rendered for other illnesses therefore leading to an assumption that HIV infection will not be an exception [6, 19]. This belief and culture influence the patient orientation for seeking therapy for illness especially chronic infection like HIV/AIDS [6, 16-19]

Poor regulation

There is no strict regulation on use of herbal medicine by herbal therapists or the patients when compared to orthodox drugs. There is no need for prescription to buy herbal medicine. Many of the herbal medicines are not registered by government agency. There is no formal entry or qualification or registration of herbal therapist dispensing herbal medicine [16, 17, 20]. The porosity of herbal medical practice has aided the patronage of HIV patients who want service for their health by all means.

Herbal medicines and HIV infection (efficacy)

Herbal medicines are used for HIV infection as alternative or complementary therapy to orthodox antiretroviral therapy (HAART). The use of herbal medicine is very popular among symptomatic (moderate and advanced) HIV patients [21, 22]. It was reported that about 70% of HIV infected patients had use herbal remedies before commencing ARV [21]. Herbal medicines are usually used for HIV infection symptoms like diarrhea, fever, pain, anxiety, cough, weight loss, insomnia, weakness, etc [23-25]. Despite the fact that there is paucity of scientific evidence for the use of many herbal medicines, very few had been well documented. Some herbal medicines have been documented to be effective for HIV infection [26-29]. It was reported that some HIV patients used herbal remedies that contained the components or whole of garlic (*Allium sativum L.*) *Neem* , *Baissea hua*, *Nigella sativa*, hypoxis, ginger (*Zingiber officinale*), and moringa (*Moringa stenopetala*), *Acacia karroo Hayne* etc. [12, 21, 31]. These herbal medicines may be taken alone or in different combination formulations as complementary or alternative to ARV. These herbal combination formulations are marketed in different names e.g Fuzheng Paidu, Jobelyn that contained *Sorghum bicolor* plant leaves (13.8%), Garlic containing Allicin, ã-glutamyl- (s)-ally-L-Cysteine (10.3%), Ginger of 17.2% and *Aloe vera* [Hydroxyanthracene derivatives expressed as Barbaloin] (10.3%), [32-34]. Some of these herbal medicines had been used as complementary therapy with ARV. It was reported that some herbal medicines were used to relieve nausea, vomiting, diarrhea and anaemia associated with HAART [22-24, 35]. Some components of HAART had been associated with pain, depression and anxiety thus Cannabis had been in use by some HIV patients to relieve these problems [36]. It was documented that some herbal remedies ameliorated the opportunistic diseases associated with advanced HIV infection like candidiasis [37-39]. Some herbal medicines eg *Nigella sativa*, Jia-Wei-Xiao-Yao-San, Ge-Gen-Tang, Yin-Qiao-San have been documented to lower the risk of hyperlipidemia and hypertension associated with ARV [40, 41].

There are many herbal remedies that have been documented to have efficacy like HAART or its components [24, 25]. It was reported that Chinese herbal medicines caused sero-reversion in eight HIV patients [42]. Lamiaceae herbal families that are used for aromatic spices like thyme, savory, lemon balm, sage, mint, basil, hyssop, oreagano, rosemary, etc., act on HIV envelope antigens thus preventing attachment and entrance into cell (fusion inhibitor). They also act on some enzymes that inhibit viral cycle replicative cycle [43]. Arylnaphthalide lignans (ANL) glycosides obtained from fractionated stems and barks of Acanthaceae (*Justcia gendarussa*) is a potent anti-HIV medicinal plant better than Zidovudine [7]. Arylnaphthalide lignans glycosides was documented to inhibit nucleoside reverse trancriptase inhibitor (NRTI) and non nucleoside reverse transcriptase inhibitor (NNRTI) resistant strains of HIV isolates: HIV- $1_{1617\text{-}1}$ (Zidivudine analogue) and HIV-1_{N119} (Nevirapine analogue) respectively [7]. *Asteraceae* herbal family likes *Bidens pilosa* and *Sonchus oleraceus* plants have work acid which is a potent anti-HIV integrase inhibitor [44]. Medicinal plants of *Guttiferae* family, *Hypericum* genus with carbocyclic nucleosides from iridoid glucosides have been reported to have potent anti-HIV activities [45]. It was documented that stem, bark, root, seeds and fruits of *Combretaceae, Anacardiaceae , Mimosaceae and Ebanaceae* families of medicinal plants that were used to treat herpes simplex, herpes zoster, diarrhea, skin infection, malaria, candidiasis, tuberculosis and meningitis in Namibia are potent anti- HIV medicinal agents [10, 46]. Cameroonian medicinal plant extracts of root and bark of Pierre (Anacardiaceae) *Antrocaryon klaineanum* that has anti-parasitic effects on plasmodium and trypanosome had been documented

to be a potent anti-HIV integrase inhibitor [47]. The methanol extracts of *Alchornea laxiflora extracts from roots, stem and leaves are potent integrase inhibitor [48]*. *Sennoside A, a constituent of Rheum palmatum* L. and *Rheum officinale* from Rhubarb have been documented to be a potent reverse transcriptase inhibitor [49]. A fungal endophyte of *Quercus emoryi* (*Alternaria tenuissima*) and its epoxyperylene derivative in altertoxins at low concentrations that is not toxic to T cells is an effective anti-HIV agent [50]. The Chinese herb derivative, Sparstolonin B (SsnB) was found to effectively inhibit HIV-1 transcription when used alone or in combination with Zidovudine (AZT) [51]. Fusion inhibition is very important to HIV prevention and control, Cinnamon derivative, type A procyanidin polyphenol has been documented to be a potent HIV-1 entry blocker of CXCR4 and CCR5 [52]. Lichen, a methanol extract from *Ramalina farinacea* is a potent antiretroviral medicinal plant [53].

Drug interaction

It is highly important that health practitioners should be aware that many of the HIV patients take herbal medicines. It has been documented that many HIV patients denied during history taking when asked about the use of herbal medicine [17, 21, 24]. Health practitioners should be aware that despite availability of HAART, some HIV patients take herbal medicine as alternative or complementary medicine to orthodox medicines [17]. It was observed that level of education does not deter HIV patients from seeking herbal medicine for HIV infection [17]. Awareness of use of herbal medicine as complementary therapy by medical practitioners will guide in case of negative drug interaction. The earlier reported studies that there was negative interaction when garlic, St John's wort and hypoxis were used with orthodox antiretroviral therapy had been guiding medical practitioners in assessing HIV patients on the listed herbal remedies [54].

The herbal remedies may cause decrease in metabolism of ARV, this may be beneficial by prolonging the antiviral effects of the drug [55]. However, this may also cause prolonged side-effects of the ARV in HIV patients. The hepatic inducer herbal medicines will accelerate metabolism thereby reducing efficacy of ARV thus leading to serious problems [56]. Declaration of concomitant drug use with orthodox or herbal medicines will be of help in HIV management thus reducing possible negative herbal-orthodox drug interactions [57]. *Hypericum perforatum* (St John's Wort) significantly reduced protease inhibitors eg indinavir. In this study, it was observed that St John's wort significantly caused reduction in extrapolated 8-h trough and area under the curve when used as complementary therapy with Indinavir, an anti-HIV protease inhibitor [58]. However, not all herbal medicines negatively interact with orthodox medicines. *Moringa Oleifera* that is widely used by many people as herbal medicine for common illnesses did not alter nevirapine pharmacokinetics [59]. Likewise African potato *(Hypoxis hemerocallidea*) that is widely available and popular in Africa as medicinal plant and used for many illnesses including HIV infection does not negatively interact with orthodox medications [60]. Some HIV/AIDS patients use this traditional medicine together with their antiretroviral therapy and it was documented that *H. hemerocallidea* did not affect Lopinavir and Indinavir concentrations [60-62].

Problems

There are potential problems associated with HIV management especially when herbal medicines are used with HAART. Belief and attitude of HIV patients to herbal medicines, there may be skipping of HAART which may lead to drug resistance [63, 64]. It was reported that about one third of patients on ARV will use traditional medicine as complementary or alternative therapy thus causing problem with adherence [65-67]. It has been well documented that many of the HIV infected patients using herbal remedies denied when asked by orthodox health practitioners therefore making wrong management of drug resistance [17, 64, 68]. The possible negative drug interaction between HAART and undocumented herbal medicine could lead to organ damage [55].

Solution

There is no doubt that the use of herbal medicines cannot be stopped therefore there is need to develop solutions to the problems associated with the herbal practice [69]. Since the use of herbal medicine is not restricted to races or continents, the concerted efforts to standardize and regulate the practice as done for orthodox medicine will be the best approach. Human immunodeficiency virus infection is a chronic illness and pandemic led to well-coordinated concerted efforts from all nations [1]. Since HIV patients cannot be stopped from seeking herbal remedies globally, there is need to document and develop all the potential

medicinal plants into acceptable and standard medications that will be available and affordable to all like HAART [70, 71]. These medicinal plants can be categorized into complementary and alternative therapy to HAART having passed through required minimum research standard. Since wide availability and affordability of HAART, there are more tendencies that HIV patients may take herbal medicines as complementary therapy thus the need for extensive research on common medicinal products interaction with HAART by appropriate institutions [72-74]. The use of modern technologies in research could facilitate development of potential herbal medicines into standard form like orthodox medicines [75-77]. With the advent of HIV drug resistance, there is need to use multiple targets antimicrobial agents which herbal medicines are known to be very useful [78-80].

There is lack of trust and the level of Western education that will be required to communicate their findings by herbal therapists to orthodox health practitioners, many facts have been kept without access thus hampering traditional drug development [16]. There is need to have herbal medicine side-by-side with orthodox care at all levels of health facilities. Any potential herbal medicine for HIV infection should be incorporated as complementary or alternative to orthodox medicine after research has confirmed the efficacy and safety of such products [22, 81]. Orthodox medical education should incorporate herbal medicine into their programmes at all level. There is need for orientation on co-existence and practice of both medical practitioners and herbal therapists rather than passing blames on each other [82].

Conclusion

Herbal medicines are widely available in our environment and are used by HIV patients because of their potentials as complementary or alternative to orthodox medicines. Some of these herbal medicines efficacy have been documented and there is need for translational research so that they can be available to other HIV patients that are not accessible to these medicinal plants. Integration of herbal medicines into Western education and health care system at all cadres will help in accessing many hidden knowledge and increase the confidence of herbal practitioners. Herbal medicines are potent and could serve as complementary to HAART after safety profiles of such products have been established. With proper regulation of herbal medicine practice, research and orientation of medical practitioners and herbal therapists, HIV patients will benefit more, communities and nations will be happier because HIV infection will be well controlled if not eradicated

References

1. UNAIDS/WHO. AIDS epidemic update: 2018, July; pp. 1–376
2. Bannerman R Traditional Medicine and Healthcare. Geneva. WHO, 1993
3. Kisangau D, Lyaruu H, Hosea K, Joseph C Use of traditional medicines in the management of HIV/ AIDS opportunistic infections in Tanzania: a case in the Bukoba rural district. J Ethnobiol Ethnomed; 2007 10: 24-27
4. World Health Organization. Traditional medicine; growing needs and potential. WHO Policy perspectives on medicines, WHO, Geneva; 2002, 1-6
5. WHO. Traditional Medicine Strategy 2014-2023; WHO, Geneva; 2013, 1-78
6. Zhang X . Integration of traditional and complementary medicine into national health care systems. J Manipulative Physiol Ther; 2000, 23: 139-140
7. David M. Advising Patients who seek alternative medical therapies. Ann Intern Med; 1997, 27(1): 61-69.
8. Stephen M, Margaret L and Robert M. Complementary and alternative medical practices: training, experiences, and attitudes of a primary care medical school faculty. J Am Board Fam Pract; 2003, 16: 318-326
9. Ostrowski M. A., Krakauer D. C., Li Y., *et al*. Effect of immune activation on the dynamics of human immunodeficiency virus replication and on the distribution of viral quasispecies, *Journal of virology*, 1998, *72*(10), 7772-7784.
10. Gail H, Tarryn B, Oluwaseyi A, *et al*. An ethnobotanical survey of medicinal *plants* used by traditional health practitioners to manage *HIV* and its related opportunistic *infections* in Mpoza, Eastern Cape Province, South Africa Journal of Ethnopharmacology, Volume 171 (2) 109-115.
11. Maroyi A. Acacia karroo Hayne: Ethnomedicinal uses, phytochemistry and pharmacology of an important medicinal plant in southern Africa. Asian Pac J Trop Med. 10 (4):351-360. doi: 10.1016/ j.apjtm.2017.03.021. Epub 2017 Apr 6.

12.Pandey H, Pandey P, Singh S, Gupta R and Banerjee S. Production of anti-cancer triterpene (betulinic acid) from callus cultures of different Ocimum species and its elicitation; 2015, 252(2):647-655.

13 Saeki H, Hara R, Takahashi H, *et al*. An Aromatic Farnesyltransferase Functions in Biosynthesis of the Anti HIV Meroterpenoid Daurichromenic Acid. Int J Mol Sci. 2018, 14;19(5). pii: E1459. doi: 10.3390/ijms19051459.

14. Pang X, Kang LP, Fang XM, *et al*. Polyoxypregnane Glycosides from the Roots of Marsdenia tenacissima and Their Anti-HIVActivities. ; 2017, 83(1-02):126-134.

15. Afolayan AJ, Otunola GA. Ultrastructure and elemental analysis of Hypoxis hemerocallidea: a multipurpose medicinal plant. Afr J Tradit Complement Altern Med. 2014, 11 (4):39-43.

16.Bamidele J, Adebimpee O and Oladele. Knowledge, attitude and use of alternative medical therapy amongst urban residents of Osun State SouthWestern Nigeria. Afri J Trad Compl Altern Med. 2009, 6 (3):281-288

17. Onifade A.A., Ajeigbe K.O., Omotosho I.O., Rahamon S.K and Oladeinde B.H. Attitude of HIV patients to herbal remedy for HIV infection in Nigeria Niger. J. Physiol. Sci. 2013, 28(2) 109 –112

18. Tocco JU. The Islamification of antiretroviral therapy: Reconciling HIV treatment and religion in northern Nigeria. Soc Sci Med. 2017,. 190:75-82.

19. Weintraub A, Mantell JE, Holt K, et al. 'These people who dig roots in the forests cannot treat HIV': Women and men in Durban, South Africa, reflect on traditional medicine and antiretroviral drugs. Glob Public Health, 2018, 13(1):115-127.

20. Omowunmi A, Nkiru O, Yekeen R, *et al*. Knowledge, attitudes and perceptions of HIV/AIDS among traditional birth attendants and herbal practitioners in Lagos State, Nigeria. Afr J AIDS Res. 2004, 3(2):191-196.

21. Haile KT, Ayele AA, Mekuria AB, *et al*. Traditional herbal medicine use among people living with HIV/AIDS in Gondar, Ethiopia: Do their health care providers know? Complement Ther Med. 2017, 35:14-19.

22. Langlois-Klassen D, Kipp W, Jhangari GS and Rubaale T. Use of traditional herbal medicine by AIDS patients in Kabarole District, Western Uganda. Am J Trop Med and Hyg. 2007,77: 757-763.

23. Hodgson T and Rachanis C. Oral fungal and bacterial infections in HIV-infected individuals: an overview in Africa. J Oral Dis, 2002, 8: 80-87.

24. Furler M, Einarson T, Walmsley S, Millson M and Bendayan R. Use of complementary and alternative medicine by HIV-infected outpatients in Ontario, Canada. AIDS Patient Care STDs 2003, 17(4): 155-168.

25 Dhalla S, Chan KJ, Montaner JS and Hogg RS. Complementary and alternative medicine use in British Columbia- a survey of HIV positive people on antiretroviral therapy. Compl Therap Clin Pract, 2006, 12(4): 242-248.

26. Ahwinahwi US, Odili VU, Ogubere J. Benefits and extent of CAM use among persons living with HIV attending an antiretroviral therapy clinic in Warri, Nigeria. Int J Pharm Pract. 2018, 26(4):351-355.

27. Zhibin L, Changhai M, Jiping Y, Xiumin C and Yantao J. Survival rate: an indicator of the management of acquired immune deficiency syndrome using Traditional Chinese Medicine. J Tradit Chin Med. 2015, 35(4):473-477.

28. Zou W, Wang J and Liu Y. Effect of traditional Chinese medicine for treating human immunodeficiency virus infections and acquired immune deficiency syndrome: Boosting immune and alleviating symptoms. Chin J Integr Med. 2016, 22(1):3-8.

29. Liu Z and Yang J. Health related quality of life: is it another comprehensive evaluation indicator of Chinese medicine on acquired immune deficiency syndrome treatment? J Tradit Chin Med. 2015, 35(5):600-605.

30. Liu ZB, Yang JP, Xu LR. Effectiveness and safety of traditional Chinese medicine in treating acquired immune deficiency syndrome: 2004-2014; 2015, 23;4:59.

31. Liu Z, Li X, Yang J, Xu L and Guo H (2015) Differences in acquired immune deficiency syndrome treatment and evaluation strategies between Chinese and Western Medicine 2015, 35(6):718-722.

32. Mbah A U, Udeinya IJ, Shu EN, Chijioke CP, Nubila T, Udeinya F, Muobuike A, Mmuobieri A and Obioma MS. Fractionated *neem* leaf extracts is safe and increases CD4+ cell levels in HIV/AIDS

patients. America Journal Ther; 2007, 14 (4):369-374.

33. Wang Y, Jin F, Wang Q and Suo Z. Long. Term Survival of AIDS Patients Treated with Only Traditional Chinese Medicine. AIDS Res Hum Retroviruses; 2017,. 33(2):90-92.
34. Ayuba GI, Jensen GS, Benson KF, Okubena AM and Okubena O. Clinical efficacy of a West African sorghum bicolor-based traditional herbal preparation Jobelyn shows increased hemoglobin and CD4+ T-lymphocyte counts in HIV-positive patients; 2014, 20(1):53-56
35. Salehi B, Kumar NVA, [a]ener B, *et al*. Medicinal Plants Used in the Treatment of Human Immunodeficiency Virus. Int J Mol Sci. 2018, 14;19(5). pii: E1459.
36. Miao M, Cheng B, Guo L and Shi J. Effects of Fuzheng Paidu tablet on peripheral blood T lymphocytes, intestinal mucosa T lymphocytes, and immune organs in cyclophosphamide-induced immunosuppressed mice; 2015, 11(11):2659-2663.
37. Forgarty A, Rawstorne P, Prestage G, *et al*. Marijuana as therapy for people living with HIV/AIDS: social and health aspects. AIDS Care; 2007, 19 (2):295-301
38. Okechukwu DC, Momoh MA and Esimone CO. Evaluation of the anti-candidal activity of methanolic leaf extract of cleistopholis patens (fam. Annonaceae) on candida species isolated from stage II HIV patients. Afr Health Sci. 2015,. 15(3):789-796.
39. Mgbeahuruike EE, Holm Y, Vuorela H, Amandikwa C and Fyhrquist P. An ethnobotanical survey and antifungal activity of Piper guineense used for the treatment of fungal infections in West-African traditional medicine, 2018, 15;229:157-166.
40. Tsai FJ, Li TM, Cheng CF, *et al.* Effects of Chinese herbal medicine on hyperlipidemia and the risk of cardiovascular disease in HIV-infected patients in Taiwan J Ethnopharmacol.2018, 12;219:71-80.
41. Nemmar A, Al-Salam S, Zia S, Marzouqi F, *et al.* Contrasting actions of diesel exhaust particles on the pulmonary and cardiovascular systems and the effects of thymoquinone. Br J Pharmacol; 2011, 164(7): 1871-1882.
42. Lu WB. A report on 8 seronegative converted HIV/AIDS patients with traditional Chinese medicine. Zhongguo Zhong Xi Yi Jie He Za Zhi Zhongguo Zhongxiyi Jiehe Zazhi;1997, 17 (5):271–273. Chinese.
43. Bekut M, Brkiæ S, Kladar N, Dragoviæ G and Božin B. Potential of selected Lamiaceae *plants* in anti (retro)viral therapy. Pharmacological Research, 2018, 133: 301-314.
44. Zhang HJ, Rumschlag-Booms E, Guan YF, Liu KL and Rong L. Anti-*HIV* diphyllin glycosides from Justicia gendarussa.. Phytochemistry, 2017, 136: 94-100
45. Nobela O, Renslow RS, Thomas DG, Colby SM and Madala NE. Efficient discrimination of natural stereoisomers of chicoric acid, an *HIV*-1 integrase inhibitor Journal of Photochemistry and Photobiology B: Biology, 2018, 189: 258-266
46. Ornano L, Feroci M, Guarcini L, Venditti A and Bianco A. Chapter 6: Anti-*HIV* Agents From Nature: Natural Compounds From Hypericum hircinum and Carbocyclic Nucleosides From Iridoids Studies in Natural *Products* Chemistry, 2018, Volume 56, Pages 173-228
47. Fouokeng Y, Feusso HMF, Teinkela JEM, Noundou XS and Vardamides JC. In vitro antimalarial, antitrypanosomal and *HIV*-1 integrase inhibitory activities of two Cameroonian medicinal *plants*: Antrocaryon klaineanum (Anacardiaceae) and Diospyros conocarpa (Ebenaceae) South African Journal of Botany, In press, corrected proof, Available online 23 October 2018
48. Siwe-Noundou X., Ndinteh DT, Olivier DK, Mnkandhla D and Krause RWM. Biological activity of plant extracts and isolated compounds from Alchornea laxiflora: Anti-HIV, antibacterial and cytotoxicity evaluation South African Journal of Botany, In press, corrected proof, Available online 7 September 2018.
49. Esposito F, Carli I, Del Vecchio C, *et al.* Sennoside A, derived from the traditional chinese medicine plant Rheum L., is a new dual HIV-1 inhibitor effective on HIV-1 replication. Phytomedicine. 2016, 23 (12): 1383-1391.
50. Bashyal BP, Wellensiek BP, Ramakrishnan R, *et al.* Altertoxins with potent anti-HIV activity from Alternaria tenuissima QUE1Se, a fungal endophyte of Quercus emoryi. Bioorg Med Chem. 2014, 22(21):6112-6116.
51. Deng X, Zhang Y, Jiang F, *et al.* The Chinese herb-derived Sparstolonin B suppresses HIV-1 transcription. Virol J.;2015, 12:108.

52. Connell BJ, Chang SY, Prakash E, *et al.* Cinnamon-Derived Procyanidin Compound Displays Anti-HIV-1 Activity by Blocking Heparan Sulfate- and Co-Receptor- Binding Sites on gp120 and Reverses T Cell Exhaustion via Impeding Tim-3 and PD-1 Upregulation. PLoS One. ;11(10):e0165386. doi: 10.1371/journal.pone.0165386. eCollection 2016.
.53. Esimone CO, Grunwald T, Wildner O, *et al.* In vitro pharmacodynamic evaluation of antiviral medicinal plants using a vector-based assay technique. J Appl Microbiol. 2005, 99(6):1346-1355.
54. Chen XW, Serag ES, Sneed KB, *et al.* Clinical herbal interactions with conventional drugs: from molecules to maladies. Curr Med Chem.2011, 18(31):4836-4850.
55. Chen XW, Sneed KB, Pan SY, *et al.* Herb-drug interactions and mechanistic and clinical considerations. Curr Drug Metab. 2012, 13(5):640-651.
56. Walubo A. The role of cytochrome P450 in antiretroviral drug interactions. Expert Opin Drug Metab Toxicol. 2007, 3(4):583-598.
57. Ladenheim D, Horn O, Werneke U, *et al.* Potential health risks of complementary alternative medicines in HIV patients. HIV Med. 2008, 9(8): 653-659.
58. Piscitelli S, Burstein A, Welden N, Gallicano K and Falloon J. Indinavir concentrationsand St. John's wort. Lancet, 2000, 255: 547-548.
59. Monera-Penduka TG, Maponga CC, Wolfe AR, *et al.* Effect of *Moringa oleifera* Lam. leaf powder on the pharmacokinetics of nevirapine in HIV-infected adults: a one sequence cross-over study. AIDS Res Ther. 14:12. doi: 10.1186/s12981-017-0140-4. eCollection 2017.
60. Havenga K, Abay E, Wiesner L, *et al.* The In Vitro and In Vivo Effects of Hypoxis hemerocallidea on Indinavir Pharmacokinetics: Modulation of Efflux. Planta Med. 2018, 84(12-13):895-901.
61. Jegede AI, Offor U, Onanuga IO, Naidu EC and Azu OO. Effect of co-administration of Hypoxis hemerocallidea extract and antiretroviral therapy (HAART) on the histomorphology and seminal parameters in Sprague Dawley rats. Andrologia 49(2). doi: 10.1111/and.12640. Epub 2016 Jul 12.
62. Gwaza L, Aweeka F, Greenblatt R., *et al.* Co-administration of a commonly used Zimbabwean herbal treatment (African potato) does not alter the pharmacokinetics of lopinavir/ritonavir. International Journal of Infectious Diseases, 2013, 17,(10) Pages e857-e861.
63. Nlooto M. Comorbidities of HIV infection and health care seeking behavior among HIV infected patients attending public sector healthcare facilities in KwaZulu-Natal: A cross sectional study. PLoS One. 12(2):e0170983. doi: 10.1371/journal.pone.0170983, 2017.
64.Wanyama JN, Tsui S, Kwok C, *et al.* Persons living with HIV infection on antiretroviral therapy also consulting traditional healers: a study in three African countries. Int J STD AIDS. 2017, 28(10):1018-1027.
65.Peltzer K, Friend-du Preez N, Ramlagan S and Anderson J. Antiretroviral treatment adherence among HIV patients in KwaZulu-Natal, South Africa. BMC Public Health.2017, 10:111. doi: 10.1186/1471-2458-10-111
66.Peltzer K, Friend-du Preez N, Ramlagan S, Fomundam H and Anderson J. Traditional complementary and alternative medicine and antiretroviral treatment adherence among HIV patients in Kwazulu-Natal, South Africa. Afr J Tradit Complement Altern Med. 2009, 7(2):125-37
67. Oku AO, Owoaje ET, Ige OK and Oyo-Ita A. Prevalence and determinants of adherence to HAART amongst PLHIV in a tertiary health facility in south-south Nigeria. BMC Infect Dis. 2013, 13:401. doi: 10.1186/1471-2334-13-401.
68. Dwyer JT, Salvato-Schille AM, Coulston A, Casey VA, Cooper WC and Selles WD. . The use of unconventional remedies among HIVpositive men living in California. J Assoc Nurses AIDS Care, 1995, 6:17-28.
69. Astin J. Why patients use alternative medicine: results of a national study. JAMA, 1998, 279:1548-1553.
70. Drew A and Myers S. Safety issues in herbal medicine: implications for the health professions Med J Aust. 1997, 166(10): 538-541.
71. Hollenburg D, Zakus D, Cook T, Xu X. Re-positioning the role of traditional, complementary and alternative medicine as essential health knowledge in global health: do they still have a role to play? World Health Population, 2008, 10 (4): 62-75.

72. Awodele O, Olayemi SO, Adeyemo TA, Sanya TA and Dolapo DC. Use of complementary medicine amongst patients on antiretroviral drugs in an HIV treatment centre in Lagos, Nigeria. Curr Drug Saf. 2012, 7(2):120-125.
73. Hughes GD, Puoane TR, Clark BL, *et al*. Prevalence and predictors of traditional medicine utilization among persons living with AIDS (PLWA) on antiretroviral (ARV) and prophylaxis treatment in both rural and urban areas in South Africa. Afr J Tradit Complement Altern Med. 2012, 9(4):470-484.
74. Mncengeli S, Manimbulu NM and Panjasaram N. Concurrent use of Antiretroviral and African traditional medicines amongst people living with HIV/AIDS (PLWA) in the eThekwini Metropolitan area of KwaZulu Natal. Afr Health Sci. 2016, 16(4):1118-1130.
75. Hensel G, Floss DM, Arcalis E, *et al*. Transgenic Production of an Anti HIV Antibody in the Barley Endosperm. PLoS One. 10(10):e0140476. doi: 10.1371/journal.pone.0140476. eCollection 2015
76. Md-Mustafa ND, Khalid N, Gao H, Peng Z, Alimin MF, Bujang N, Ming WS, Mohd-Yusuf Y, Harikrishna JA, Othman RY (2014) Transcriptome profiling shows gene regulation patterns in a flavonoid pathway in response to exogenous phenylalanine in Boesenbergia rotunda cell culture. BMC Genomics. 15:984. doi: 10.1186/1471-2164-15-984
77. Moghadam A, Niazi A, Afsharifar A, Taghavi SM (2016) Expression of a Recombinant Anti-HIV and Anti-Tumor Protein, MAP30, in Nicotiana tobacum Hairy Roots: A pH-Stable and Thermophilic Antimicrobial Protein. PLoS One. 26;11(7):e0159653.
78. Ortega JT, Suárez AI, Serrano ML, *et al*. The role of the glycosyl moiety of myricetin derivatives in anti-HIV-1 activity in vitro. AIDS Res Ther. 2017, 14(1):57. doi: 10.1186/s12981-017-0183-6.
79. Dwevedi A, Dwivedi R and Sharma YK. Exploration of Phytochemicals Found in *Terminalia* sp. and their Antiretroviral Activities. Pharmacogn Rev. 2016, 10(20):73-83
80. Kumari A, Baskaran P and Van Staden J. Enhanced HIV-1 Reverse Transcriptase Inhibitory and Antibacterial Properties in Callus of Catha edulis Forsk. Phytother Res. 2015, 29(6) :840-3.
81. Ajaiyeoba EO and Ogbole OO. A phytotherapeutic approach to Nigerian anti-HIV and immunomodulatory drug discovery. Afr J Med Med Sci. 2006, 35 Suppl:71-76.
82. Batisai K. Towards an integrated approach to health and medicine in Africa. SAHARA J. 2016, 13(1):113-122.

Afr. J. Med. Med. Sci. (2020) **49,** 263-270

Predictors of quality of life among informal caregivers of children with cerebral palsy: A cross-sectional survey in Northeastern Nigeria

UM Bello[1], M Chutiyami[2] and D Salihu[2]

Department of Physiotherapy[1], Yobe State University Teaching Hospital and Shehu Sule College of Nursing and Midwifery[2], Damaturu, Yobe State, Nigeria

Abstract

Background: Cerebral palsy is the most frequently reported motor impairment in childhood, with a high prevalence in African countries. Children with cerebral palsy require long-term care from their caregivers. The long-term dependence may lower the level of quality of life of the caregivers.

Aim: This study aimed to assess the level of quality of life and its determining factors among caregivers of children with cerebral palsy.

Methods: A cross-sectional survey design was conducted with fifty-one caregivers of children with cerebral palsy. Hausa translated version of World Health Organization Quality of Life-Bref (WHOQOL-Bref) was used to assess the quality of life of the participants. Functional ability of the children with cerebral palsy whose caregivers were recruited in the study was assessed using Gross Motor Function Classification System Expanded and Revised (GMFCS-E&R). A multiple regression analysis was used to predict different domains of the caregiver's quality of life.

Results: Majority of the caregivers (72.0%) were females. They presented with lower level of quality of life (<60 points in all domains of WHOQOL-Bref). Findings from multiple regression analysis indicated that the educational status of the caregivers of children with cerebral palsy significantly predicts (p=0.00) different domains of their quality of life, including; psychological, environmental and physical health. Other significant predictors of psychological domain of the caregiver's quality of life are child birth order (p=0.02) and caregiver's age (p=0.00).

Conclusion: Caregivers of children with cerebral palsy have low levels of quality of life. Child birth order, caregiver's age and educational status are strong predictors of quality of life among caregivers of children with cerebral palsy.

Correspondence: Mr. U.M. Bello, Department of Physiotherapy, Yobe State Teaching hospital, Along Potiskum road, Damaturu, Yobe State, Nigeria.

Keywords: *Quality of life; Cerebral palsy; WHOQOL-Bref; GMFCS-E&R; Caregivers*

Résumé

Contexte: La paralysie cérébrale est la déficience motrice la plus fréquemment signalée dans l'enfance, avec une prévalence élevée dans les pays africains. Les enfants atteints de paralysie cérébrale ont besoin de soins de longue durée de la part de leurs soignants. La dépendance à long terme peut abaisser le niveau de qualité de vie des soignants.

Objectif : Cette étude visait à évaluer le niveau de qualité de vie et ses facteurs déterminants chez les soignants d'enfants atteints de paralysie cérébrale.

Méthodes: Un plan d'enquête transversal a été mené auprès de 51 soignants d'enfants atteints de paralysie cérébrale. La version traduite en haoussa de Qualité de vie - Bref de l'Organisation Mondiale de la Santé (WHOQOL-Bref) a été utilisée pour évaluer la qualité de vie des participants. La capacité fonctionnelle des enfants atteints de paralysie cérébrale dont les soignants ont été recrutés dans l'étude a été évaluée à l'aide du Système de Classification des Fonctions Motrices Brutes Elargi et Révisé (GMFCS-E & R). Une analyse de régression multiple a été utilisée pour prédire différents domaines de la qualité de vie du soignant.

Résultats: La majorité des soignants (72,0%) étaient des femmes. Ils présentaient un niveau de qualité de vie inférieur (<60 points dans tous les domaines de WHOQOL- Bref). Les résultats de l'analyse de régression multiple ont indiqué que le niveau d'éducation des soignants aux enfants atteints de paralysie cérébrale prédit de manière significative (p = 0,00) différents domaines de leur qualité de vie, y compris; santé psychologique, environnementale et physique. D'autres prédicteurs significatifs du domaine psychologique de la qualité de vie du soignant sont l'ordre de naissance des enfants (p = 0,02) et l'âge du soignant (p = 0,00).

Conclusion: Les soignants d'enfants atteints de paralysie cérébrale ont un faible niveau de qualité de vie. L'ordre de naissance des enfants, l'âge et le niveau

d'éducation du soignant sont de solides prédicteurs de la qualité de vie des soignants d'enfants atteints de paralysie cérébrale.

Mots-clés: *Qualité de vie; Paralysie cérébrale; WHOQOL- Bref ; GMFCS-E&R; Soignants*

Introduction

Cerebral palsy is the most commonly observed motor impairment in childhood and its effects continue throughout lifespan [1,2]. It is caused by affectation of the central nervous system [3], commonly characterized by delay in developmental milestones, motor impairment, mental and physical dysfunctions [1]. Cerebral palsy affects 2 in every 1000 child worldwide [4]. Thus, indicating higher prevalence of the disease condition. According to the Cerebral Palsy Foundation, about 764,000 children were diagnosed with cerebral palsy in United States [1]. Furthermore, approximately 650,000 families in Europe take care of an adult with cerebral palsy or have a child diagnosed with the condition [4].

Higher prevalence of cerebral palsy is evident in Africa and very little of this condition has been reported from the member countries [5]. In Nigeria, a retrospective epidemiological study conducted by Ogunlesi *et al*. [6] had shown that cerebral palsy accounted for 50.3% of the cases reported in pediatric neurological clinic from the year 2000 to 2006. This indicates higher prevalence of the disease in Nigeria. It is a serious health issue in this country [5] and most individuals with cerebral palsy have associated symptoms such as epilepsy and intellectual impairments [4]. For these reasons, children with the condition require special assistance during schooling period, and about 50% face difficulty securing a job and living independently as they grow [4].

Cerebral palsy is a long term disabling pediatric neurological condition which leads to delay in growth and development of the child as well as functional dependence, leading to some social and financial implications on the caregiver [6]. Unfortunately, even with regular rehabilitation, overall recovery from cerebral palsy is not achieved [5]. Most children/adolescents with cerebral palsy rely solely in full or partial on their caregivers for day-to-day lively needs such as feeding, toilet use, transfer and mobility. Informal caregivers of children with cerebral palsy may be faced with a burden of providing long term care to the child due to nature of the condition. Characteristic of this condition in terms of functional dependency of the child and level of overall expected recovery may also place extra burden on the caregivers [6].

There are numerous studies conducted in different parts of the world that reported caring for a child with cerebral palsy has a tremendous negative effect on quality of life of the caregiver [5,7-13]. However, limited number of studies went further to assess factors that may contribute to the decrease in quality of life among the caregivers, especially in African context. This necessitates the need to carry out the present study. This study aimed to examine the level of quality of life among informal caregivers of children with cerebral palsy in the Northeastern part of Nigeria, and to assess the influence of caregiver's socio-demographic characteristics and child characteristics on the quality of life of the caregivers.

Methods

The study was a cross-sectional descriptive survey and participants were drawn from population of informal caregivers of children with cerebral palsy in outpatient Physiotherapy units of selected hospitals in Maiduguri (University of Maiduguri Teaching Hospital, UMTH; State Specialist Hospital Maiduguri, SSHM). The G-power software (http://www.gpower.hhu.de/) was adopted in calculating the sample size for the study; assuming 80% power, 5% type I error and effect size (f^2) of 0.15 [https://ncss-wpengine.netdna-ssl.com/wp-content/themes/ncss/pdf/Procedures/PASS/Multiple_Regression_using_Effect_Size.pdf], forty-three caregivers were needed for the seven independent variables in the study to significantly predict the domains of quality of life among the caregivers. We recruited fifty-one caregivers into the study to control for missing data. Ethical approvals for this study was obtained from the research ethics committee of SSHM (reference number: SSH/GEN/641/Vol. 1) before commencing the study. Adult caregivers, both males and females having a responsibility of looking after a child with cerebral palsy were recruited in the study.

A purposive sampling technique was adopted to recruit participants in the study after the objectives and procedure were explained to them. Participants were checked for inclusion criteria which included (a) informal adult caregivers, caring for a child with cerebral palsy (b) attending outpatient Physiotherapy unit of UMTH or SSHM and (c) being able to understand and speak Hausa language. Verbal informed consent was obtained from caregivers that had difficulty in writing, while a written informed consent

was obtained from those that were able to write, before being included into the study. Socio-demographic characteristics of the caregivers and child's birth order were recorded for each caregiver. Hausa translated version of World Health Organization Quality of Life-Bref (WHOQOL-Bref) was administered to the caregivers by the researchers. The questionnaire was translated into Hausa language, which is the native language that is predominantly spoken in the area [14]. This is because it was perceived that majority of the caregivers would not be able to speak, read or write in English language. The English version of WHOQOL-Bref was translated to Hausa language by a lecturer from the linguistic Department of University of Maiduguri, who can speak, read and write in both Hausa and English language. Hausa translated version of the instrument was then back translated into English language by an independent translator. The back translated version and the original English version were then compared by senior Physiotherapists for construct and conceptual equivalence.

The WHOQOL-Bref comprises of 26 items [15]. The first two questions ask about the general health and overall quality of life while the remaining 24 questions are domain specific [16]. Physical health, psychological, social relationship and environment are the domains of WHOQOL-Bref [17]. The questions were scored on 5-points Likert scales which were converted to a scale of 0-100 based on the domains as provided in the scoring manual [18]. A cut-off score of 60 points in each domain of WHOQOL-Bref had been reported elsewhere [19]. Age of the child with cerebral palsy whose caregiver was recruited in the study was recorded and present functional ability of the child was assessed using Gross Motor Function Classification System Expanded and Revised (GMFCS-E&R). Higher domain scores in WHOQOL-Bref are indicative of higher quality of life, whereas lower scores in GMFCS-E&R signify higher functional ability.

Data analysis

The socio-demographic characteristics of the caregivers, child's level of functional ability, age of the child, child's birth order and quality of life scores were summarized using descriptive statistics of mean, standard deviation, frequencies and percentages. Multiple regressions (using the "standard method") was utilized to assess whether socio-demographic variables of the caregivers (sex, age, highest educational status occupational status), age of the child, child's birth order and functional ability of the child were predictive variables of caregiver's quality of life. This analysis was conducted based on the domains of quality of life in WHOQOL-Bref. Therefore, four regression analyses were carried out. Data analysis was performed using SPSS version 21 (SPSS Inc., Chicago, IL, USA) and level of significance was set at $p \leq 0.05$.

Results

The socio-demographic characteristics of the participant were analyzed using descriptive statistics (table 1). Fifty-one participants were recruited for this study and female caregivers had the highest frequency 37 (72%). Mean age of the overall sample was 34.37 years (SD: 10.87; range: 19-73) and most of the caregivers (70.6%) were between the age of 18 and 38.

Table 2 reports the characteristics of the children whose caregivers were recruited in the study. The mean age of the children was 46.73 months (SD: 37.87; range: 10-204). Most of the children 18 (35.3%) were less than 2 years old, while only 1 (1.9%) was greater than 12 years. Concerning position of the child in the family, most of the children 19 (37.3) were 1st child. Participants in the study had mean quality of life score below 60 in all the domains of WHOQOL-Bref (table 3).

This is indicative that the caregivers presented with low level of quality of life. Psychological and environmental domains of WHOQOL-Bref had the highest (54.0) and lowest (47.92) mean scores respectively.

Table 4 presents four regression analysis predicting domains of WHOQOL-Bref. Only psychological (model 2) and environmental (model 4) domains had statistically significant variance, $R^2 = 0.36$ ($p = 0.00$) and $R^2 = 0.27$ ($p = 0.05$) respectively. A more detailed examination of individual model showed that

Table 1: Socio-demographic variables of the caregivers of children with cerebral palsy

Socio-demographics	Frequency (%)	Mean (SD)	Range
Primary Caregiver (n=51)			
Sex			
Male	14 (27.5)		
Female	37 (72.5)		
Age (years)		34.37 (10.87)	19-73
Age group (years)			
18-38	36 (70.6)		
39-59	14 (27.4)		
60-80	1(2.0)		
Highest Educational Status			
Islamic School	14 (27.5)		
Never Attended School	3 (5.9)		
Primary School		8 (15.7)	
Secondary School	13 (25.5)		
Tertiary Institution	13 (25.5)		
Occupational Status			
Unemployed	1 (2.0)		
Housewife	28 (54.9)		
Students	5 (9.8)		
Retired	2 (3.9)		
Employed	15 (28.4)		

Table 2: Characteristics of the children whose caregivers were recruited in the study

Socio-demographics	Frequency (%)	Mean (SD)	Range
Child, (n=51)			
Age (months)		46.73 (37.87)	10-204
Age group (years)			
< 2	18 (35.3)		
2-4	14 (27.5)		
5-6	7 (13.7)		
7-12		11 (21.2)	
>12	1 (1.9)		
Position of child in the family			
1st	19 (37.3)		
2nd	8 (15.7)		
3rd	10 (19.6)		
4th	3 (5.9)		
5th	2 (3.9)		
6th	2 (3.9)		
7th	2 (3.9)		
8th	3 (5.9)		
9th	1 (2.0)		
10th	1 (2.0)		
GMFCS-E&R levels			
Level I		-	
Level II	1 (2.0)		
Level III	9 (17.6)		
Level IV	24 (47.1)		
Level V	17 (33.3)		

GMFCS-E&R levels: lower levels signify better functional ability in child with cerebral palsy

Table 3: Descriptive statistics of domain-specific analysis for transformed scores of WHOQOL-Bref

Quality of life domains (WHOQOL-Bref)	N	Mean (SD)	Range of scores
Physical health	51	50.98 (17.38)	0-100
Psychological	51	54.0 (17.04)	0-100
Social relationships	51	51.63 (16.67)	0-100
Environmental	51	47.92 (15.20)	0-100

In the quality of life domains of physical health, psychological, social relationships and environmental, higher scores signify better quality of life.

Table 4: Regression analysis predicting the domains of WHOQOL-Bref

(n=51)	R^2	β	*p*
Model 1			
WHOQOL-BREF (Physical health)	0.23		0.97
Caregiver age		-0.31	0.12
Sex		0.16	0.56
Educational Status		0.43	0.00**
Occupational Status		-0.09	0.73
Position of child in the family		0.21	0.17
Age of the child		-0.15	0.36
GMFCS-E&R levels		-0.92	0.17
Model 2			
WHOQOL-BREF (Psychological)	0.36		0.00**
Caregiver age		-0.56	0.00**
Sex		0.14	0.58
Educational Status		0.42	0.00**
Occupational Status		-0.08	0.74
Position of child in the family		0.33	0.02*
Age of the child		0.28	0.07
GMFCS-E&R levels		0.51	0.06
Model 3			
WHOQOL-BREF (Social Relationships)	0.26		0.06
Caregiver age		-0.37	0.06
Sex		0.00	0.99
Educational Status		0.39	0.07
Occupational Status		-0.58	0.83
Position of child in the family		0.26	0.90
Age of the child		0.11	0.48
GMFCS-E&R levels		0.23	0.10
Model 4			
WHOQOL-BREF (Environmental)	0.27		0.05*
Caregiver age		-0.35	0.76
Sex		0.15	0.58
Educational Status		0.45	0.00**
Occupational Status		-0.06	0.84
Position of child in the family		0.20	0.19
Age of the child		0.14	0.40
GMFCS-E&R levels		-0.23	0.10

**p dH 0.05*
***p dH 0.001*

only caregiver's age (β = -0.56, p = 0.00), position of child in the family (β = 0.33, p = 0.02) and educational status of the caregiver (β = 0.42, p = 0.00) significantly predicts psychological domain of WHOQOL-Bref. The first and fourth models showed that only educational status significantly predicts physical health (β = 0.43, p = 0.00) and environmental domains (β= 0.45, p = 0.00).

Discussion

Finding from this cross-sectional survey has shown that caregivers of children with cerebral palsy have lower level of quality of life. This conclusion was reached based on the findings from the study of Silva *et al*. [19] which provided 60 points as a cut-off point for each domain of WHOQOL-Bref, when the scores are transformed to scale of 0 to 100. Consistent findings have been reported from previous studies conducted in different parts of the world [5,7-13]. The reduced level of quality of life among caregivers of children with cerebral palsy could be due to provision of long-term special care to the children, thereby placing much burden on different aspects of life of the caregivers [3]. Similarly, caregivers of children with cerebral palsy may lower their quality of life while trying to improve that of the child [9]. In addition to the factors mentioned above, the present study was conducted in Africa, where people mostly live in communal setting. Most communities in Africa perceive having a child with disability as disgraceful. Living with such feeling may place extra emotional burden on the caregivers. Moreover, Hamzat and Osundiya [20] reported that caregivers of children with disabilities in African settings may likely have poor quality of life due to stigma from other members of the community in which they live.

Among the different constructs of quality of life assessed by WHOQOL-Bref, the participants reported having better psychological status, which indicates that caregivers of children with cerebral palsy have better psychological wellbeing when compared to other domains of quality of life assessed. This finding is surprising due to lack of adequate social care support services in most Africa countries [5]. Nonetheless, psychological support provided by extended family members [13] in the form of counselling and advices might have resulted in the positive impact on the psychological status of the caregivers. More so, religious inclination may also play a vital role in improving psychological status of the caregivers. It may be argued that religious background of caregivers recruited in this study was not assessed. However, it is well established that majority of populace in the Northern part of Nigeria are either followers of Christianity or Islam [14] Skinner *et al*. [21] reported that most parents of children with developmental delays view religious faith as being supportive in coping with the stress of caregiving. To further stress the link between religious faith and psychological wellbeing, Plante *et al*. [22] reported that strength of religious faith is significantly associated with adopting positive coping strategies, lower anxiety level and higher optimism.

Environmental domain of WHOQOL-Bref had the least mean score in this study (Table 3), which connotes that environmental domain of caregiver's quality of life was the most affected. The finding could arise because the caregivers might have difficulty in moving around freely due to high dependence of the child for assistance in activities of daily living. This situation is likely to have a negative impact on the caregiver's overall wellbeing.

Looking at the second aim of this study, educational status was found to be the most significant predictor of quality of life among all the independent variables analyzed (see table 4). This is an indication that higher educational status is related to better quality of life. Interestingly, this finding is consistent with that of Vincent-Onabajo *et al*. [23] which reported a significant positive correlation between educational status and physical health of caregivers of stroke survivors in Northeastern part of Nigeria.

Review of the existing literature has shown that child's level of functional ability has no correlation with quality of life of the caregiver [9-11]. Outcome of the present study in this regard is consistent with the above literature. This shows that poorer functional ability of a child with cerebral palsy does not add a negative effect on the quality of life of the caregivers. It was further hypothesized that age of the child will be a predictor of caregiver's quality of life. However, all the regression models generated findings that are contrary to the proposed hypothesis. This study has shown that age of the child with cerebral palsy is not a predictor of caregiver's quality of life across all domains assessed by WHOQOL-Bref. However, position of the child with cerebral palsy in the family (child's birth order) is a significant predictor (β = 0.33,

$p = 0.02$) of psychological domain of WHOQOL-Bref as shown in Table 4. This finding shows that caregivers caring for children with cerebral palsy that are 1st or 2nd born in the family were having poorer psychological wellbeing compared to those caring for children that are 4th or 5th born. This finding may be due to anxiety among the caregivers caring for children with lower birth order. Moreover, caregivers caring for a child with cerebral palsy having a higher birth order may have less psychological distress because of the feeling that the child has other siblings.

A key strength of this study is that the questionnaire (WHOQOL-Bref) was translated into Hausa language which is predominantly spoken language in the area where data was collected. The translation process was done to avoid unnecessarily excluding potential participants that cannot speak, read and write in English language. Although, lack of psychometric assessment of translated version of the questionnaire may serve a limitation of this study. It was stated that comparison was made between the back-translated version and the original English version by senior physiotherapists to ensure that actual meaning of questions asked in the questionnaire were not lost during the translation process. Another limitation of the study is its focus on caregivers that regularly attend out-patient physiotherapy services in the selected hospitals. As such, findings from this study may not be generalizable to caregivers who do not attend the physiotherapy outpatient unit, as they may be having other forms of caregiving burdens different from those recruited in the present study. Nevertheless, this study provides an insight into the subject area, but it is recommended that future studies should incorporate both community- and hospital-based approaches.

Conclusion

Caregivers of children with cerebral palsy have low levels of quality of life. Educational status of the caregivers is a significant predictor of physical health, psychological and environmental domain of WHOQOL-Bref. This shows that caregivers with higher educational status have better quality of life with respect to physical health, environmental and psychological statuses. More so, caregiver's age and birth order of the child with cerebral palsy are predictors of caregiver's psychological wellbeing. Therefore, future government policies should incorporate social care support services to enhance the quality of life of the caregivers.

Acknowledgements

The authors would like to thank the management of State Specialist Hospital Maiduguri (SSHM) and University of Maiduguri Teaching Hospital (UMTH) for the grant of ethical clearance and the permission to collect data at the healthcare facilities. We would also like to thank all the participants that took part in the study.

References

1. Krigger K.W. Cerebral palsy: an overview. American Family Physician 2006; 73(1): 91-100.
2. Guillamon N., Nieto R., Pousada M., *et al.* Quality of life and mental health among parents of children with cerebral palsy: the influence of self efficacy and coping strategies. Journal of clinical nursing 2013; 22(11-12): 1579-1590.
3. Raina P., O'Donnell M., Rosenbaum P., *et al*. The health and well-being of caregivers of children with cerebral palsy. Pediatrics 2005; 115(6): e626-e636.
4. Cans C., De-la-Cruz J. and Mermet M.A. Epidemiology of cerebral palsy. Paediatrics and Child Health2008; 18(9): 393-398.
5. Fatudimu M.B., Hamzat T.K. and Akinyinka O.O. Comparative quality of life of Nigerian caregivers of children with cerebral palsy. International Journal of Therapy and Rehabilitation 2013; 20(3): 131-135.
6. Ogunlesi T., Ogundeyi M., Ogunfowora O. and Olowu, A. Socio-clinical issues in cerebral palsy in Sagamu, Nigeria. South African Journal of Child Health 2008;2(3): 120-124.
7. Eker L. and Tüzün E. H. An evaluation of quality of life of mothers of children with cerebral palsy. Disability and Rehabilitation 2004; 26(23): 1354-1359.
8. Tuna H., Ünalan H., Tuna F. and Kokino, S. Quality of life of primary caregivers of children with cerebral palsy: a controlled study with Short Form-36 questionnaire. Developmental Medicine and Child Neurology 2004; 46(09): 647-648.
9. Ones K., Yilmaz E., Cetinkaya B. and Caglar N. Assessment of the quality of life of mothers of children with cerebral palsy (primary caregivers). Neurorehabilitation and Neural Repair 2005; 19(3): 232-237.
10. Davis E., Shelly A., Waters E., *et al*. The impact of caring for a child with cerebral palsy: quality of life for mothers and fathers. Child: care, health and development 2009; 36(1): 63-73.

11. Kaya K., Unsal-Delialioglu S., Ordu-Gokkaya N. K., *et al*. Musculo-skeletal pain, quality of life and depression in mothers of children with cerebral palsy. Disability and Rehabilitation 2010; (20): 1666-1672.
12. Guillamon N., Nieto R., Pousada M., *et al.* Quality of life and mental health among parents of children with cerebral palsy: the influence of self efficacy and coping strategies. Journal of clinical nursing 2013; 22(11-12): 1579-1590.
13. Adegoke B.O.A., Adenuga O.O., Olaleye O.A. and Akosile C.O. Quality of life of mothers of children with cerebral palsy and their age matched controls. African Journal of Neurological Sciences 2014; 33(1): 71-78.
14. National Population Commission (NPC) [Nigeria] and ORC Macro (2004): Nigeria Demographics and Health Survey 2003. Calverton, Maryland: National Population Commission and ORC Macro. Accessed 01 July 2019. Available: http://www.dhsprogram.com/pubs/pdf/FR148/FR148.pdf
15. Power, M., Bullinger, M. and Harper, A. The World Health Organization WHOQOL-100: Tests of the universality of quality of life in 15 different cultural groups worldwide. Health psychology 1999; 18(5): 495.
16. Chiu, W.T., Huang, S.J., Hwang, H.F., *et al.* Use of the WHOQOL-BREF for evaluating persons with traumatic brain injury. Journal of Neurotrauma 2006; 23(11): 1609-1620.
17. Hwang H.F., Liang W.M., Chiu Y.N. and Lin M.R. Suitability of the WHOQOL-BREF for community-dwelling older people in Taiwan. Age and ageing 2003; 32(6): 593-600.
18. WHOQoL Group.. Study protocol for the World Health Organization project to develop a Quality of Life assessment instrument (WHOQOL). Quality of life Research, 1993; *2*(2), 153-159.
19. Silva P.A.B., Soares S.M., Santos J.F.G. and Silva L.B. Ponto de cortepara o WHOQOL-brefcomopreditor de qualidade de vida de idosos. Revista de SaúdePública 2014;48(3): 390-397.
20. Hamzat T. K. and Osundiya O. C. Musculoskeletal pain and its impact on motor performance among stroke survivors. Hong Kong Physiotherapy Journal 2010; 28(1): 11-15.
21. Skinner D.G., Correa V., Skinner M. and Bailey Jr, D.B. Role of religion in the lives of Latino families of young children with developmental delays. Journal Information 2001;106(4).
22. Plante T. G., Yancey S., Sherman A. and Guertin M. The association between strength of religious faith and psychological functioning. Pastoral Psychology 2000; 48(5): 405-412.
23. Vincent Onabajo G., Ali A. and Hamzat T. Quality of life of Nigerian informal caregivers of community dwelling stroke survivors. Scandinavian journal of caring sciences 2013; 27(4): 977-982.