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Clinical skills acquisition by medical graduates: a prerequisite for good practice …

Approximately half of the seventeen manuscripts appearing in this last issue of Volume 48 of this journal present information on non-communicable diseases. They include glycaemic control (correlating blood viscousity, age and anaemia; relationship between ghrelin level and glucagon-like peptide-1 release); adherence to therapy for systemic hypertension, benefit of diuretic therapy stored at low temperature and protected from light for treating pulmonary hypertension in children, bladder cancer trends, frailty and ageing and haemoglobinopathy. Three of the remaining manuscripts cover interesting topics in dentistry such as sequence of tooth eruption, use of acrylic dentures for improved well-being of partially edentulous individuals and overcoming shyness as one of the peculiar reasons for prolonged indulgence in oral habits by school children aged 6 to 12 years. Two other manuscripts highlight traditional practices for childbirth and male circumcision. These articles reinforce the emerging health problems posed by non-communicable diseases.

The article by Abdur-Rahman and colleagues from University of Ilorin deserves special attention. It was based on data obtained from a questionnaire survey of 163 new interns, and it showed dismal performance in pre-training self-assessed proficiency level particularly with nasogastric intubation, chest tube insertion and fracture management. The poor performance was attributed to inadequate training facilities, reluctant patients and competition between undergraduate and postgraduate trainees. These procedures, among others, are essential and should be within the competence list of most graduates. The essential professional duties of medical and dental graduates in sub-Saharan Africa was published as a review article in the September 2016 edition of the journal and there was an editorial titled "Ensuring professional competence of medical and dental graduates in sub-Saharan Africa" to highlight the key points

This is a time for sober reflection on our training programmes and we must find ways to ensure that all the needed competences are acquired by the time a student graduates from our training institutions. In the era of globalization, the products of our medical schools must be competitive and should not be short-changed in their training. Use of manikins for simulation and the acquisition of clinical skills laboratories will go a long way in overcoming some of the highlighted factors in the article. Interns who are found deficient should have extra teaching during the internship year and residency training.

The focus of the national template for undergraduate medical education is patient-centred, competency-based teaching and many medical schools have adopted this new curriculum. This article therefore serves as a reminder to all training institutions to place the right emphasis on formative assessment to ensure that necessary skills are acquired to ensure smooth professional practice and quality care of patients.

Reference

1. Olapade-Olaopa EO, Sewankambo N, Iputo JE *et al.* Essential professional duties for the sub-Saharan medical/dental graduate: An Association of Medical Schools of Africa initiative. Afr. J Med med sci. 2016; 45: 221-227

A. Ogunniyi
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Effect of fasting plasma ghrelin level on glucagon-like peptide-1 release in healthy male adults following ingestion of selected Nigerian meals

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Abstract

Introduction: Glucagon-like peptide 1 (GLP-1) and ghrelin play crucial roles in energy homeostasis control. Although they appear to have differing functions, emerging reports show that there is an important interplay between the 2 hormones as ghrelin could enhance GLP-1 release. This study was therefore carried out to determine the plasma changes in GLP-1 and ghrelin levels following ingestion of selected Nigerian meals.

Materials and ethod: Twelve adult males were recruited into this randomized cross-over study. Meal tolerance testing (MTT) was carried out using 50g available carbohydrate of yam flour paste (amala), wheat paste and cooked cowpea with 50g of glucose serving as the reference meal (RM). Plasma levels of GLP-1 and ghrelin were determined at 0 minute and then postprandially, at 30, 60, 90 and 120 minutes.

Result: The median $AUC_{Ghrelin}$ of wheat meal, cowpea meal and amala were not significantly different when compared with RM and with one another. However, the median AUC_{GLP-1} of wheat meal and cowpea meal were significantly higher compared with RM but no significant differences were observed when the meals were compared with one another. There were significant positive correlations between fasting ghrelin level and 30 min GLP-1 level following ingestion of amala and RM.

Conclusion: The meals appear to have similar appetite induction due to their comparable ghrelin levels but ingestion of cowpea meal or whole, unprocessed wheat might have some benefits in maintaining normoglycaemia probably because of their effects on GLP-1 release. Also, fasting level of ghrelin appears to have some stimulating effect on postprandial release of GLP-1.

Keywords: *Ghrelin, Glucagon-like peptide 1, Incretin, Meal tolerance testing, Metabolic diseases, Nigerian meals*.

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Résumé

Introduction : Le peptide 1 de type glucagon (GLP-1) et la ghréline jouent un rôle crucial dans le contrôle de l'homéostasie énergétique. Bien qu'ils semblent avoir des fonctions différentes, les rapports récents montrent qu'il existe une interaction importante entre les 2 hormones car la ghréline pourrait augmenter la libération de GLP-1. Cette étude a donc été réalisée pour déterminer les modifications plasmatiques des taux de GLP-1 et de ghréline suite à l'ingestion de certains repas nigérians.

Matériel et méthode : Douze hommes adultes ont été recrutés pour cette étude croisée randomisée. Le test de tolérance des repas (TTR) a été réalisé avec 50 g de glucides disponibles de la pâte de farine d'igname (amala), de la pâte de blé et du niébé cuit, avec 50 g de glucose servant de repas de référence (RR). Les taux plasmatiques de GLP-1 et de ghréline ont été déterminés à 0 minute puis de manière postprandiale à 30, 60, 90 et 120 minutes.

Résultat : L'$ASC_{Ghréline}$ médiane du repas de blé, repas de niébé et d'amala n'étaient pas significativement différents par rapport au RR et avec les unes aux autres. Cependant, l'ASC_{GLP-1} médiane du repas de blé et du repas de niébé était significativement plus élevée par rapport au RR, mais aucune différence significative n'a été observée lorsque les repas ont été comparées les unes aux autres. Il y avait des corrélations positives significatives entre le niveau de ghréline à jeun et le niveau de GLP-1 après 30 minutes après l'ingestion d'amala et de RR.

Conclusion : Les repas semblent avoir une induction d'appétit similaire en raison de leurs niveaux de ghréline comparables, mais l'ingestion du repas de niébé ou entier, non transformé de blé pourrait avoir certains avantages à maintenir une normo-glycémie probablement en raison de leurs effets sur la libération de GLP-1. En outre, le taux de ghréline à jeun semble avoir un effet stimulant sur la libération postprandiale de GLP-1.

Mots - clés : *Ghréline, peptide 1 de type glucagon, incrétine, test de tolérance des repas, maladies métaboliques, repas nigérian*.

Introduction

Diet remains an important aetiological factor implicated in the development of metabolic diseases such as type 2 diabetes mellitus (T2DM). Interestingly, it is also a key component in their management as it can be controlled and, can directly influence health [1].

Diets with high calories have been shown to contribute to the current epidemic of metabolic diseases. For example, diets high in saturated fats are implicated in weight gain, insulin resistance, and hyperlipidemia in humans and animals [2, 3]. Similarly, evidences abound that uncontrolled consumption of carbohydrate especially, the refined form predisposes to metabolic diseases. Interestingly, carbohydrate food sources form the greatest percentage (50-60%) of the daily diet for different segments of the population [1]. In Nigeria, starchy staples (cereals, roots and tubers) and legumes constitute the major part of the traditional diets up to 70% and 25% respectively [4]. Legumes constitute a natural protein supplement to staple diets, and in Africa, cowpea represents the legume of choice [5].

The gastrointestinal tract (GIT) plays a crucial role in the control of energy homeostasis through its role in the digestion, absorption, and assimilation of ingested nutrients. Hormones from the GIT, which are regulated in part by nutrients, are important in regulating gut motility and satiety which play important roles in the pathogenesis of metabolic diseases. Furthermore, the emerging therapeutic roles of gut hormones as well as their biological roles in regulating glucose homeostasis highlight their importance in effective management of diseases such as T2DM [6, 7].

One of the important gut hormones with crucial roles in glucose and energy metabolism is glucagon-like peptide 1 (GLP-1). It is a 30 amino acid peptide secreted by the L cells of the GIT in response to nutrient ingestion [8]. GLP-1 rapid degradation by proteases confers on it a short half-life hence; approximately 10-20% of total plasma biologically active GLP-1 are usually quantified [9].

The incretin effect of GLP-1 was first reported in 1932 by La Barre [10]. Once released, it potentiates glucose-stimulated insulin secretion from the pancreatic β-cells, even before blood glucose levels rise [11, 12]. It also facilitates improved glucose clearance by inhibiting glucagon secretion, inducing satiety, promoting insulin gene transcription, stimulating pancreatic β-cell proliferation and neogenesis, inhibiting β-cell apoptosis, preventing gastric emptying and enhancing skeletal muscle glucose disposal [9, 13, 14].

Usually, presence of food in the lumen regulates GLP-1 secretion. The regulation is finely regulated via nutrient transporters, receptors and metabolism [12]. The meal-induced release of GLP-1 has 2 peaks. The first peak appears before nutrients access the L cells in the intestine, this occurs within 15 min after meal initiation while the second peak, which is larger, occurs later when the nutrients have had direct contact with intestinal L cells. Irrespective of these biphasic release, the insulinotropic effect of GLP-1 is limited as its level decreases as normal glycaemic level is attained thereby reducing the risk of hypoglycaemia [9].

Although secretion of GLP-1 is largely meal dependent, it has been reported that neural and hormonal activated pathways, which are still poorly understood, play vital roles in GLP-1 regulation. Some of the implicated hormones are leptin, glucose-dependent insulinotropic peptide (GIP) and cholecystokinin. Recently, ghrelin was also shown as a regulator of GLP-1 [12].

Ghrelin is a 28 amino acid peptide involved in appetite induction. It is secreted from the stomach in response to hunger hence, serving as a peripheral signal to stimulate desire for food. Unlike GLP-1, ghrelin peaks during fasting at the sight of food, just immediately before meal ingestion [15].

Aside from the established role of ghrelin in appetite induction, ghrelin also has strong growth hormone releasing activity, increases gastric acid secretion and stimulates gastric motility. It also, has some effects on insulin secretion albeit with some controversies [16-18].

Although GLP-1 and ghrelin appear to have differing functions, Gagnon *et al*. [12] showed that there exists an important interplay between the 2 hormones. They hypothesized that L cell response to meal ingestion may be primed by the high levels of ghrelin that occur immediately before a meal. Interestingly, they showed that ghrelin enhances GLP-1 release in response to a subsequent oral glucose load. Tong *et al*. [19] reported that ghrelin increases GLP-1 release but impairs prandial glucose tolerance by decreasing insulin sensitivity and impairing β-cell function. These reports although seemingly controversial, suggest that there exists an important, but poorly understood, relationship between these two hormones.

This study was therefore designed to assess the interplay between these two gut hormones following ingestion of selected Nigerian meals. Availability of this information, in conjunction with GI knowledge, could facilitate informed dietary recommendation with a view to preventing metabolic

diseases such as T2DM as well as enhancing their effective management.

Methodology

Details of the study participants, meal preparation, execution of the meal tolerance testing and blood sample collection have earlier been reported [20]. Briefly, twelve apparently healthy male adult volunteers were recruited, using convenient sampling method, into the randomized cross-over study. Meal tolerance testing was carried out using 3 commonly consumed Nigerian diets; amala, wheat meal and cowpea. Fifty gram (50 g) of glucose was used as the reference meal. The meal tolerance testing was done on separate days, with a washout period of one week between each meal.

Ethical approval was obtained from the University of Ibadan/University College Hospital Joint Ethics Committee and written informed consent was obtained from the study participants.

Laboratory analysis

Plasma levels of ghrelin and glucagon like peptide 1 (GLP-1) were determined using ELISA (WKEA Med Supplies Corp., Changchum, China).

Statistical analysis

Data obtained from the study were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 20.0. Area under the Curve (AUC) was determined using trapezoidal rule. Since the levels of the hormones did not obey Gaussian distribution, Mann Whitney *U* was used to determine the differences in their levels following ingestion of the meals. Correlation between variables was determined using the Spearman's rho correlation. Results are reported as median (interquartile range). *P*-values less than 0.05 were considered as statistically significant.

Results

Eleven participants completed the study; one participant was excluded. His plasma levels of ghrelin and GLP-1 were unexpectedly elevated and there was no immediate possible explanation.

The pattern of GLP-1 response following ingestion of the meals was slightly different from that of the reference meal. Following ingestion of the reference meal, there was steady release of GLP-1 between 0 min and 30 min. At about 30 min, the concentration rose progressively and reached its peak at about 90 min after which it started declining (Fig. 1). In contrast, there was a sharp rise in GLP-1 concentration following ingestion of amala. The peak was reached at about 30 min. Thereafter, the concentration started declining and surprisingly, rose again at about 90 min. Similarly, GLP-1 concentration rose following ingestion of cowpea meal and at about 30 min, the concentration started declining paralleling the basal concentration at 120 min. Following ingestion of wheat meal, there was a steady rise in GLP-1 concentration from 0 min through 120 min with a sharp rise in concentration observed between 60 min and 120 min (Fig.1).

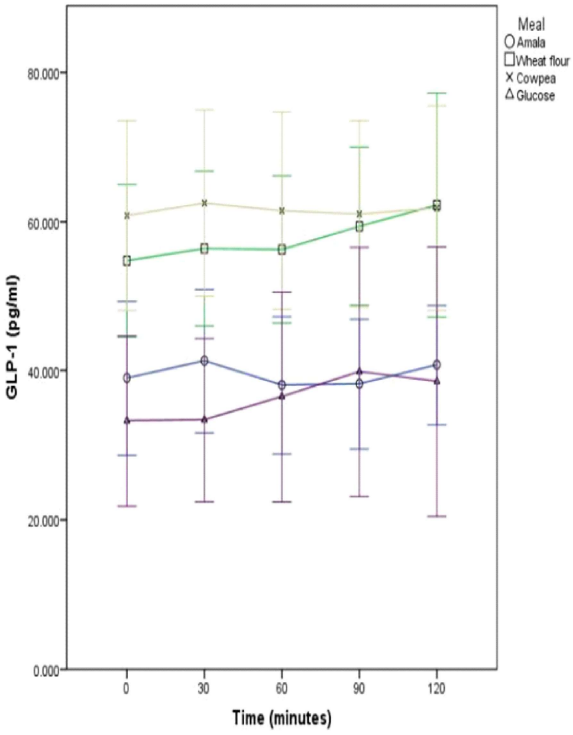

Fig. 1: GLP-1 responses following ingestion of amala, wheat paste, cowpea and glucose

The pattern of changes in ghrelin concentrations following ingestion of the test and reference meals are shown in Figure 2. There was a sharp drop in ghrelin concentration 30 min after ingestion of the reference meal compared with the fasting level. Thereafter, the concentration rose between 30 min and 60 min after which it started declining again. Changes in ghrelin concentration following ingestion of amala and wheat meal were similar. The concentrations of ghrelin steadily declined from 0 min through 90 min after which the concentrations rose again. In contrast, ghrelin concentration following cowpea meal ingestion steadily declined from 0 min through 60 min and thereafter, the concentration rose again but started declining at about 90 min post ingestion of cowpea meal.

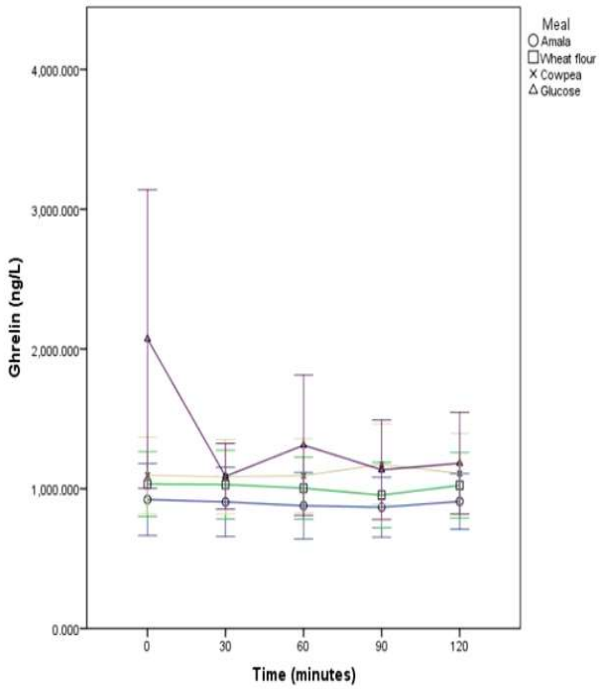

Fig. 2: Ghrelin responses following ingestion of amala, wheat, cowpea and glucose

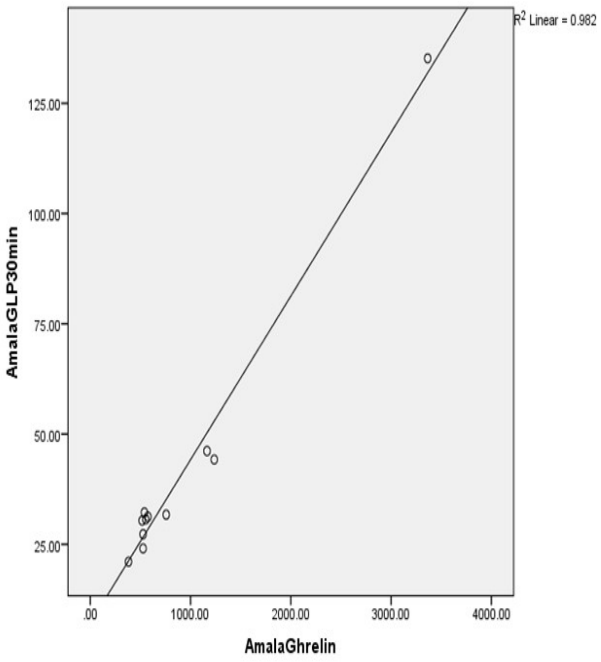

Fig. 3: Correlation between fasting ghrelin level and GLP-1 level 30 min post-ingestion of amala

Table 1: Areas under the curve for glucagon like peptide 1 (GLP-1) and ghrelin following ingestion of the test meals and the reference meal

	GLP-1 (pg/ml)	Ghrelin (ng/L)
Amala	3944.0 (2948.6 – 5324.3)	77772.8 (54272.5 - 136511.7)
Glucose	2266.4 (1757.6 - 4228.6)	86976.8 (77269.1 - 196241.9)
P-value	0.071	0.279
Wheat meal	3938.7 (3004.1- 8272.6)	101423.9 (59432.1 - 128284.4)
Glucose	2266. 4 (1757.6 - 4228.6)	86976.8 (77269.1 - 196241.9)
P-value	0.020*	0.922
Cowpea meal	6814.4 (3596.2 - 9366.4)	88918.3 (62701.6 - 139147.5)
Glucose	2266.4 (1757.6 - 4228.6)	86976.8 (77269.1 - 196241.9)
P-value	0.028*	0.768
Amala	3944.0 (2948.6 - 5324.3)	77772.8 (54272.5 - 136511.7)
Wheat meal	3938.7 (3004.1 - 8272.6)	101423.9 (59432.1 - 128284.4)
P-value	0.375	0.922
Amala	3944.0 (2948.6 - 5324.3)	77772.8 (54272.5 - 136511.7)
Cowpea	6814.4 (3596.2 - 9366.4)	88918.3 (62701.6 - 139147.5)
P-value	0.224	0.279
Wheat meal	3938.7 (3004.1 - 8272.6)	101423.9 (59432.1 - 128284.4)
Cowpea	6814.4 (3596.2 - 9366.4)	88918.3 (62701.6 - 139147.5)
P-value	0.669	0.922

*Significant at $P<0.05$

Table 1 shows the areas under the curve (AUC) for GLP-1 and ghrelin following the ingestion of test and reference meals. There were no significant differences in the median AUCs of ghrelin when the meals were compared with one another and when compared with the reference meal. However, the median AUCs of GLP-1 were significantly higher following ingestion of wheat and cowpea meals compared with the reference meal.

In order to assess the possible influence of fasting ghrelin level on postprandial GLP-1 release, correlation between the fasting ghrelin level and 30 min

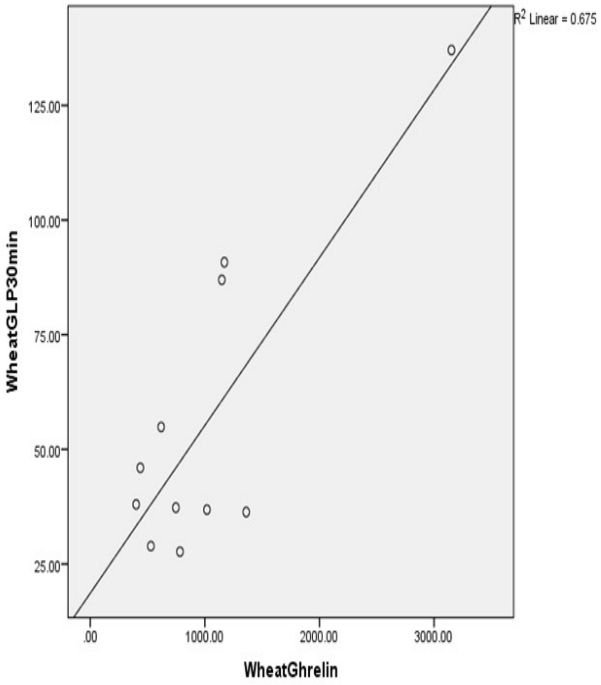

Fig.4: Correlation between fasting ghrelin level and GLP-1 level 30 min post-ingestion of wheat meal

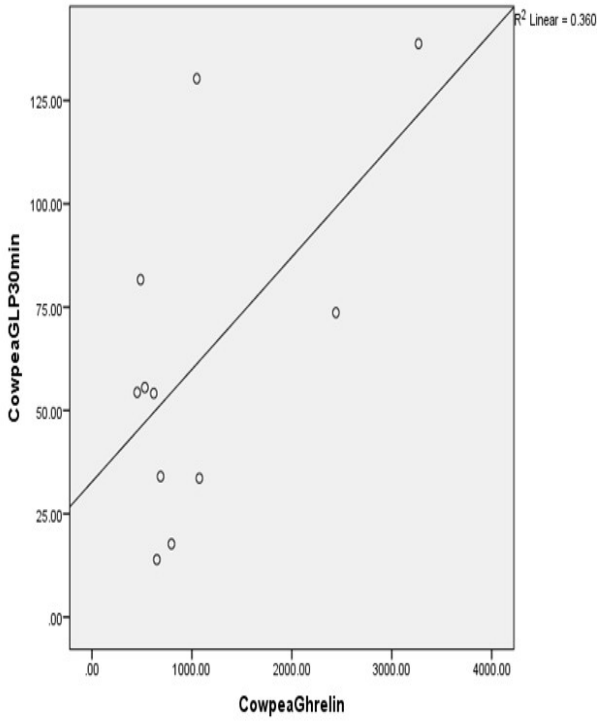

Fig. 5: Correlation between fasting ghrelin level and GLP-1 level 30 min post-ingestion of cowpea meal

level of GLP-1 post-meal ingestion was determined. The bivariate correlation plots are shown in Figures 3, 4, 5 and 6.There was significant positive correlation (r = 0.909, p = 0.000) between fasting ghrelin level and 30 min GLP-1 level following ingestion of amala. Similarly, significant positive correlation (r = 0.682, p = 0.021) between fasting

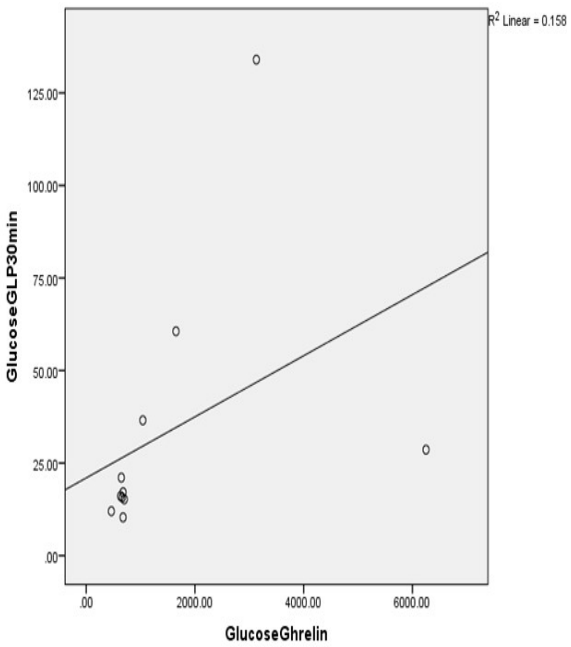

Fig.6: Correlation between fasting ghrelin level and GLP-1 level 30 min post-oral glucose ingestion

ghrelin level and 30 min GLP-1 level following ingestion of the reference meal. However, there were positive, but insignificant, correlations (r = 0.309, p = 0.355, r = 0.182, p = 0.593) between fasting ghrelin levels and 30 min GLP-1 levels following ingestion of wheat and cowpea meals respectively.

Discussion

Regulation of energy intake and appetite is a dynamic physiologic process involving a fine interplay between the orexigenic and anorexigenic hormones. Usually, there is low GLP-1 (an anorexigenic peptide) concentration in the fasting state but increases multifold after nutrient ingestion [21]. Similar observations were made in this study as there were increases in GLP-1 levels following ingestion of the four meals.

The observed dissimilar pattern of GLP-1 responses over the course of 120 min meal tolerance testing compared with the oral glucose tolerance testing might not be surprising as the report of Calanna *et al*. [22] showed that there is differential GLP-1 response following solid meal ingestion compared to oral glucose. This is evident in this study as GLP-1 release was noticeable within 30 min of ingesting the solid meals unlike the reference meal. This observation might be due to the fact that no sampling was done within the first 20 min post oral glucose load and hence, we probably missed the peak secretion period. Kim and Egan [23] reported that GLP-1 levels generally reach maximum secretion between 17 to 20 min post oral glucose ingestion.

Although direct interaction of luminal nutrients with L-cells appears to be key in the production of GLP-1, nutrients, neural and hormonal factors have also been shown to play important roles in the mechanisms regulating incretin release [24]. This might be responsible for the observed irregular patterns in the rise and fall of GLP-1 levels following the ingestion of amala and cowpea meals compared with the reference meal. This observation could be due to the biphasic nature of GLP-1 secretion [11] and might suggest that the peaks of GLP-1 secretion, especially the second peak, vary according to the nutrients in a meal. Furthermore, the continuous rise in GLP-1 concentrations, even at 120 minutes, post wheat meal ingestion was unexpected. This may suggest that the second peak of GLP-1 release following wheat meal ingestion extends beyond 120 min. This may further buttress our suggestion that the peaks of GLP-1 release could be meal dependent. Usually, the first peak of GLP-1 secretion appears within 15 min after meal initiation while the second peak, which is larger, occurs later when nutrients had had contact with intestinal L cells [11].

Consumption of whole wheat products has been reported to be a useful dietary intervention in diabetes prevention [25]. The observed significant elevations in the AUC_{GLP-1} of wheat and cowpea meals compared with the reference meal might indicate that there is slower nutrient release following ingestion of these meals. This probably culminated in slower stimulation of L cells which resulted in a larger second peak of GLP-1 secretion since the first peak of GLP-1 secretion is largely reached before nutrients even have access to the L cells [11]. Our observation could be due to the high contents of fiber and protein in wheat and cowpea respectively. In contrast, the observed similar AUC_{GLP-1} of amala and reference meal might indicate that nutrient release following amala ingestion is rapid thereby stimulating rapid GLP-1 production. Due to the incretin effect of GLP-1, it might mean that there is rapid insulin release following ingestion of amala. Therefore, there might be the need for some caution in amala consumption as diets that provoke more insulin secretion have adverse effect on glycaemic control [26].

Ghrelin, a somatotrophic orexigenic hormone, is secreted mainly from the stomach in a pulsatile manner [27]. Its level increases steadily before meal and during fasting, but decreases after feeding [28]. In contrast to GLP-1, ghrelin concentrations expectedly decreased following ingestion of all the meals, although there were differences in the pattern of responses to the meals. There has been controversial reports on changes in ghrelin concentration following ingestion of protein rich meals. These controversies have mainly been attributed to variation in meal composition [29]. However, unlike amala and wheat meals, the unordered changes in ghrelin concentrations over the course of 120 min following cowpea ingestion might be due to the protein content of cowpea which has the highest protein content among the meals selected for this study. Erdmann *et al*. [30] reported that a protein rich meal increases ghrelin level. At 120 min, the ghrelin levels following ingestion of the 3 meals paralleled the baseline values. This could mean that the three meals have similar appetite induction.

The high levels of ghrelin that occur immediately before a meal, is reported to prime the L cells and thereby enhance GLP-1 release following feeding [12]. The positive correlation observed between the fasting levels of the meals and the 30 min GLP-1 levels following ingestion of the meals might indicate that the higher the level of fasting ghrelin, the higher the level of GLP-1 released. This observation appears to be in line with the report of Tong *et al*. [19] which showed that ghrelin raises postprandial GLP-1 secretion.

Our study has a number of limitations. These include small sample size, lack of satiety score, and non-determination of hormones such as glucagon, glucose-dependent insulinotropic peptide (GIP) and des-acyl ghrelin which could add more information to our observations.

It could be concluded from this study that ingestion of 50g of available carbohydrate of cowpea meal, whole, unprocessed wheat meal and amala have similar appetite inducing potential due to their comparable ghrelin levels while ingestion of cowpea meal or whole, unprocessed wheat meal might have some benefits in maintaining normoglycaemia because of their effects on GLP-1 release. Additionally, fasting level of ghrelin appears to have some stimulating effect on postprandial release of glucagon-like peptide 1.

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Survey of proficiency and factors mitigating clinical skills acquisition during medical school training

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Abstract

Background: Traditionally, the art and science of medical skills acquisition occur through an apprenticeship model where trainers supervise trainees who are learning on the patients exposed to variety of risk. The concern for patient safety and other limitations in provision of adequate training has necessitated the introduction of skills simulation for trainees to acquire certain proficiency before encounter with live patients.

Objectives: The study is aimed to determine the level of skills acquired and constraints experienced by newly graduated medical doctors during their training in various medical schools in Nigeria.

Method: Structured questionnaires were administered to interns undergoing orientation training programme at the University of Ilorin Teaching Hospital, Nigeria. Items were set to determine the frequency of practice and proficiency attained in basic clinical procedures during medical school training; and the factors that influenced their attempts of the procedures. The data was entered in SPSS for Windows version 17.0 and p value d" 0.05 was taken as statistically significant.

Results: There were 163 new interns who graduated from 11 medical schools (three outside Nigeria). The participants were aged between 22 and 35 years with no significant statistical difference between the mean ages of interns trained at home or abroad. Mean attempt of basic procedures ranged between 1.73 and 3.93 overall among 9.8 to 81.5% of the trainees. Most of them performed poorly on the pre-training self-assessed proficiency level. Urethral catheterization and intravenous cannulation were the commonest procedures done while the least performed procedures were nasogastric intubation, chest tube insertion; and fracture reduction and splinting (1.53-2.10 mean attempt) among less than 25% of trainees. Inadequate training facilities and competition between undergraduate and postgraduate trainees for procedures on the available but reluctant patients were considered as limiting factors in the acquisition of skills. However, inadequate number of trainers was considered least of a preventive factor.

Conclusion: Most medical graduates had inadequate exposures to skills acquisition from various medical training institutions due to inadequate volunteers (patients) and lack of students' call rooms for proximity to where and when the activity is taking place. We recommend that Clinical Skills acquisition through simulation should be integrated into the curricula of medical training institutions to facilitate acquisition of skills and ease practice on and safety of patients.

Keywords: *Patient safety; medical errors, clinical skills, simulation; internship*

Résumé

Contexte : Traditionnellement, l'art et la science de l'acquisition des compétences médicales reposent sur un modèle d'apprentissage dans lequel les formateurs supervisent les stagiaires qui apprennent sur des patients exposés à une variété de risques. Le souci de la sécurité des patients et d'autres limitations dans la fourniture d'une formation adéquate ont nécessité l'introduction d'une simulation des compétences permettant aux stagiaires d'acquérir certaines compétences avant de rencontrer des patients vivants.

Objectifs : L'étude a pour objectif de déterminer le niveau de compétences acquises et les contraintes rencontrées par les médecins récemment diplômés au cours de leur formation dans diverses facultés de médecine au Nigéria.

Méthode : Des questionnaires structurés ont été administrés à des stagiaires prenant part à une formation de programme d'orientation à l'Hôpital d'Enseignement de l'Université d'Ilorin, au Nigeria. Des éléments ont été définis pour déterminer la fréquence de pratique et de maîtrise des procédures cliniques de base au cours de la formation en médecine ; et les facteurs qui ont influencé leurs tentatives des procédures. Les données ont été entrées dans SPSS pour Windows version 17.0 et la valeur p d" 0,05 a été considérée comme statistiquement significative.

Résultats : Il y'avait 163 nouveaux stagiaires qui ont été diplômés de 11 facultés de médecine (trois hors du Nigéria). Les participants étaient âgés de 22 à 35 ans et ne présentaient aucune différence statistique significative entre les âges moyens des stagiaires

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formés au Nigeria ou à l'étranger. Le nombre moyen de tentatives de procédures de base variait globalement entre 1,73 et 3,93 chez 9,8 à 81,5% des stagiaires. La plupart d'entre eux ont eu de piètres résultats au niveau de compétence auto-évalué avant la formation. Le cathétérisme urétral et la canulation intraveineuse étaient les procédures les plus courantes, alors que les procédures les moins pratiquées étaient l'intubation nasogastrique, l'insertion d'un drain thoracique ; et réduction de la fracture et attelles (tentative moyenne de 1,53 à 2,10) parmi moins de 25% des stagiaires. Le manque de facilités de formation et la concurrence entre les stagiaires du premier cycle et des cycles supérieurs pour les interventions sur les patients disponibles mais réticents ont été considérés comme des facteurs limitants dans l'acquisition de compétences. Cependant, le nombre insuffisant de formateurs a été considéré comme moins d'un facteur préventif.

Conclusion : La plupart des diplômés en médecine ont été exposés de manière inadéquate à l'acquisition de compétences auprès de divers établissements de formation en médecine en raison du nombre insuffisant de volontaires (patients) et du manque de chambres d'appel pour les étudiants, à proximité du lieu et du moment de l'activité. Nous recommandons que l'acquisition de compétences cliniques par simulation soit intégrée aux programmes des établissements de formation médicale afin de faciliter l'acquisition de compétences et de faciliter la pratique sur et la sécurité des patients.

Mots-clés : *sécurité des patients ; erreurs médicales, compétences cliniques, simulation ; stage*

Introduction

Historically, medical students and graduates learn clinical skills primarily by practice on live patients through an apprenticeship model. These patients are exposed to certain risks possibly regulated by seniors who supervise the juniors while learning on the job. Medical apprenticeship provides effective knowledge translation under supervision of experts [1,2]. The apprenticeship is championed by a mentor who is expected to possess not just superior skills and knowledge but also high moral and professional values [3].

In this model, the students start by observing clinical practitioners and are gradually given more tasks to perform as their competence grows, however, this is dependent on the day-to-day demands of the workplace where learning opportunities and supervision do not have first priority.[2,4] Hence, there are agitations for better methods to provide the optimal learning experience for students during their clerkships [2].

Skillful performance of practical skills, which could be lifesaving by junior doctors is fundamental to the delivery of quality service to patients [5]. Observed deficiencies in undergraduate programmes have been blamed on overpopulation in medical schools and lack of training facilities. Non-availability of volunteers (patients); and students' presumption of reliance on rote learning and chance have led to inadequacy in the skills [6]. These deficiencies often times result in junior doctors suboptimal performance of skills that they have not been prepared for [7,8]. This can be a significant source of stress for them[5] and a potential source of risk to their patients.

These patients are also becoming increasingly concerned and worried about potential harm that they are exposed to when medical trainees 'practise' on them. The emphasis on patients' safety and improved quality of care make the whole idea of bedside teaching and education to be gradually fizzling out [9-11].

The aim of this study was to determine the level of skills acquired and constraints experienced by newly graduated medical doctors during their training in various medical schools in Nigeria.

Materials and method

Structured questionnaires were self-administered to newly employed interns at the University of Ilorin Teaching Hospital, Nigeria during the orientation training programme in the Clinical Skills and Simulation Laboratory of the College of Health Sciences. All interns who resumed together participated in the orientation training program and participated in the survey. The questionnaires were administered before commencement (as a pre-test) and after completion (post-test) of a 2-day clinical skills' training. Items in the questionnaires were meant to determine the frequency of practice of basic clinical procedures during medical school training and the proficiency attained; and to determine the factors that influenced their attempts of the procedures. The lead author (ALO) designed the scoring of proficiency as follows:

None = 0 (No knowledge and skill of procedure)
Low = 1 (vague theoretical knowledge and no exposure to skills of procedure)
Moderate = 2 (Good theoretical knowledge and have performed procedure under supervision)
High = 3 (Good theoretical knowledge and competency in procedure; can perform procedure without supervision).

The data was entered into SPSS for Windows version 17.0 and p value ≤ 0.05 was taken as statistically significant.

Results

One hundred and sixty new interns comprising of 65 in 2014, 57 in 2015 and 40 in 2016 participated in study. These were graduates from 8 Nigerian medical schools and 3 overseas medical schools. They were aged between 22 and 35 years with insignificant statistical difference among the groups (Table 1). Of the minimum of 30 attempts (10 per year of clinical training of 3 years) of basic procedures mandatory for students, mean attempt

Table 1: Analysis of mean number of attempts at practice of procedures during medical school training

	2014 n= 66	% of participants with 3 attempts	2015 n= 57	% of participants with 3 attempts	2016 n=40	% of participants with 3 attemps	Sig. P-value
Age (years)	25.8 ±3.61		26.2±2.55		25.23±1.94		0.34
Sex (Male:Female)	48:18		2:1		2:1		0.72
Nasogastric_Intubation	1.95	23.6	2.18	33.4	1.83	19.4	0.33
Suturing_of_Wound	2.52	50	2.62	48.9	2.53	55.6	0.70
Cannulation	3.74	80.8	3.37	81.5	3.56	83.4	0.07
Blood_Transfusion	3.02	67.2	2.33	38.8	2.47	55.6	0.04*
Digital_Rectal	2.64	55.4	2.89	65.9	2.86	69.4	0.54
Cardiopulmonary	2.66	38	2.19	32	2.0	33.3	0.37
Urethral_Catheter	3.93	80	3.40	80	3.25	80.6	0.67
Chest_Tube_Insertion	1.73	9.8	1.53	13.2	1.08	11.1	0.03*
Lumbar_Puncture	2.26	38.3	2.43	45.9	1.75	36.1	0.27
Incision_and_Drainage	2.19	35.1	2.05	35.7	1.86	27.7	0.38
Scrubbing_and_Gowning	2.88	60.4	2.83	53.8	2.28	44.5	0.52
Aseptic_Gloving	2.92	62.7	3.09	68.2	2.92	68.5	0.58
Airway_Section	2.76	54.3	2.65	55.8	2.39	55.6	0.71
Airway_Access	2.08	25.6	1.90	20.5	1.58	22.2	0.26
Bone_Fracture	1.97	26.3	2.10	30.7	1.69	25.0	0.80

Table 2: Analysis of self-assessed proficiency of the three sets of interns

Year	2014		2015		2016		p-valve
Variables	Mean sxore	% of participants with moderate score	Mean score	% of participants with moderate score	Mean score	% of participants with moderate score	
Nasogastric Tube	2.14	30.2	2.2	38.6	2.3	38.9	0.63
Suturing	2.0	25.0	2.1	28.1	2.18	36.1	0.64
Cannulation_and_Infusion	3.18	86.0	3.0	77.2	3.12	88.9	0.35
Blood Transfusion	2.8	65.6	2.35	41.8	2.3	50.0	0.01*
Digital_Rectal_Exam	2.9	37.8	2.6	54.5	2.7	69.5	0.83
Cardiopulmonary_ Resuscitation	2.22	33.9	2.36	40.3	2.18	36.2	0.58
Urethral Catheter	3.15	81.6	2.95	68.5	2.9	77.8	0.31
Chest Tube Insertion	1.39	3.3	1.57	3.6	1.33	0	0.12
Lumbar Puncture	1.66	15.0	1.69	11.3	1.52	8.3	0.54
Incision And Drainage	1.97	31.2	2.0	24.5	1.94	22.3	0.95
Scrubbing	2.58	55.6	2.76	68.4	2.36	52.8	0.14
Aseptic Gloving	2.78	59.4	2.95	78.2	2.61	71.2	0.18
Recognition_of_Abnormal_ Heart Sounds	2.29		2.55		2.55		0.06
Recognition_of_Abnormal_ Breath Sounds	2.72		2.75		2.67		0.88
Recognition_of_Normal_ Bowel Sounds	2.9		2.8		2.85		0.58

(actual) ranged between 1.73 and 3.93 overall among 9.8-81.5% of the trainees in all the groups in the 3 years, Table 1. Most of them performed poorly on the pre-orientation training self-assessed proficiency level, (Table 2). There is statistical difference among groups in the performance of blood transfusion (p value = 0.04) and chest tube insertion (p value = 0.03). The overseas trained interns confirmed that they learnt some of the procedures on mannequins as they never had contact with patients for legal reasons.

Urethral catheterization and intravenous cannulation were the commonest procedures done during medical school training in the three groups, though moderate to high proficiency level was up to 80%. The least performed procedures were nasogastric intubation, chest tube insertion; and fracture reduction and splinting (1.53-2.10 mean attempts) among less than 25% of trainees among whom were just 30% who had moderate pre-orientation training proficiency.

The factors that prevented adequate attempts and practice of procedures during training included competition between undergraduate and postgraduate trainees for procedures on available patients (73.6%), overpopulation and lack of training facilities in medical schools (60% each), and refusal of patients to be "used as guinea pigs". Inadequate number of trainers was considered least as a preventive factor (Fig.1).

The participants suggested that greater supervision, provision of clinical skills simulation laboratory and provision of call rooms would have assisted them in observing and doing more procedures during training.

Discussion

Medical internship which is also called housemanship is a compulsory phase in medical training in Nigeria and many countries in the world.[11] The duration is a year period in Nigeria but can be up to two years in other countries when a newly minted doctor is trained under a supervising consultant in an accredited medical facility.[12] During this period, interns participate fully in patients' management, which also includes performance of a number of procedures some of which are invasive.

In this study, the three sets of interns (2014, 2015 and 2016) graduated from eight medical schools in Nigeria, which gives a fair mix of experience and distribution of perception of medical training in the country.

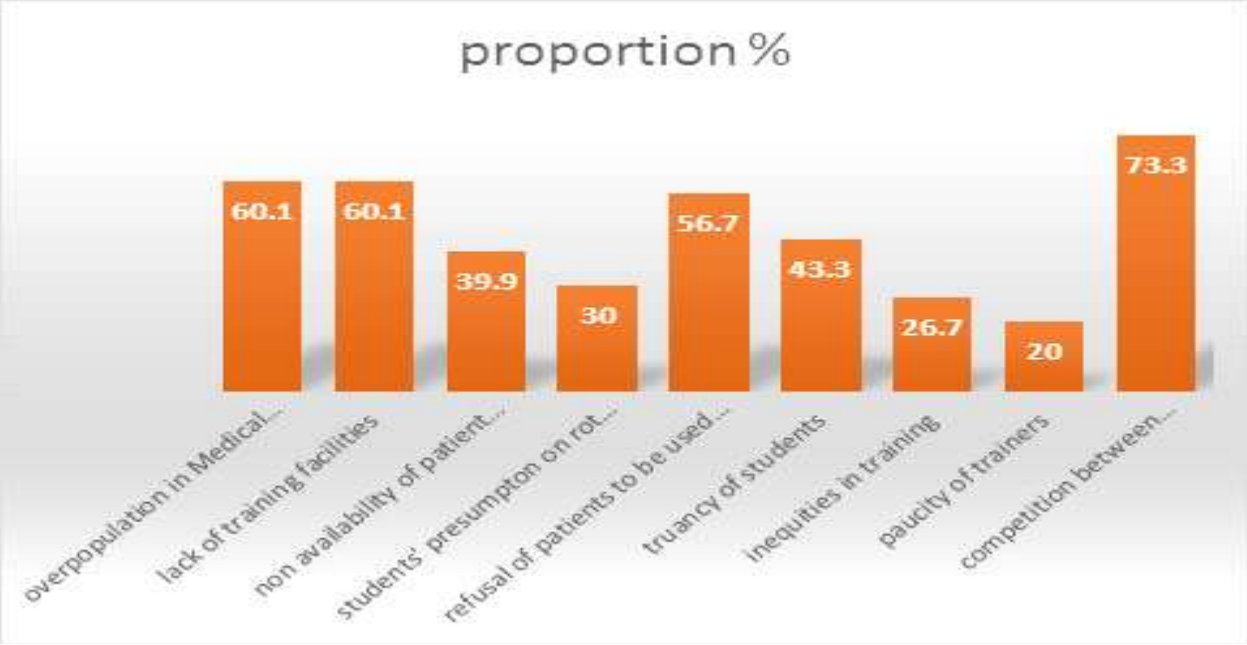

Fig. 1: The factors that influenced the attempts and proficiency of the participants

This study showed that many of the trainees had not attained at least 3 (10% percent) attempts on recommended basic procedures that should have been learnt before graduation. This goes to confirm that students do not see or perform enough basic procedures under supervision as expected during their training in the medical schools. The foreign

trained interns commented that they had restriction and exclusion from participation in patient care and procedures for legal reasons. This obviously will lead to several inadequacies in skills and can lead to major errors in patient care as alluded to in the previous studies.[6-9] The statistical difference among groups in the performance of blood transfusion and chest tube insertion confirmed restriction on some live saving procedures, which students should readily be conversant with the art and practice.

Some of the reasons given for inadequate skills acquisition were competition between undergraduate and postgraduate trainees for procedures on few available patients, overpopulation and lack of training facilities in their medical schools; and refusal by patients to be "used as guinea pigs" for trial of procedures. This is in consonance with other studies [6,7]. Most of the participants denied 'truancy' of students and inadequate trainers as causes of poor students' acquisition of skills in medical schools but reported that the distance of the hall of residence to the teaching hospital facilities prevented them from being present at the bedside when procedures were being done. They therefore, suggested that call rooms should also be provided for students so that they are available most times to participate in carrying out procedures. Ideally, medical students are expected to be offered accommodation on site appropriate to the placement they are doing with access to use of all amenities on site including internet access, well stocked library facilities and excellent catering and restaurant facilities [13,14].

Errors in medical practice are associated with great losses which might be apparent or concealed [15] Kaldjian *et al* [16]. reported that most faculty and resident physicians in US teaching hospitals were inclined to report harm-causing hypothetical errors, but only a minority have actually reported an error. More often than not these medical errors result in morbidities that hampers patients' capabilities and quality of life. These could be prevented by adequate training, drills and pre-procedure practice on mannequins, prefabricated and reconstructed models, animal experimental laboratory and virtual simulation laboratory [17].

Most participants in this study were exposed adequately to venipuncture and intravenous cannulation, urethral catheterization and sterile gloving during medical school training, however; the rated proficiency was low. This low proficiency might be blamed on inadequate practice and supervision, which could be mitigated by exposure to training and practice on mannequins in the simulation laboratory as suggested by many of the participants. Evidence based projects like the Capstone project provides evidence that information in conjunction with simulation improve the competency of nurses in medication administration [18]. This training demonstrated that high proficiency in clinical skills and transfer of knowledge could be attained by using appropriate simulation tools in a safe environment. It has been proven that provision of learning resources, in the form of simulators and computer-based learning modules could successfully be adopted and integrated into medical schools' curriculum if well planned and adapted as may be necessary [17, 19-21]. Simulation-based medical education enables knowledge, skills and attitudes to be acquired for all healthcare professionals in a safe, educationally orientated and efficient manner [22].

Limitations of this study include our inability to objectively ascertain the impact of this short time training on the clinical practice on live patients in the hospital. However, we received commendation from the staff (nurses, doctors, etc.) on the wards describing the interns that had gone through the orientation training as 'new breed' who have made patients' care seamless through prompt and efficient performance of basic procedures as directed by their seniors. The other limitation is that we could not also compare the foreign trained students skills because their numbers were few (<5%/ group).

Conclusion

Most medical graduates had inadequate exposure to skills acquisition from various medical training institution across the country. This was reflected in their low self-rated proficiency which they claimed was due to few available volunteering patients and lack of students call rooms for proximity to where and when the activities are taking place. Though, they claimed trainers were adequate, they requested for more supervision of performance of procedures. We recommend that simulation centres should be established and properly integrated into the curricula of training institutions in Nigeria to facilitate skills acquisition to optimal proficiency level in a safe environment. This is not a replacement for clinical exposure to live patients but will enable understanding of the details of the procedures and boost the confidence of the learners when approaching the live patients with ultimate elimination of errors.

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Predictors of adherence to hypertension treatment among adult patients attending Medical Out-Patient Clinics of a secondary health care facility in Southwestern Nigeria

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Abstract

*Background***:** Hypertension has been found to be one of the preventable risk factors for renal, cardiac and blood vessel diseases and hence there is a need to achieve control. Despite new guidelines and development of new drugs in treatment of hypertension, a significant number of patients remained uncontrolled. Adherence has been found to affect blood pressure control according to literature. Demographic characteristics, severity of disease, number of drugs and doses prescribed and side effects of some drugs have been found to affect adherence. Achieving good control of hypertension will reduce rate of emergency admissions, health care expenses, strain in family income, days off work, depression and invariably improve quality of life in patients with hypertension.

Aims: To evaluate the predictors of adherence to treatment of hypertension among patients attending Medical Outpatients clinic at a secondary health care facility in southwest Nigeria.

Methods: The study was a cross sectional study of 386 randomly selected adults with uncontrolled hypertension aged between 18years and 70years on treatment and follow up conducted at the Medical Outpatient clinic of the State Hospital Oyo. Chi-square test was used for bivariate analyses to test the significance of the association between categorical variables and adherence to medications. Logistic regression analysis was performed for the various factors to show the predictors of adherence to treatment of hypertension. Data was analyzed using Statistical Package for Social Sciences (SPSS) soft-ware version 15 and a p-value of ≤ 0.05 was considered to indicate statistical significance.

Results: Hypertensive patients with monthly income of $\geq$ N13, 600 were about three times more likely to have good treatment adherence compared to those who were earning < N13,600 monthly. (OR= 2.815 ; 95% CI= 1.103 – 7.186). Also, hypertensive patients on single medication were about six times more likely to have good adherence to medications compared to those on three drugs(OR= 6.184; 95%CI= 1.141 - 33.533).

Conclusion: The predictors of good adherence to anti-hypertensive therapy included monthly income and the number of drugs used by the patients. The prescriptions of efficacious, cost-effective medications, single dose daily therapy with minimal side effects will improve patient adherence to therapy.

Keywords: *Hypertensive, adults, treatment, adherence*

Résumé

Contexte **:** L'hypertension s'est avérée l'un des facteurs de risque évitables des maladies rénales, cardiaques et des vaisseaux sanguins ; il est ainsi nécessaire de parvenir à un contrôle. Malgré les nouvelles directives et le développement de nouveaux médicaments pour le traitement de l'hypertension, un nombre important de patients sont restés non contrôlés. L'adhérence affecte la régulation de la pression artérielle selon la littérature. Les caractéristiques démographiques, la gravité de la maladie, le nombre de médicaments et les doses prescrites, ainsi que les effets indésirables de certains médicaments ont des effets sur l'adhérence. Un bon contrôle de l'hypertension réduira le taux d'admission d'urgence, les dépenses de santé, la pression sur le revenu familial, les journées de congé, la dépression et améliorera invariablement la qualité de vie des patients hypertendus.

Objectifs: Pour évaluer les facteurs prédictifs de l'adhérence au traitement de l'hypertension chez les patients fréquentant une clinique de consultations externes dans un établissement de soins de santé secondaire situé dans le sud-ouest du Nigéria.

Méthodes : L'étude était une étude transversale portant sur 386 adultes sélectionnés aléatoirement, atteints d'hypertension non contrôlée et âgés de 18 à 70 ans, traités et suivis à la clinique de consultations externes de l'hôpital public de l'État à Oyo. Le test du chi carré a été utilisé pour les analyses bivariées afin de tester la signification de l'association entre

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les variables catégorielles et l'adhérence aux médications. Une analyse de régression logistique a été réalisée pour les différents facteurs afin de montrer les facteurs prédictifs de l'adhérence au traitement de l'hypertension. Les données ont été analysées à l'aide de la version 15 du logiciel SPSS (Statistical Package for Social Sciences) et une valeur-p $\leq$ 0,05 a été considérée comme indiquant une signification statistique.

Résultats : Les patients hypertendus avec un revenu mensuel > N13.600 étaient environ trois fois plus susceptibles d'avoir une bonne adhérence au traitement par rapport à ceux gagnant moins de N13.600 par mois. (OR = 2,815; IC à 95% = 1,103 à 7,186). En outre, les patients hypertendus qui prenaient un seul médicament avaient environ six fois plus d'adhérence au traitement que ceux qui prenaient trois médicaments (OR = 6,184; IC à 95% = 1,141 - 33,533).

Conclusion : Les prédicteurs de la bonne adhérence au traitement antihypertenseur comprenaient le revenu mensuel et le nombre de médicaments utilisés par les patients. Les prescriptions de médicaments efficaces et rentables, une thérapie quotidienne à dose unique avec des effets secondaires minimes amélioreront l'observance du traitement par le patient.

Mots - clés : *Hypertension, adultes, traitement, adhérence*

Introduction

Hypertension has been found to be one of the preventable hazards for renal, cardiac and blood vessel diseases and therefore there is a need to achieve control [1]. Various researchers in Nigeria have documented a myriad of cardiac complications of hypertension (such as left ventricular hypertrophy, diastolic dysfunction, congestive heart failure, ischemic heart disease, stroke) and renal failure [2.3]. Adherence is a term used to describe the patients' behaviour of taking drugs correctly based on mutual agreement between the patient and health care provider [4-,6]. Ramli *et al* reported that poor knowledge of hypertension and its treatment, increasing number of medications and dose frequencies were associated with poor adherence [7]. They recommended multi-disciplinary approach with patients' involvement in their own treatment to improve adherence. Demographic characteristics, severity of disease, number of drugs and doses prescribed, drug classes, patients' forgetfulness and lack of understanding of the nature of disease affect adherence [8]. Adherence might be affected by side effects of some drugs. According to some studies done in Nigeria, some patients developed headaches after using nifedipine. Some developed dizziness, drowsiness, nightmares and insomnia after using methyldopa and brinerdin [5,8].

Patients' adherence to prescribed therapy and advice is a strong predictor of achieving blood pressure control. The number of medications prescribed and the complexity of the treatment regimen are two important determinants of patient adherence. This has been shown in patients with a variety of different diseases. Adherence improves with fewer medications or pills prescribed [9,10]. Taking antihypertensive drugs once daily has been shown to have the highest adherence rate compared with multiple daily dosing [11]. It has been found that adherence and compliance appear to be reduced with complex, multiple-dose regimens [12]. Tamuno and Fadare reported poor adherence to therapy which could have been responsible for poor blood pressure control [13]. Literature search has shown that the predictors of good blood pressure control were diuretics and beta- blockers and the predictors of poor blood pressure control were diabetes, chronic kidney disease, diabetic nephropathy and cerebrovascular disease [13].

It was reported from developed countries that rigorous patient education can result in improved adherence to therapy reducing morbidity and mortality. It has been reported that a major cause of treatment failure or poor control of hypertension is non-adherence to treatment [14]. Factors associated with good adherence to hypertensive management include regular clinic attendance, use of drugs prescribed by the doctors and strong social support from the community [6]. According to a study conducted in Kano, poor adherence to treatment was associated with poor knowledge of treatment of hypertension, poverty and side effect of drugs [15]. In another study conducted in Kano by Tamuno and Babashani, there was poor adherence to medications and subsequently poor control of hypertension [16]. Also in another study, it was reported that patients were not educated about life-style modifications and they had low adherence to medications [17]. Women have been found to be more likely to take less alcohol, smoke less and adhere more to medications than men and therefore have better controlled blood pressure [18]. Poor adherence to medications has been shown to contribute significantly to poor blood pressure control. Poor adherence to anti-hypertensive was also reported in two Nigerian studies [19,20]. However, a study carried out in Jos showed that patients had high level of knowledge of life style practices and good compliance to treatment [21].

Poverty is usually measured and quantified as an income below the minimum level of income

considered necessary to meet the basic needs of life. The income threshold varies from one country to another. A new poverty line of $1.25 a day (N13,600 monthly by current exchange rate) was pronounced by the World Bank in 2008 [22]. Poverty may contribute to poor adherence to management of hypertension and monthly income is one of the variables considered in this study. The medications used for treatment of hypertension are costly and that can cause major economic burden on patients and their families. Despite new guidelines on the management of hypertension, there is growing failure of control due to diverse factors and hence the need to assess predictors of adherence to management. Hypertension is a major public health burden, because of its increasing prevalence and the resulting medical resource consumption. Achieving better control of hypertension will decrease rate of emergency admissions, health care expenses, strain in family income, and invariably improve quality of life in patients with hypertension. Due to an increasing failure of blood pressure control, the burden of hypertension is growing in epidemic proportions in Africa over the past few decades [23]. The economic burden of long term antihypertensive therapy appears large, cost reduction strategies are needed to improve hypertension management in societies with inadequate funds. Hypertensive treatment consequently requires a response adjusted to the local environment [24]. The aim of this study was to evaluate the predictors of adherence to treatment of hypertension among adult patients attending Medical Outpatient clinic at the State Hospital Oyo.

Materials and methods

The study was conducted at the State Hospital Oyo in Oyo East Local government. Oyo is a sub-urban community located in Oyo central senatorial zone of Oyo State in the South-Western Nigeria in which the Yorubas are the predominant ethnic group. There are artisans, traders, civil servants, teachers and farmers living in the town. The study was carried out at the Medical outpatient clinic of the State Hospital Oyo. The Hospital is a secondary heath care center and has 170 beds capacity with various specialty units, paramedical and outpatient services. Most of the new patients come into the Hospital through General Outpatient Clinic which acts as the gateway of the hospital. Patients are referred to the State Hospital Oyo from other hospitals around Oyo town such as General hospital Fiditi and General hospital Ilora. Patients are also referred to Medical Out-patient clinic from other units within the hospital. The study was a cross-sectional study of 386 patients with uncontrolled hypertension. Respondents were recruited from April 2015 to July 2015.

Sample size estimation

Sample size was estimated using the formula

$n = \frac{Z^2pq}{d^2}$ [25]. Quoting n= minimum sample size

Z_α=the standard normal deviate, usually set at 1.96, which corresponds to the 95% confidence level. P = the prevalence of controlled hypertension to be 34.5% for Nigeria [13], q=1.0- p

d=degree of accuracy desired usually set at 0.05.

$n = \frac{(1.96)^2(0.345)(1-0.345)}{(0.05)^2} = \frac{(3.84)(0.226)}{(0.05)^2} = 347$

q= 1/1-f q is the adjustment factor f = non response rate, if f =10% q = 1/0.9 =1.11

n = 1.11 x 347 = 385.5 = 386

For the purpose of this study, a minimum 386 patients was recruited

Z_α= the standard normal deviate, usually set at 1.96, which corresponds to the 95% confidence level. Zα is standard normal deviate corresponding to level of significance (usually 5%)

A pretest of the questionnaire was carried out at the General hospital, Ilora, seven kilometers away from the study site on 40 patients to identify potential problems and amendments were done where necessary. Incomplete filling of questionnaires observed during the pretest leading to missing values were corrected during the main study.

The study population was composed of adults 18years to 70years with an established diagnosis of hypertension. Inclusion criteria included patients who were 18-70 years with uncontrolled arterial hypertension and office blood pressure of e”140 D 90 mm Hg. Exclusion criteria included patients with Systolic blood pressure >180 mm Hg and Diastolic blood pressure > 110 mm Hg who would need immediate adjustment of treatment, patients with renal insufficiency, pregnant and lactating women and patients with Diabetics mellitus.

Sampling technique

A simple random sampling technique with computer generated random numbers was used for selection. Medical Outpatient Clinic holds twice in a week at the State Hospital Oyo. About 110 patients per day were seen at the Medical outpatient clinic out of which about 66(60%) have been found to have

uncontrolled hypertension. Random numbers within the range of the number of registered patients with uncontrolled hypertension was generated using the random number function of Microsoft Excel 2007. (The soft-ware was opened, equal to= and r was clicked on the computer. Then RANDBETWEEN was clicked twice and randomisation was done between 1 and 66. The numbers were sorted from the smallest to largest and on each clinic day 24 patients with serial numbers corresponding to the random numbers generated was selected for recruitment from about 66 patients until the calculated sample size of 386 was achieved.

Scoring of Adherence among respondents

Adherence to treatment was assessed by using modified Morisky Medication-taking Adherence questionnaire which has a Cronbach's alpha of 0.753[26]. The assessment was done on a scale of 0-21 by asking the following questions: "How often do you forget to take your medicine"? "How often do you decide not to take your medicine"? "How often do you miss taking your medicine because you feel better"? "How often do you decide to take less of your medicine"?" How often do you stop taking your medicine because you feel sick due to the effect of the medicine"? "How often do you forget to bring along your medicine when you travel away from home"? "How often do you not take your medicine because you run out of them at home"? Questions were assessed on a scale of four. None of the time was scored three, some of the time was scored two, most of the time was scored one and all of the time was scored zero. Statistical analysis showed the mean score to be 20. Individual scores were totaled and categorized into two groups. Patients with adherence score less than 20 were categorized as having poor adherence while those with scores of 20 and above were classified as having good adherence.

Knowledge, Attitude and Practice Survey questionnaire of Hypertensive Patients was used to assesses Knowledge, Attitude and Practice of respondents. It is a validated instrument used in a previous study in Nigeria [27]. The Cronbach alpha coefficient is 0.82 [28]

Knowledge score

Knowledge of hypertension and its management among the respondents was assessed on a scale of 0-29 by asking to what extent the respondents agreed or disagreed with the following statements: Physically inactive lifestyle can contribute to increase of blood pressure; Alcohol abuse can contribute to increase in blood pressure; Smoking cigarettes can lead to blood pressure increase; Salt rich diet is one of the factors that contribute to hypertension; High vegetable and high fruit diet can increase blood pressure; Usage of high fat dairy products can cause increase in blood pressure; Excess use of fats and oils cannot increase blood pressure; Reduction of excess weight at least by 5 kg will lead to control high blood pressure more effectively; Compared with persons of your own age and sex, who do not have high blood pressure, how would you rate your risk of developing stroke? Can hypertension cause other health related problems, in case of absence of treatment or not adhering to treatment?

The responses to the statements were scored 0-2 irrespective of the responses been true or false. Also, for the last two questions, correct answers were scored one irrespective of the response been "yes or no", while incorrect answers were scored zero. Statistical analysis showed the mean score to be 19. Scores were totaled and categorized into two groups. Patients with knowledge scores less than 19 were classified as having poor knowledge while those with knowledge scores of 19 and above were classified as having good knowledge.

Attitude score

Attitudes of respondents towards hypertension and its management was assessed with total scores ranging between 0-18 by asking them to what extent they believed the following: Eating healthy food will help you to decrease your blood pressure; Reducing salt intake in food is important for controlling your high blood pressure; Using doctors prescribed medicine will help you to control your blood pressure more effectively; During the treatment, people who have high blood pressure should not stop the usage of prescribed medicines even in case of short term improvements; Main responsibility for ensuring your blood pressure balanced is yours; Main responsibility for ensuring your blood pressure balanced is your doctor's. The responses to the statements were scored 0-2 depending on the answers. Statistical analysis showed the mean score to be 16. Scores were totaled and categorized into two groups. Respondents with attitude scores less than 16 were classified as having poor attitude while those with attitude score of 16 and above were classified as having good attitude.

Practice score

Practices of hypertensive in management of hypertension were assessed by asking the following questions: Do you visit your doctor to monitor your blood pressure? How often do you visit your doctor

for your hypertension care? How often do you measure your blood pressure? During the last 7 days, on how many days did you do physical activities such as brisk walking or walking? On the days that you exercised, how many minutes did you usually spend exercising per day? Do you currently smoke cigarettes? How long have you been smoking? How many cigarettes did you smoke per day? How often do you add salt to your food without trying it? How much salt do you think you consume? What do you do on a regular basis to control your salt intake? Practice was assessed with total scores ranging from eight to 35. Statistical analysis showed the mean score to be 23. Scores were totaled and categorized into two groups. Respondents with scores of less than 23 were classified as having poor practices while those with scores above 23 were classified as having good practices.

Data was analyzed using Statistical Package for Social Sciences (SPSS) soft-ware version 15. The dependent variable was adherence and the independent variables included age, sex, level of education, monthly income, knowledge of hypertension, attitude and practice of hypertensive towards hypertension and its management. Frequency tables were used for relevant variables. Chi-square test was used for bivariate analyses to test the significance of the association between categorical variables and adherence to drugs. Binary logistic regression analysis was performed for the various factors to show the predictors of adherence to anti-hypertensive. A p-value < 0.05 was considered to indicate statistical significance.

This study was approved by the Ethical Review Committee of Oyo State Ministry of health, State Secretariat Ibadan, Nigeria. Informed consent was obtained from eligible patients before administration of the questionnaires and examinations. Privacy and confidentiality of the respondents were guaranteed by anonymity of respondents.

Results

Distribution of levels of adherence to treatment and number of anti-hypertensive drugs used by the patients

Table 1 shows that thirty four (8.8%) respondents had poor adherence to treatment while 352(91.2%) had good adherence to treatment. Fifty eight (16.40%) patients were on one anti-hypertensive drug while 158(44.60%) patients were on two anti-hypertensive drugs. Also one hundred and four (29.40%) patients were on three antihypertensive drugs while 34(9.60%) patients were on more than three anti-hypertensive drugs.

Table 1: Distribution of levels of adherence to treatment and number of anti-hypertensive drugs used by the patients

	Frequency (n)	Percentage (%)
Adherence scores		
Good adherence	352	91.2
Poor adherence	34	8.8
Number of drugs used		
One drug	58	16.4
Two drugs	158	44.6
Three drugs	104	29.4
More than three drugs	34	9.6

Factors associated with adherence to treatment of hypertension

Table 2 shows factors associated with adherence to treatment of hypertension.

A significantly higher proportion of hypertensive patients (87.2%) with monthly salary of $\geq$ N13, 600 had good adherence to treatment compared to hypertensive patients (5.8%) with monthly salary of < N13, 600. Majority (92.7%) of the respondents that had good knowledge of hypertension had good adherence to treatment compared with respondents (89.5%) that had poor knowledge of hypertension. A significantly higher proportion 257(93.8%) of the 274 respondents that had good attitude toward hypertension had good adherence compared with 84.8% that had poor attitude. A higher proportion of hypertensive patients (92.0%) with no formal education had good adherence to treatment compared to 82.0% with primary education. A higher proportion of hypertensive patients who were using one drug 53(91.4%) had good adherence to therapy compared with hypertensive patients (89.4%) who were using three drugs.

Logistic regression analysis of good drug adherence to hypertension treatment on selected variables

Table 3 shows the results of binary logistic regression of good drug adherence on selected variables. After adjusting for other variables, the predictors of good adherence to anti-hypertensive therapy include monthly income and using one drug for treatment of hypertension.

Respondents who were on one anti-hypertensive drug were about six times and one and half times respectively more likely to have good adherence to therapy compared to those who were

Table 2: Factors associated with adherence to treatment of hypertension

		Adherence to treatment of hypertension			
Variable		Poor (n)	Good (n)	X^2	p-value
Sex	Male	6(10.9%)	58(89.1%)	0.433	0.511
	Female	28(8.4%)	294(91.6%)		
Age in years	<454	5(6.2%)	33(93.8%)	0.824	0.844
	5 to 54	12(11.4%)	120(88.6%)		
	55 and above	19(7.9%)	197(92.1%)		
Monthly income	<13,600	210(94.2%)	13(5.8%)	5.643	0.018*
	≥13,600	20(12.8%)	136(87.2%)		
Knowledge	Poor	15(7.3%)	162(89.5%)	1.210	0.286
(Naira)	Good	19(10.5%)	190(92.7%)		
Attitude	Poor	17(15.2%)	95(84.8%)	7.971	0.005*
	Good	17(6.2%)	257(93.8%)		
Practice	Poor	18(12.0%)	132(88.0%)	3.111	0.078
	Good	16(6.8%)	220(93.2%)		
levels of education	No education	15(8.0%)	172(92.0%)	0.824	0.844
	Primary	7(8%)	80(82.0%)		
	Secondary	6(10.2%)	53(89.8%)		
	Tertiary	6(11.5%)	46(88.5%)		
Number of drugs	One drug	5(8.6%)	53(91.4%)	9.418	0.024*
used by the patients	Two drugs	3(1.9%)	155(98.1%)		
	Three drugs	11(10.6%)	93(89.4%)		
	More than three drugs	3(8.8%)	31(91.2%)		

**Significant at 5% level of significance*

Table 3: Logistic regression analysis of good drug adherence on selected variables

	Variable	Odd Ratio	95% CI	p-value
Number of drugs used	One drug	6.184	1.141- 33.533	0.035*
by patients	Two drugs	1.416	0.296 - 6.783	0.663
	Three drugs	1		
Monthly income	≥ ₦13,600	2.815		
	< ₦ 13,600	1	1.103 – 7.186	0.030*
Attitude	Good attitude	0.414		
	Poor attitude	1	0.161 – 1.064	0.067
Practice	Good practice	0.952		
	Poor practice	1	368 – 2.464	0.920
Sex	Female	0.680	0.222 – 2.082	0.499
	Male	1		

*Significant at 5% level of significance

on three anti-hypertensive drugs.(OR= 6.184; 95%CI= 1.141 - 33.533 and OR= 1.416; 95% CI= 0.296 - 6.783).

Patients who were earning ≥ 13,600 monthly were about three times more likely to have good adherence to therapy compared to those who were earning < 13,600 monthly. (OR= 2.815 ; 95% CI= 1.103 – 7.186). Attitude, practice and sex were however not associated with adherence to treatment of hypertension

Discussion

Despite improved awareness of hypertension and accessibility of many efficacious antihypertensive agents, only one third of patients achieved their target blood pressure. One of the reasons recognized for

the poor control of high blood pressure was poor adherence to therapy [29]. This study showed that majority of the respondents had good adherence to treatment of hypertension which was in agreement with the results of two studies conducted in Nigeria [30, 31]. It was reported that a little above average of patients had good compliance with therapy in a study conducted in Ibadan whereas a very high proportion had good adherence to therapy in this study [31]. The results of a study conducted in Kano also showed that majority of hypertensive patients had good adherence to therapy [15]. The findings of the Kano study conducted by Kabir et al was similar to the findings of this study which showed that patients who were on one type of anti-hypertensives had a higher proportion with good adherence to treatment compared with other patients. Shaikh and others in their work reported a lower proportion of their respondents having good adherence to pharmacotherapy which was contrary to the findings of this study [29].

Majority of the respondents in this study who had good attitude toward hypertension and its management had good adherence to treatment compared with those who had poor attitude toward hypertension. The group of hypertensives with good attitude and good adherence towards treatment of hypertension would be expected to have good control of their blood pressure. The association between attitude of respondents toward hypertension and their adherence to therapy was statistically significant. However, the results of a Nigerian work done by Iyalomhe et al showed that patients with hypertension had poor attitude toward hypertension and its management which was contrary to the results of this study [27]. They also reported low adherence among the respondents that were recruited which might have resulted to poor blood pressure control. The level of adherence to treatment in hypertensive patients was also said to be unacceptably low according to the results of work done in Nigeria [19].

It was found in this study that patients who were on one class of anti-hypertensives had better adherence than those on more than one class of drugs. It was reported that the lower the number of medications the higher the adherence to therapy which was similar to the findings of this study [10]. This was corroborated by Flack and Nasser who reported that taking anti-hypertensive once daily has highest level of adherence compared with multiple dosing [11]. This was also corroborated by Potchoo et al that adherence appeared to be reduced with multiple complex dosing of medications [12]. So Physicians should prescribe the lowest number of doses and classes of drugs to patients for better adherence to treatment and better blood pressure control.

This study has shown that poverty is associated with adherence, the higher the income the better the adherence. The new poverty line of $1.25(approximately N250 in 2015) a day was announced by the World Bank in 2008[22]. According to this study, those who earned N7500 and above monthly had better adherence to treatment than those who earned less than ¦ 7500 monthly. In a work done in Kano, Kabir and others found that poor adherence to treatment was mainly associated with ignorance of the need to take medications as prescribed, lack of funds to buy drugs and side effects of drugs. It was reported that patients with insufficient funds would have low adherence to treatment and consequently poor control of their blood pressures[33]. Majority of the respondents had good adherence to anti-hypertensive therapy irrespective of their level of education according to the results of this study.

In conclusion, the level of adherence to therapy was found to be high among respondents. The predictors of good adherence to anti-hypertensive therapy include monthly income and the number of drugs used by the patients. There is a need for the government to improve the socio-economic status of the populace by job creation and also to subsidize cost of drugs so that patients with hypertension would be able to afford to buy their drugs.

Conclusion

Based on the findings of this study**,** health care providers must update themselves on Evidence Based Medicine by reading and also doing more researches in Behavioural Medicine. There is a need to launch a comprehensive approach of educating patients to take their drugs regularly as prescribed. Doctors should consider the financial position of their patients in prescribing antihypertensive medications. The prescriptions of efficacious, cost-effective medications, single dose daily therapy with minimal side effects will increase patient adherence to therapy.

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Determination of the role of patient satisfaction on glycaemic control among persons with diabetes attending the Family Medicine Clinic of Federal Medical Centre, Ido-Ekiti, Nigeria

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Abstract

*Background***:** Diabetes mellitus in sub-Saharan Africa is a chronic and debilitating disease with increasing morbidity and mortality and health care costs.

Aim: This study focused on determination of the role of patient satisfaction on glycemic control among persons with diabetes attending the Family Medicine clinic of Federal Medical Centre, Ido-Ekiti, Nigeria

*Materials and methods***:** A cross-sectional descriptive study was conducted on 156 adults with diabetes diagnosed in the hospital and had been attending the clinic for at least 6 months. Relevant data were collected using interviewer-administered semi-structured questionnaire and clinical parameters measured include fasting plasma glucose (FPG). Data were analyzed using statistical package for the social sciences (SPSS) software version 17.

Result: In this study, 127 (81.4%) of the participants were satisfied with services provided while 134 (86%) had good glycemic control. There was significant difference between the satisfied and dissatisfied participants with regard to age group, ethnicity, glycaemic control (based on FPG) as well as in the pattern of medication adherence (based on Morisky medication adherence scale MMAS). The age of participants is a predictor of satisfaction while the level of patient satisfaction and age of the patients are predictors of pattern of glycaemic control and medication adherence of the participants. A positive association existed between patient satisfaction, medication adherence and glycaemic control in persons with diabetes.

Conclusion: Therefore, physicians and health care providers ought to seek ways of improving patient satisfaction with a view to enhancing good glycemic control.

Keywords: *Diabetes mellitus, satisfaction, medication adherence, Fasting Plasma Glucose, Glycaemic control.*

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Résumé

Contexte **:** Le diabète sucré en Afrique subsaharienne est une maladie chronique et débilitante qui entraîne une morbidité et une mortalité croissantes, ainsi que des coûts en soins de santé.

But : Cette étude portait sur la détermination du rôle de la satisfaction du patient sur le contrôle glycémique chez les personnes atteintes de diabète fréquentant la clinique de médecine familiale du Centre Médical Fédéral, Ido-Ekiti, Nigéria.

Matériels et méthodes **:** Une étude descriptive transversale a été menée sur 156 adultes atteints de diabète diagnostiqué à l'hôpital et fréquentant la clinique depuis au moins 6 mois. Les données pertinentes ont été collectées à l'aide d'un questionnaire semi-structuré administré par intervieweur et les paramètres cliniques mesurés incluent la glycémie à jeun. Les données ont été analysées à l'aide du logiciel SPSS (Statistical Package for Social Sciences) version 17.

Résultat : Dans cette étude, 127 (81,4%) des participants étaient satisfaits des services fournis, tandis que 134 (86%) avaient un bon contrôle de la glycémie. Il existe une différence significative entre les participants satisfaits et insatisfaits en ce qui concerne le groupe d'âge, l'appartenance ethnique, le contrôle glycémique (basé sur la glycémie à jeun) ainsi que sur le schéma d'adhérence thérapeutique (basé sur l'échelle d'adhérence thérapeutique, MMAS de Morisky). L'âge des participants est un facteur prédictif de satisfaction, tandis que le niveau de satisfaction du patient et l'âge des patients sont des facteurs prédictifs du modèle de contrôle glycémique et de l'adhérence thérapeutique des participants. Une association positive existait entre la satisfaction du patient, l'adhérence thérapeutique et le contrôle glycémique chez les personnes atteintes de diabète.

Conclusion : Par conséquent, les médecins et les prestataires de soins de santé doivent rechercher des

moyens d'améliorer la satisfaction des patients afin d'améliorer le contrôle de la glycémie.

Mots-clés : *diabète sucré, satisfaction, adhérence thérapeutique, glucose plasmatique à jeun, contrôle glycémique.*

Introduction

Diabetes mellitus (DM) is an important cause of morbidity and mortality worldwide affecting approximately one in ten United States adults at an estimated cost in 2007 of 174 billion dollars [1] and is projected as the sixth leading cause of death globally [2]. Although a lower prevalence (about 1-7%) is reported in Nigeria, the burden associated with it is felt more with an overall mortality rate of 32.5% with mean age at death being 57.07± 14.29years [3] and it poses major public health and socioeconomic challenges in the face of scarce resources [2,4-6]. In 2008, global age-standardized adult diabetes prevalence was 9·8% in men and 9·2% in women [7]. Estimates from 2009 by the International Diabetes Federation (IDF) suggest that the number of adults with diabetes in the world will expand by 54%, while for Sub-Saharan Africa is 98%, from 2010 to 2030 [7]. Globally 366 million people had diabetes in 2011; by 2030 this will have risen to 552 million [4]. The number of people with type 2 diabetes is increasing in every country and 80% of people with diabetes live in low- and middle-income countries [8].

Health is the most precious of all things, and the foundation of all happiness [11]. Health care includes both clinical and non-clinical care. Traditionally, the practice of medicine and assessments of quality of care in hospitals had concentrated on the former which tend to look only at cure, but certain other non-clinical aspects of care such as amenities and accessibility of care are equally important in determining the outcome of health care [12]

Patient satisfaction has been defined as the degree of congruency between a patient's expectations of ideal care and his/her perceptions of the real care he/she receives [13]. It is a summation of all the patient's experiences in the hospital [12]. It is derived from the patient's evaluation of how well the provider meets his or her personal and emotional as well as physical needs. Glycaemic control remains the major therapeutic objective for prevention of acute and chronic complications related to the disease [49]. Operationally, a patient was defined to have good glycaemic control if his or her fasting blood glucose in the study visit was less than 110 mg/dL (6.1mmol/L). This ordering was based on the standard of the Diabetes Association of Nigeria (DAN) as desirable glycaemic targets [47]. A similar value was used as standard for the United Kingdom Prospective Diabetes Study Group definition of intensive control for diabetes patients [48]. Present study therefore focused on determination of the role of patient satisfaction on glycemic control among persons with diabetes attending the Family Medicine clinic of Federal Medical Centre, Ido-Ekiti, Nigeria.

A transformation of healthcare is underway, from a sellers' market to a consumers' market, where the satisfaction of the patients' needs is part of the definition of quality [21]. While the business community has been involved in assessing customer satisfaction for at least a much earlier, the medical community has lagged considerably in assessing patient satisfaction. More recent developments in the medical environment have prompted the health care profession to recognize patients as valuable customers [22]. Discussions about how the quality of health care should be measured increasingly include patient satisfaction, which may be a predictor of whether patients follow their recommended treatments, re-attend for treatment or change their provider of health care. This is one principal goal of this research to show if patient satisfaction has any influence on the glycemic control of diabetes patients

Materials and methods

Study area

The study was conducted in the Family Medicine department of the Federal Medical Centre; Ido-Ekiti, Nigeria which is a Federal Government owned tertiary health care facility. The facility is located in Ido-Ekiti, the semi-urban headquarters of Ido-Osi Local Government Area of Ekiti State, Nigeria. The facility provides qualitative and efficient health care services and is a referral centre for all the health institutions (Specialist Hospitals, General Hospitals, and Comprehensive Health Centres etc.) in Ekiti State and environs.

Study design

This was a descriptive cross-sectional hospital-based study. The study was conducted during the period from April to June 2013. All persons with diabetes aged 20 years and above attending the Family Medicine clinic at FMC, Ido-Ekiti were used for this study. Questionnaire and other instruments were used to collect data.

Inclusion criteria

All those aged 20 years and above [14], who had been diagnosed to have DM and were receiving

treatment in family medicine clinic for at least 6 months.

Exclusion criteria

1. Those too ill and/or with acute complication(s) of DM such as diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS)
2. Pregnant patients (due to presence of gestational diabetes of pregnancy as a confounder)
3. Mentally impaired persons [15].

Scoring system for assessment of overall satisfaction

Dimension

Satisfied with all dimensions- 4, Satisfied with at least 3 of the dimensions- 3, Satisfied with at least 2 of the dimensions- 2, Satisfied with at least 1 of the dimensions – 1, Satisfied with none of the dimensions- 0. Score of 2 and above is satisfied, Score of 1 and below is dissatisfied [16]

Social classification

Subjects were allotted into one of five social classes based on each individual's occupation, employment, monthly family income and educational level according to a scoring system designed by Olusanya and Okpere [17] for Nigeria and other African countries as follows.

Occupation score

1. Professionals, Top civil servants, Politicians and Businessmen.
2. Middle-level bureaucrats, Technician, Skilled artisan, and well-to-do traders.
3. Unskilled workers, those in general whose family income would be at or below the National minimum wage of N18, 000.00 per month and the unemployed.

Level of educational attainment Score

0. University Education
1. Secondary or Tertiary level below University (e.g. College of Education, Polytechnic etc.)
2. No schooling or primary level only.

Fasting plasma glucose determination

The patients routinely came fasting. Fasting was defined as no caloric intake for at least 8 hours. A patient who came to the clinic unfasted, was asked to return the next morning for collection of sample for FPG. Venous blood (2.5 ml) was collected by the researcher into fluoride-oxalate bottle and transported to the chemical pathology laboratory of the hospital within 30 minutes for the determination of fasting plasma glucose (FPG) by the glucose oxidase method [21].

Height and weight

The height and weight of subjects were measured using a combined weighing scale and stadiometer manufactured by Surgifield Medical England. The weight was calibrated in kilograms and height in centimeters. The subjects stood erect against the height scale, wore no shoes and looked straight ahead and had their arms hanging loosely by their sides [20]. Height and weight were measured to the nearest 1cm and 0.1kg respectively.

The Body mass index

The Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared and categorized according to World Health Organization classification.

Blood pressure

This was measured with an Accoson® brand mercury sphygmomanometer with appropriate cuff size and a Littman's stethoscope. At least 5 minutes after the patient had arrived the clinic, the BP was measured with an appropriately sized sphygmomanometer cuff (A cuff with bladder that is 12-13cm x 35cm and a larger one for obese individuals was used at the upper two-third (2/3) of the arm).

Assessment of blood pressure control

Measured systolic and diastolic blood pressure values were judged as either well controlled or uncontrolled based on systolic blood pressure (SBP) being <140mmHg or e"140mmHg and/or diastolic blood pressure (DBP) being <90mmHg or e"90mmHg respectively

Data analysis

All data collected were analysed using the statistical Package for the social sciences (SPSS) for windows software version 17.0. Means, modes medians, standard deviations, proportions and percentages were determined as appropriate. Test of significance was done using Pearson's Chi-Square and Student's t-test as appropriate. $P<0.05$ was taken to be statistically significant.

Ethical consideration

Ethical approval was obtained from the Ethical Review and Research Committee of the hospital. Informed verbal and written consent was obtained from the willing participants. To maintain confidentiality, no names appeared on the

questionnaires, but only numbers were used as identifiers. Confidentiality and privacy were respected during interview.

Results

Socio-demographic findings

One hundred and fifty-six adult patients with diabetes mellitus attending family medicine clinics of the FMC Ido-Ekiti, Nigeria from April to June 2013, who were aged 20years and above, satisfied the inclusion criteria, gave their consent and had completed data were studied. The mean age (SD) of participants was 58 (±12) years. There were more female subjects 92 (59.0%) than male subjects 64 (41%) with a male to female ratio of 1: 1.44.

(82.7%) of the participants were married, 42.3% were unskilled workers, 54.5% had secondary or tertiary level below university education and most participants in this study fell into the lower social class (53.2%). One hundred and fifty (96.2%) subjects were Yoruba and 85.3% were Christians.

Age and gender characteristics of the respondents

Table 2. Summarizes the age and gender characteristics of participants and shows that the disease is typically one of older adults, with a mean age of 58 (± 12) years. The table particularly demonstrates that females were significantly older than males and that the proportion 61 (39.1%) of the participants in the age group of 60 –

Table 1: Socio-demographic characteristics of the respondents. (N = 156)

Characteristics	Frequency	Percent
Age group (yrs)		
< 40	8	5.1
40 – 49	24	15.4
50 – 59	38	24.4
60 – 69	61	39.1
70 +	25	16.0
Gender		
Male	64	41.0
Female	92	59.0
Domicile		
Urban	46	29.5
Rural	92	59.0
Outside Ekiti	18	11.5
Marital status		
Single	7	4.5
Married	129	82.7
Widowed	14	9.0
Divorced/Separated	6	3.8
Occupation		
Professionals, etc.	28	17.9
Middle-level bureaucrats, etc.	62	39.7
Unskilled workers	66	42.3
Educational		
University Education	22	14.1
Secondary or Tertiary level below University	85	54.5
No schooling or primary level only	49	31.4
Religion		
Christianity	133	85.3
Islam	23	14.7
Ethnicity		
Yoruba	150	96.2
Non-Yoruba	6	3.8

Table 1 shows the socio-demographic characteristics of the participants. Majority (59.0%) dwelt in rural areas of Ekiti, a larger proportion

69 years was significantly higher ($p<0.001$) than their counterparts.

Table 2: Age and gender characteristics of the respondents

Age in years	Male (n = 64)	Female (n = 92)	Total	Statistic	Df	P value
Mean ± SD	53.78 ± 14.29	61.95 ± 9.37	58 .60 ± 12.28	-4.310	154	<0.001*
Age group, n (%)						
< 40 yrs	8 (12.5)	0 (0.0)	8 (5.1)	17.974	4	0.001**
40 - 49 yrs	14 (21.9)	10 (10.9)	24 (15.4)			
50 - 59 yrs	15 (23.4)	23 (25.0)	38 (24.4)			
60 - 69 yrs	20 (31.3)	41 (44.6)	61 (39.1)			
70 + yrs	7 (10.9)	18 (19.6)	25 (16.0)			
Total	64 (100.0)	92 (100.0)	156 (100.0)			

Student t test applied Chi-square test applied*

Table 3: Family and social characteristics of the respondents.

Characteristics	Frequency	Percent
Social class group		
Upper class	28	17.9
Middle class	45	28.8
Lower class	83	53.2
Type of Family		
Monogamy	101	64.7
Polygamy‘	55	35.3
Family size		
5 or less	71	45.5
6 – 9	72	46.2
10 or more	13	8.3
Number of dependants		
< 5	86	55.1
5 or more	70	44.9
Family income (NGN)		
< 18,000	46	29.5
18,000 - 24,999	23	14.7
25,000 - 49,999	37	23.7
50,000 - 74,999	10	6.4
75,000 - 99,999	11	7.1
≥ 100,000	29	18.6

*Family and social characteristics of the respondents***.** Table 3 shows the family and social characteristics of the participants. Most participants in this study were in the lower social class 83 (53.2%), from monogamous settings 101 (64.7%), had a family size of more than four members 112 (71.8%) and about a third of the participants 46 (29.5%) earned less than N18,000 monthly. More of the participants 86 (55.1%) had less than five dependants in their household.

Physical, psychometric and laboratory characteristics of participants

Table 4 shows that the median (IQR) of the systolic blood pressure of the participants was 135.0 (120.0 - 148.0) mmHg, of the BMI, 25.9 (22.8 - 28.9) kg/m2, of the overall SWOPS score,3.0 (2.0 - 4.0). The nursing care had the highest mean SWOPS score of 0.8 while the registration process had the least score of 0.5 among the dimensions of care. The median Morisky’s medication adherence score was 1.0 (0.3

Table 4 Physical, psychometric and laboratory characteristics of participants

Variables	Mean	SD	Median (IQR)
Physical characteristics			
SBP (mmHg)	134.5	18.2	135.0 (120.0 - 148.0)
BMI (Kg/m^2)	25.90	3.99	25.9 (22.8 - 28.9)
Psychometric score			
Overall SWOPS	2.7	1.3	3.0 (2.0 - 4.0)
Registration process	0.5	0.5	0.0 (0.0 - 1.0)
Nursing care	0.8	0.4	1.0 (1.0 - 1.0)
Physician care	0.7	0.4	1.0 (0.0 - 1.0)
Pharmacy services	0.7	0.5	1.0 (0.0 - 1.0)
MMAS-4	1.3	1.0	1.0 (0.3 - 2.0)
Laboratory characteristics			
Fasting plasma glucose (mmol/L)	6.4	3.6	5.3 (4.3 - 6.4)

IQR=Interquartile range

SBP= Systolic blood pressure

Table 5: Association between patients' satisfaction and socio-demographic characteristics

Characteristics	Satisfaction level		Total	$\chi 2$	df	P value
	Satisfied	Dissatisfied				
Age group (yrs)						
< 40	2 (25.0)	6 (75.0)	8 (100.0)	21.357	4	<0.001
40 – 49	22 (91.7)	2 (8.3)	24 (100.0)			
50 – 59	32 (84.2)	6 (15.8)	38 (100.0)			
60 – 69	53 (86.9)	8 (13.1)	61 (100.0)			
70 +	1 (72.0)	7 (28.0)	25 (100.0)			
Gender						
Male	49 (76.6)	15 (23.4)	64 (100.0)	1.685	1	0.194
Female	78 (84.8)	14 (15.2)	92 (100.0)			
Domicile						
Urban	35 (76.1)	11 (23.9)	46 (100.0)	2.883	2	0.237
Rural	75 (81.5)	17 (18.5)	92 (100.0)			
Outside Ekiti	17 (94.4)	1 (5.6)	18 (100.0)			
Marital Status						
Single	4 (57.1)	3 (42.9)	7 (100.0)			0.207*
Married	107 (82.9)	22 (17.1)	129 (100.0)			
Widowed	12 (85.7)	2 (14.3)	14 (100.0)			
Divorced/Separated	4 (66.7)	2 (33.3)	6 (100.0)			
Religion						
Christianity	110 (82.7)	23 (17.3)	133 (100.0)			0.382*
Islam	17 (73.9)	6 (26.1)	23 (100.0)			
Ethnicity						
Yoruba	125 (83.3)	25 (16.7)	150 (100.0)			0.011*
Non-Yoruba	2 (33.3)	4 (66.7)	6 (100.0)			
Occupation						
Professionals, etc.	25 (89.3)	3 (10.7)	28 (100.0)	1.924	2	0.382
Middle-level bureaucrats, etc.	51 (82.3)	11 (17.7)	62 (100.0)			
Unskilled workers	51 (77.3)	15 (22.7)	66 (100.0)			
Educational						
University education	19 (86.4)	3 (13.6)	22 (100.0)	0.467	2	0.792
Sec. /Ter. below University	39 (79.6)	10 (20.4)	49 (100.0)			
None / Primary only	69 (81.2)	16 (18.8)	85 (100.0)			
Social class						
Upper class	24 (85.7)	4 (14.3)	28 (100.0)	1.143	2	0.565
Middle class	38 (84.4)	7 (15.6)	45 (100.0)			
Lower class	65 (78.3)	18 (21.7)	83 (100.0)			

*Fisher's exact test applied

Table 6. Association between patient satisfaction and family characteristics

Characteristics	Satisfaction level		Total	χ2	df	P value
	Satisfied	Dissatisfied				
Type of Family						
Monogamy	79 (78.2)	22 (21.8)	101 (100.0)	1.929	1	0.165
Polygamy‘	48 (87.3)	7 (12.7)	55 (100.0)			
Family size						
5 or less	58 (81.7)	13 (18.3)	71 (100.0)	3.918	2	0.141
6 – 9	61 (84.7)	11 (15.3)	72 (100.0)			
10 or more	8 (61.5)	5 (38.5)	13 (100.0)			
Number of dependants						
< 5	66 (76.7)	20 (23.3)	86 (100.0)	2.757	1	0.097
5 or more	61 (87.1)	9 (12.9)	70 (100.0)			
Family income (NGN)						
< 18,000	38 (82.6)	8 (17.4)	46 (100.0)	1.957	5	0.855
18,000 - 24,999	20 (87.0)	3 (13.0)	23 (100.0)			
25,000 - 49,999	30 (81.1)	7 (18.9)	37 (100.0)			
50,000 - 74,999	7 (70.0)	3 (30.0)	10 (100.0)			
75,000 - 99,999	8 (72.7)	3 (27.3)	11 (100.0)			
≥ 100,000	24 (82.8)	5 (17.2)	29 (100.0)			

Table 7: Association between satisfaction and some factors of diabetes health care

Variable	Satisfaction level		Total	χ2	df	P value
	Satisfied	Dissatisfied				
Duration of anti-diabetic medication (yrs)						
< 3 yrs	70 (78.7)	19 (21.3)	89	1.042	1	0.307
> 3 yrs	57 (85.1)	10 (14.9)	67			
Number of consultations in past 6 month						
0 - 2 times	58 (84.1)	11 (15.9)	69	1.984	2	0.371
3 - 5 times	41 (83.7)	8 (16.3)	49			
6 or more times	28 (73.7)	10 (26.3)	38			
Healthcare coverage (Health insurance)						
Yes	9 (90.0)	1 (10.0)	10	0.091	1	0.763*
No	118 (80.8)	28 (19.2)	146			

** Yates' correction for continuity*

- 2.0) while the median fasting plasma glucose was 5.3 (4.3 - 6.4) mmol/L.

Association between patients' satisfaction and socio-demographic characteristics

Table 5 shows the level of satisfaction based on socio-demographic characteristics. The proportion of the participants in the age group 40 – 49 years **(p<0.001)** and of the Yoruba ethnic group (p=0.011) had significantly higher levels of satisfaction when compared with their counterparts. The participants who were female (61.4%, p=0.194), domicile in rural Ekiti, 59.1%, p=0.237), married (84.3%, p=0.266) and Christians (86.6%, p=0.317) had higher levels of satisfaction compared to their counterparts however these differences were not statistically significant. Similarly, participants who had professional jobs were more educated and in the upper social economic class were more satisfied than their counterparts were. These relationships were not statistically significant.

Association between patient satisfaction and family characteristics

Table 6 illustrates the relationship between patients' satisfaction and family characteristics. The

Table 8: Relationship between patients' satisfaction and glycaemic control

Satisfaction level	Glycaemic Control		Total
	Good	Poor	
Satisfied	114 (89.8)	13 (10.2)	127 (100.0)
Dissatisfied	11 (37.9)	18 (62.1)	29 (100.0)

$\chi 2 = 39.835$, df = 1; P value < 0.001

Table 9: Differences in fasting plasma glucose by Satisfaction level

Satisfaction level	Fasting plasma glucose Mean ± SD (mmol/L)	t*	Df	P value
Satisfied	5.5 ± 2.1	-4.771	29.855	<0.001
Dissatisfied	10.5 ± 5.6			

** Student t test with assumption of unequal variances.*

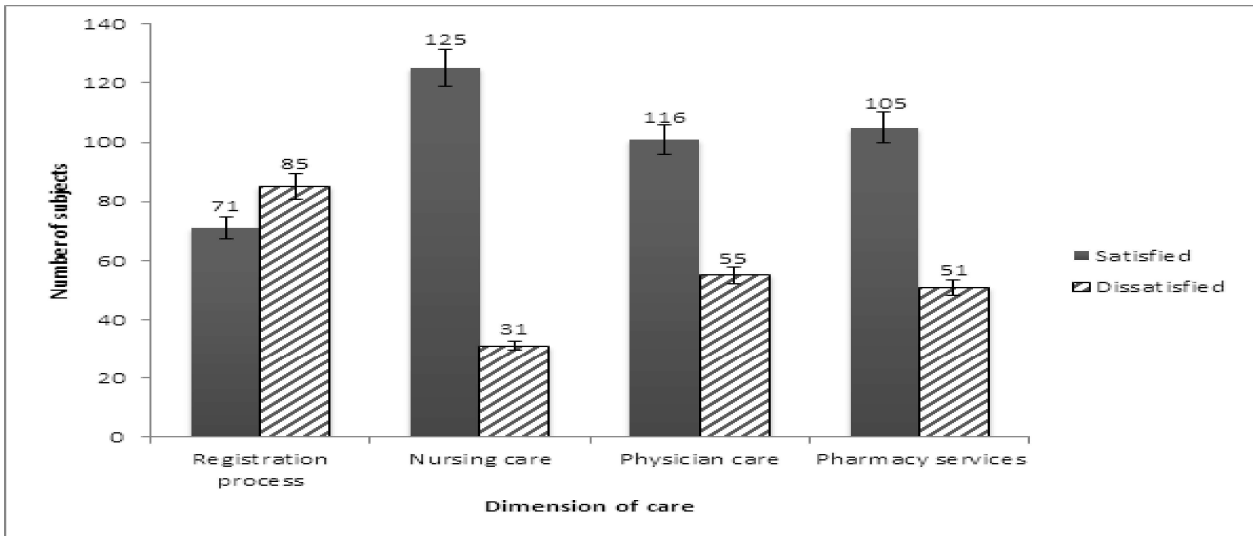

Fig. 1: Summary of patients' satisfaction by dimensions of care

participants from the polygamous setting 48 (87.3%) were more satisfied when compared to those from monogamous setting 79 (78.2%) but this difference was not statistically significant (p=0.165). Similarly, families with more than four members 93 (83.3%), more than 5 dependants 61 (87.1%) and monthly family income of N18,000 – 24,999, 17 (87%) were more satisfied than their counterparts. A significant difference does not exist between the satisfied and dissatisfied in terms of family size (p=0.141), number of dependants (p= (, 0.097) and family income (p= 0.694).

Association between satisfaction and some factors of diabetes health care

On table 7, the participants who had been on anti-diabetic medications for more than 3years, 57 out of the 67 participants accounting for 85.1% were found to be satisfied compared to the 70 of the 89 participants who have taken medications for less than 3years accounting for (78.7%) were found to be satisfied. Although this difference was not statistically significant (p = 0.307), it suggests that \satisfaction enhances medication adherence. Similarly, larger proportion of persons with diabetes who have health insurance, 9 out of 10 participants accounting for (90.0%) were satisfied compared to their counterparts who were not on health insurance,

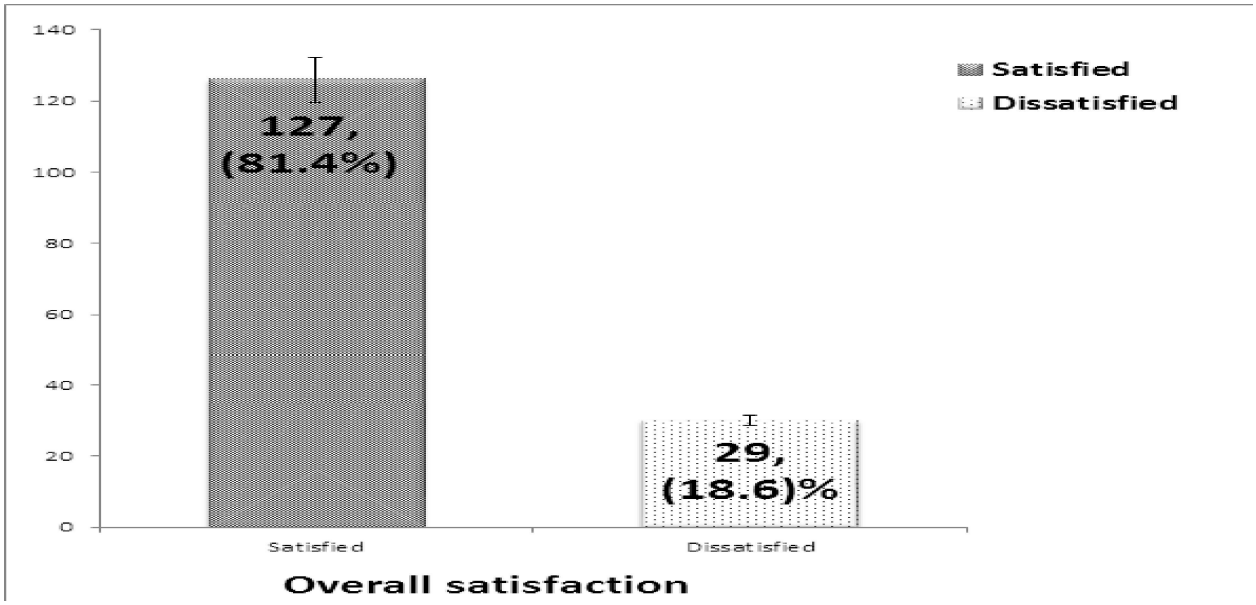

Fig. 2: Overall satisfaction of participants

118 out of 146 participants accounting for (80.0%). However, this difference was not statistically significant (p = 0.763). This also suggests that health insurance coverage is collateral to patient satisfaction and medication adherence.

Relationship between patients' satisfaction and medication adherence

In table 8, of the 127 participants who were satisfied, a larger proportion, seventy-nine (62.2%), had good adherence. There is a significant association (p<0.001) between level of satisfaction and level of adherence. The satisfied participants are more likely to adhere to their anti-diabetic medications.

Patients' satisfaction by dimensions of care

Figure 1. Following the operational definition of overall satisfaction, the nursing care recorded the highest number of satisfied participants 125 (80.1%). This was followed by the dimension of physician care, 116 (74.4%) and pharmacy care, 105 (67.3%). In contrast, more of the participants (54.5%) were dissatisfied with the registration process compared to the number of satisfied participants.

Overall satisfaction of participants

Figure 2. Overall, 81.4% representing 127 of the participants were satisfied with the services received from the outpatient services of the Federal Medical Centre, Ido-Ekiti while the remaining (29) 18.6% were dissatisfied

Discussion

The socio-demographic profile of the participants showed that majority were in the age group 60-69 years with a mean of 58 (SD= 12.28). The mean age in this study was ranked higher than the mean age of 48.9 9 ± 9.2 years obtained in a study to assess the prevalence rates of type 2 diabetes in Port Harcourt Nigeria [21] and 53.9 ± 14.4 years in Lagos Nigeria [22] .In this study, there were more female participants than male. The percentage of females attending the family medicine clinic in this study was 59% which is greater than the percentage of males (41%) attending the same clinic and in the ratio of 1.4:1. This is similar to the observation of a cross sectional descriptive study by Udonwa and Okoi [23]among persons with T2DM in a tertiary Family Medicine clinic in Southern Nigeria in which there were more females 72 (57.2%) than males 54 (42.8%) with a sex ratio of 1.3:1. Furthermore this finding of a female preponderance is in agreement to the observations from a previous study in South-western Nigeria [19].

The age characteristic of participants shows that the mean age of females (62.0 ± 9.4) years was significantly higher than that for males (53.8 ± 14.3) years. This finding is congruent with results of previous studies and a most likely explanation for this observation is the combined effect of a greater number of elderly women than men in most populations and the increasing prevalence of diabetes with age [24]. Education and income have been identified as major socioeconomic determinants of health and lower education usually begets lower

income [2]. Although the educational level in the study was good (68.6%) yet this did not translate to a high income as only a minority (17.9%) was in the high social class. Majority of the participants were of the Christian faith (85.3%); this may reflect the most predominant religion in Ekiti State Nigeria. This is similar to a study by Badejoko *et al.,* [25] in South-Western Nigeria.

In this study, the level of satisfaction of the patients with the services was generally very good as 126 (81%) of the participants were actually satisfied with the services in the Family Medicine clinics. This finding is similar to the results from previous studies where high levels of satisfaction with services accessed were observed [26]. Although, overall satisfaction in this study was very good, it was however lower than the overall satisfaction of 83% reported in Kano [27], 94.8% in Abuja [28] and 95-97% in India [29]. The reason for this variance may be due to the difference in the sample population. The patients satisfaction in this study was however higher than that recorded in Umuahia Nigeria 62% and Ethiopia where participants were similarly patients living with diabetes although the instrument for assessing patient satisfaction was different [26, 30, 31] .

This study also revealed that the participants were rather dissatisfied with the registration process. A similar result was reported by Ogunfowokan and Iloh [32] in Abuja Nigeria where they also found that patients were dissatisfied with the medical records. The dimension of nursing care recorded the highest level of satisfaction. This finding is similar to the report from Benin City, Edo state [33], Sokoto [34], and Ibadan [35]. However, this is dissimilar to the low rating of the dimension of nurses as reported in Ilorin Nigeria [36] and Eastern Ethiopia [30] The higher rating of the nurses in current and previous studies could be attributed to the interactive activities of the nursing services with the patients in the author's place of practice. It was observed that the nurses regularly organize morning prayers and health talks each day before commencement of clinical activities. Oluwadiya *et al.,*[12] suggested that patient satisfaction is influenced by how well the provider meets his or her personal, spiritual, emotional as well as physical needs beyond the biomedical aspects of their care. There is also observed positive significant association between age and patient satisfaction. A similar cross-sectional study on the experience and satisfaction of patients in Ethiopia pointed out that the relationship of age and patients' satisfaction was statistically significant [30]

Results of studies on the influence of gender on satisfaction with healthcare had been generally inconsistent [12]. Whereas a work in South Africa [37] showed that females significantly rated aspects of healthcare delivery higher than males, report in South-Western Nigeria observed that females significantly rated all indices of satisfaction lower than males in the Accident and Emergency Department of the hospital [12].

The profile of patient satisfaction with respect to different social classes indicated that the upper social class had the highest level of satisfaction while the lower class had the least level of satisfaction. The indices of social class (educational status and occupation) according to Olusanya and Okpar [17] also follow a similar pattern such that highly educated and high income professionals had a higher level of satisfaction when compared with other participants but these variations were not statistically significant in this study. However Bener *et al.,* [38] and Myburgh *et al.,*[37] in Qatar and South Africa respectively reported a comparable finding that socio-economic status of participants was significantly related to levels of satisfaction with the health care provider [37,38]. The findings of this study indicated that married and widowed subjects had a slightly higher level of satisfaction than single and divorced/separated subjects. This difference though not statistically significant is ascribed to the presence of other family members which could have resulted in health benefitting interactions which served to render family support. Cramer *et al*.,[39] and Cramer [40] respectively recognized family influence as one of the patient related factors responsible for patients' satisfaction. However Bener *et al.,*[38] found even more important result that persons with diabetes who were staying alone were significantly more satisfied with treatment than their counterparts.

In our study, the level of glycaemic control was 80.1% while only 41.8% of the patient had adequate glycaemic control in a study in Ethiopia. The reason for this difference may be due to the adherence rates of participants in the two studies. While the rate of good adherence in this study was 57.7%, it was 49% in the Ethiopian study [41].

In this study, there was significant association between patients' satisfaction and medication adherence. This is in agreement with the findings of previous research that satisfied patients were more adherent to recommendations regarding medications

and follow-up visits [42]. The majority of studies, like in this study, demonstrated the significant relationship between overall satisfaction with care and medication adherence and ultimately good glycemic control [43,44,45].

This study also found that satisfied participants were significantly more likely to have better blood glucose control than dissatisfied participants. This finding is in keeping with the results in Umuahia Nigeria and Qatar where patients who had optimum levels of glycaemic control were adjudged to be significantly more satisfied with care [26,31,38]. This finding is however predictable from the foregoing results in this study where a positive association was found between patient satisfaction and glycemic control. This suggests that if healthcare providers are more committed to the principles of patient-centred clinical method that will make for patient satisfaction, glycaemic outcome will improve. Healthcare providers and administrators need to continually reinforce and emphasize the importance of patient satisfaction at every opportunity of rendering service or care to patients.

Conclusion

Based on the results of the current study, there is a positive relationship between patient satisfaction, medication adherence and glycaemic control. Therefore, we conclude that patient satisfaction with health care services rendered is a key factor in ensuring good glycemic control and ultimately good diabetes treatment outcome.

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Assessment of design and anticipated challenges in the implementation of State Supported Health Insurance Scheme in a South West State, Nigeria

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Abstract

Background: Poor health indices in most low and middle-income countries are due to inadequate access to available health care. In Nigeria, the National Health Insurance Scheme (NHIS) devolved to State Supported Health Insurance Programme (SSHIP), a new approach aimed at improving access to health care and achieving Universal Health Coverage (UHC). Currently, not much is known about the design of SSHIP, anticipated challenges associated with its implementation, and plans to mitigate and appropriately address them. To elicit useful information about these (anticipated) challenges, the study was carried out among stakeholders who were directly involved in the design of the scheme in Oyo State, Nigeria. Findings will help to identify likely gaps needed to be addressed at the early stage of the scheme. This will contribute to efforts in implementing a sustainable health insurance scheme in the state.

*Methods***:** This is a descriptive cross-sectional study. To allow the researchers achieve the study objectives, a purposive sampling technique was employed in selecting all the 12-man Steering Committee members in the State Health Insurance Scheme for interviews. A validated In-Depth Interview (IDI) guide was used to collect qualitative data from the target population. Transcripts from the data were analysed using the thematic approach with the aid of ATLAS Ti software package version 7. Ethical approval was obtained from the Oyo State Ministry of Health Research Ethics Committee, Ibadan Nigeria. Consent was also sought and obtained from individual study participants.

Results: The concept and design of the SSHIP are fundamentally the same as any other social health insurance scheme like the NHIS, however, certain differences exist. In Oyo State, the SSHIP is made compulsory, it is supported by the organised trade unions, and policies (and benefits packages) are stratified based on the financial ability of individuals to subscribe to different premium platforms. Certain features of the scheme such as enrolment, premium determination and collection methods, and the absence of government funding support are likely areas of challenges that may militate against its sustainability. Stakeholders need to address these appropriately. Likewise, awareness and understanding the basic design of the scheme among potential beneficiaries will go a long way in the efforts to implement and sustain a successful scheme.

Conclusions: Findings in this study are suggestive that the State SSHIP enjoys good support from stakeholders in Oyo State. However, identified likely areas in the design of the scheme that could become a challenge to the scheme need to be appropriately addressed to ensure its successful implementation and sustainability. We accept as a limitation to more robust information the inability to interview certain key stakeholders such as the State Chairman of the Nigerian Labour Congress and some of the potential beneficiaries of the scheme.

Keywords*: State-supported health insurance scheme, Universal health coverage, Health financing*

Résumé

Contexte : Les mauvais indicateurs de santé dans la plupart des pays à revenu faible et intermédiaire sont dus à un accès insuffisant aux soins de santé disponibles. Au Nigéria, le régime national d'assurance maladie (NHIS) a été décentralisé en un Programme d'assurance maladie financé par l'état (SSHIP), une nouvelle approche visant à améliorer l'accès aux soins de santé et à atteindre la couverture de santé universelle. Actuellement, on en sait peu sur la conception du SSHIP, sur les défis anticipés associés à sa mise en œuvre et sur les plans pour les atténuer et les résoudre de manière appropriée. Pour obtenir des informations utiles sur ces défis (anticipés), l'étude a été réalisée auprès des parties prenantes directement impliquées dans la conception du programme dans l'État d'Oyo, Nigéria. Les

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constats aideront à identifier les lacunes susceptibles d'être traitées tout au début du programme. Ceci contribuera aux efforts déployés pour mettre en place un régime d'assurance maladie durable dans l'État.
Méthodes **:** Le plan d'étude descriptif transversal a été utilisé. Pour permettre aux chercheurs d'atteindre les objectifs de l'étude, une technique d'échantillonnage par choix raisonné a été utilisée pour sélectionner tous les membres du Comité directeur composés de 12 membres du régime d'assurance maladie de l'État pour des entretiens. Un guide validé d'interview en profondeur (IDI) a été utilisé pour collecter des données qualitatives auprès de la population cible. Les transcriptions des données ont été analysées à l'aide de l'approche thématique à l'aide du logiciel ATLAS Ti version 7. L'approbation éthique a été obtenue du Comité d'éthique de la recherche du ministère de la santé de l'État d'Oyo, Ibadan, Nigeria. Le consentement a également été demandé et obtenu des participants individuels à l'étude.
Résultats : Le concept et la stratégie du SSHIP sont fondamentalement identiques à ceux de tout autre régime d'assurance sociale de santé tel que le NHIS, toutefois, il existe certaines différences. Dans l'État d'Oyo, le SSHIP est rendu obligatoire, soutenu par les syndicats organisés et les politiques (ainsi que les paquets d'avantages) sont stratifiés en fonction de la capacité financière des individus à s'abonner à différentes plates-formes premium. Certaines caractéristiques du programme, telles que l'inscription, la détermination des primes et les méthodes de perception, ainsi que l'absence d'aide financière de la part du gouvernement sont des domaines susceptibles de poser des problèmes qui pourraient nuire à sa durabilité. Les parties prenantes doivent y répondre de manière appropriée. De même, la connaissance et la compréhension de la stratégie de base du système parmi les bénéficiaires potentiels contribueront grandement à la mise en œuvre et au maintien d'un système réussi.
Conclusions : Les résultats de cette étude sont suggestifs que le programme d'assurance maladie financé par l'état bénéficie d'un bon soutien des parties prenantes dans l'Etat d'Oyo. Cependant, les domaines identifiés dans la conception du système susceptibles de poser problème, doivent être traités de manière appropriée pour assurer sa mise en œuvre et sa durabilité. Nous acceptons comme limite aux informations plus fiables l'incapacité d'interviewer certains acteurs clés tels que le président du Congrès des Travailleurs Nigérian dans l'Etat d'Oyo et certains des bénéficiaires potentiels du programme.

Mots - clés *: Régime d'assurance maladie financé par l'État, couverture de santé universelle, financement de la santé*

Introduction

The inequity of access to available healthcare is largely responsible for the ubiquitous poor health indices in most low and middle-income countries. However, this is more pronounced in the sub-Sahara African countries [1-3]. Efforts aimed at addressing this challenge to achieve Universal Health Coverage (UHC) are the major driving forces behind the reforms to adopt and implement prepayment methods for financing health care services [4, 5]. Prepayment method of financing healthcare started in Germany and thereafter in other European countries over a century ago [6, 7]. In countries where similar structures are in place, prepayment method for paying health care services varies in structure and governance [8, 9] because of appropriate responses to different situational and structural factors in the contextual environments where they exist. Nevertheless, mutual support remains one of the fundamental reasons behind this mode of payment for health care [7].

Studies have shown that adoption and ease of transition from out-of-pocket [10] to pre-payment methods for health varies from country to country. While it took some countries over a century to achieve UHC, others were able to do the same within a considerably short period of time [6]. The facilitators and barriers in the adoption and expansion of prepayment arrangement as it exists in social health insurance schemes include the design of and awareness about schemes [11], types and structure of political institution of a country [12,13] and the political will on the part of policy-makers [14, 15]. Other factors are the size of formal to informal population, the socio-economic status of the people, as well as the technical and administrative skills of those saddled with the responsibility to administer the scheme [1, 16].

SSHIP was established in the year 2016 by the Oyo State Government to ease financial barriers of access to available health care services. A committee was set up to design an appropriate scheme with respect to this.

Upon the completion of its assignment, no assessment has been conducted on the pre-implementation phase of the scheme. This study was therefore designed to assess the design and the structure of the State-supported health insurance scheme which includes general knowledge about SSHIP, determination and collection method of set premium, implementation and expansion plan and the challenges in the implementation, sustainability of, and plans to create awareness about the scheme among potential beneficiaries in Oyo State. Findings

will be useful to guide policy decision and help to address identified gaps in this early stage of the scheme for successful implementation and sustainability.

The Context

With a population of approximately 180 million, Nigeria is Africa's most populated country. The country operates a federal system of governance at three levels: federal (national), state and the Local Government Areas (LGAs). The country is divided into 36 states and the Federal Capital Territory, which has the status of a state. These states are grouped into six geopolitical zones of the northeast, northcentral, northwest, southeast, south-south and the southwest [17]. Like other countries with a federal/presidential system, the sub-national governments (States and the LGAs) are autonomous and thus, possess legislative power to determine the direction of low politics policy sectors, except for defence and the economy which are considered high politics policy sectors and are thus under the control of the national government. The health sector is one of low politics policy [18].

Nigeria has a Gross Domestic Product of $568.5 million and is currently classified as a lower middle-income country (LMIC). However, available health indices are poor with a high infant and child mortality rate, maternal mortality ratio and low life expectancy at birth among others [3]. One of the factors attributed to this is a prevalent gross inequity of access to available health care services in the country (19).

To correct this, the NHIS was established in 2005 by the Federal Government of Nigeria. Since its establishment, population coverage of the scheme is less than ten per cent [19, 20]. Majority of the present beneficiaries are civil servants working with the federal government. Because the health sector is a low politics policy, the national government could not enforce enrolment into the scheme. As a result of this, subscription to the scheme by the States, as well as by interest groups, such as the organised labour unions is voluntary with a resultant poor population coverage [20].

To facilitate the adoption of the scheme at the sub-national levels, the National Council on Health (NCH) in Nigeria approved the devolution of the scheme to the states in 2015, whereby each state implements its own SSHIP with technical assistance from the National Health Insurance Scheme [21]. Subsequent to this, in the year 2016, Oyo State Government established an agency saddled with the responsibility to design, implement and perform oversight function on the scheme for which a committee made up of stakeholders from the health and insurance industries as well as the state law making establishment was constituted to execute the design and implementation plans. Implementation and management of the scheme is a tripartite public-private arrangement among the trio of the SSHIP agency, the Health Maintenance Organisations (HMOs) and health care providers. While the state agency plays an oversight function of policy-making and ensures quality health care is delivered to the enrollees who are the beneficiaries, The HMOs purchase health care service from healthcare providers (both private and public) for the enrollees. The scheme is designed in such a way that HMOs reimburse healthcare providers for the services rendered to enrollees and the HMOs in turn, are paid by the agency for the cost incurred through what they pay the healthcare providers.

Methods

The study was qualitative and cross-sectional in design, using a 12-man Steering Committee members' interviews on the SSHIP in Oyo State, Nigeria. This study was carried out in Oyo State, located in the South West geopolitical zone of Nigeria. The State consists of 33 Local Government Areas (LGAs) and has a population of 5.5 million [22]. It is located approximately on longitude 3°54'E of the Greenwich meridian and latitude 7°23'N of the equator. There was a total of 1,237 health facilities in the State made up of both the public and private facilities, across the three levels of care: primary, secondary and tertiary. Like in the other States of Nigeria, most of the people in the state pay for healthcare through Out of Pocket (OOP) [19, 23].

Ethical approval was obtained from the Oyo State Ministry of Health Research Ethics Committee, Ibadan Nigeria.

Purposive sampling technique was employed for this study, all the 12-man Steering Committee members were identified and scheduled for in-depth interviews. However, only nine members were available at the time of the interviews. Consent was obtained from individuals after study objective was provided. The nine were interviewed. Those interviewed included officials of the State health insurance agency, NHIS officials, representatives of HMOs and healthcare providers, a member of the public and a member of the State House of Assembly's Committee on Health. The other three members who were not available for the interview were the Chairman,

Oyo State branch of the Nigerian Labour Congress and two officials of the NHIS.

A validated In-Depth Interview (IDI) guide which included sections on participants' socio-demographics, data information on the basics of the SSHIP, potential beneficiaries, premium determination, and mechanisms of the premium collection, was used to collect data. Using the same tool the benefit packages, anticipated challenges on implementation and plans to overcome them. The themes in the guide were developed based on the objectives of the study while the question items were formed after the review of the relevant literature [24-26]. Two trained Research Assistants conducted the interviews and transcribed recorded audios. Interviews, which were conducted in the English Language, were tape-recorded with the consent of the participants. One interview session lasted an average of one hour. Data collection started in February 2017 and was completed in May of the same year. The long duration interval was because of the difficulty in securing booked appointments with some members of the Committee. Data collected and transcribed were stored in a passworded computer accessible only to the research team members. Data analysis was done using a deductive thematic approach [27]. Codes were developed from the date by two independent data analysts. Themes were generated from the codes thereafter. ATLAS Ti version 7 software was used to analyse the data. Outputs and reports were generated for specific codes, and sub-themes and narratives were identified. Themes and narratives were interpreted within the context of the study.

Results

Purpose of State Supported Health Insurance Programme

All the participants were in unison about the purpose of the (SSHIP), which according to them, was established to attain Universal Health Coverage (UHC) in the State. Participants affirmed that the National Council on Health (NCH), Nigeria highest decision-making body on health, authorized the establishment of the SSHIP to enable States in the country who hitherto had failed to subscribe to the national scheme (NHIS) design, implement and manage their health insurance schemes. According to one of the participants,

It's all about bringing and attaining universal health coverage. It came about because of, let me say, failure of the NHIS to attain universal health coverage. So barely two years ago, the highest decision-making body, the National Council on Health, decided that if NHIS could not achieve universal health coverage they should allow states to introduce alternative health insurance schemes. (A male, State government official).

Another participant said,

The SSHIP was created basically because, let me use the word, failure of the various State governments to key into the national health insurance all along, you know, they have always argued, why should they send their money into Federal Government account? (A male, National Health Insurance Scheme official)

Similarities and differences between the National Health Insurance Scheme and State Supported Health Insurance Programme

There were divergent views on the similarities between the National Health Insurance Scheme (NHIS) and the (SSHIP). One of the important features mentioned was that while the NHIS was voluntary, the SSHIP is made compulsory for everyone in the state. One other feature mentioned was the understanding that the SSHIP is closer to the people than the NHIS, and therefore more likely to have better acceptance and achieve more coverage than the NHIS.

NHIS is a national scheme. NHIS has not made it mandatory for anybody to subscribe, but SSHIP is mandatory for everyone in the state to subscribe. It is a programme that has all the people involved, and I think that is a major difference. The whole idea is just to drive health insurance and to reach more people which can only be done through the states. (A male, Chairman House Committee on Health, Oyo State House of Assembly)

The establishment of the SSHIP was viewed to have some advantages over the NHIS. According to some participants, the establishment of the SSHIP bring health insurance programme closer to the people within a state and would be able to meet their health finance needs. Quoting one of the participants,

At least, we are closer to the grassroots. We can talk to them; they know us more than those people (NHIS). They can believe in us more than them . . . Most people do not even know where NHIS office is, but for SSHIP, they believe it is a State programme, that they own it. They believe more in their own local scheme. (A female, State Health Insurance official)

Premium determination

Participants were of the opinion that premium will be determined based on socio-economic class stratification. For this, it was mentioned that the scheme has different plans, namely, the standard,

platinum, and gold plans; an individual can buy into any of the plans depending on his or her ability to pay. For civil servants in the state, for instance, a certain percentage of their basic salary will be deducted from source for the scheme. For artisans and others in that category, they are expected to make payments as it is financially convenient. According to one of the participants,

It's supposed to be a percentage of your basic salary. It is a contributory scheme; the employee and the employer are supposed to contribute, I think, 10% from the employer and 5% from an employee. For non-salaried people, the premium has been determined by the actuarial committee. It depends on the package you are choosing. The package determines what you are going to pay. (A male, Medical Doctor, Health Management Organisation Representative)

Fund collection mechanisms

In terms of premium payment, the deduction will be made from monthly payrolls of government workers. As for employees in the informal sector, it was stated that the State government will employ the use of electronic prepayment cards. With this method, individuals in the informal sector can pay their premium by purchasing appropriate cards worth the subscribed monthly premium. This will be done in partnership with banks and other suitable financial institutions. Participants suggested instalment payment of the subscribed premium especially for those who may not have the financial ability to pay at once. Some participants opined that subsidy will be provided for some citizens while the total cost of care will be waived for some others. According to some of the participants,

For government employees and others in the organised private sector, the premium will be deducted from source on a monthly basis. The arrangement will be made with banks and other financial institutions to enable those in the informal sector pay. We want to design payment vouchers that will be purchased through dedicated banks. People can pay for the premium of choice through this means. Remember that we will also cover a very small percentage of the population who will not be able to pay anything at all (A male, Member House of Assembly)

According to another member of the committee who has this to say;

We are making arrangement for internet connectivity to enable those who may be reluctant leaving their wares (shops or outlets) to pay where they sell (through e-payment). Someone selling palm oil or pepper or groundnut who cannot go to the bank can easily pay without leaving their kiosks (shops). The only thing they must do is to go to any health facility nearest to them, then register there, after which they can pay anywhere. We will also allow them to pay in the most convenient mode especially for those who cannot afford to pay their premium at once. And we are considering this modality presently. (A female, State Government Official).

Enrolment methods

It was found that enrolment into the scheme was designed to be flexible, both individual and family/ group registration will be available. However, registration for a family will accommodate a principal, the spouse and four children under the age of eighteen years. In situations where a spouse especially, a man has more than one wife and or other dependents, they will be registered as dependents for which each one of them will be paid for to enjoy the appropriate benefits package under the scheme. According to a participant:

We are putting a seal on the family size (which is made up of six family members). The next question is what happens to people (men) who have more than one wife as it were? So, the only thing to do is, ehm, to ask them to register other individuals as dependents. Let me give you an example, a standard family is six, we have the father, mother and four children. This same man has one other wife and three other kids, he will have to register the second wife and her kids as dependents (A male, Health Maintenance Organisation Representative)

Role of stakeholders

Findings showed that study participants were of the opinion that other stakeholders who are likely to be engaged in this scheme are the HMOs who will register prospective enrollees, the healthcare providers who deliver the services, while the SSHIP agency will be responsible for policy decision and provide oversight function to the HMOs and the health care providers. As mentioned by some participants, the NHIS provides technical assistance to the State agency where and when the need arises. Although other organisations such as the civil society organisations, faith-based organizations were mentioned as partners in ensuring that enrollees are provided with quality health care, the specific names of these organizations were not mentioned. Few participants opined that:

The enrollees, the HMOs, the providers; these are the key people. The HMOs will assist in registration, quality control, data collection. The providers are to provide care to the enrolees whenever care is needed, ensure quality service and treatment, so we are going to use both public and private care providers. The NHIS will assist in training, mobilization, sensitization, and regulations. (A female, State Government Official).

Another participant pointed out that,

We are aware of the oppositions against health insurance scheme by the organised labour unions such as the Nigeria Labour Union and the Trade Union Congress, in the uptake of health insurance under the NHIS. So, we partner with these groups to forestall such obstacles in the State when the scheme is eventually launched, so we don't expect opposition from them. The president of the State branch of the Nigerian Labour Union is a stakeholder in this scheme. He was involved in the design of this scheme and he has been nominated as a board member of the agency and accepted to serve in this capacity. The inauguration ceremony of the board is just a few days away. (A male private medical practitioner).

Benefit package

In respect of the types and categories of illnesses that would be covered under the scheme, most study participants were of the view that not all illnesses will be covered at this initial stage of the scheme. The NHIS was cited as an example where some illnesses were not covered by the scheme. They stated that the State government plan is to cover minimum care in the scheme and as such, the scheme might not cover all health conditions but only the commonc ones. They also pointed out that benefits might not be the same for all enrollees as they would be subscribing to different plans and premiums. Quoting one of the study participants,

Like I said, ideally there is no way or there is nowhere in the world that you will have a social insurance package, even in a private health insurance package, which covers everything. If it will cover everything, it is going to be too expensive. So, the idea is just to start from something, just design something, design a basic minimum package, start with that, then you build on it with time. (A male, Medical Doctor, National Health Insurance Scheme official).

Implementation, expansion and financial sustainability plan for the scheme

Finding also shows that some of the participants were hopeful that the programme will be sustainable and self-sustaining. Thus, it will reduce government expenditure on health, although the State government and the NHIS will make financial provision for the scheme at the initial stage. It was also pointed out that the scheme will reinvest whatever fund is available to generate more funds. According to a participant,

You see now, . . . from the start, we are not relying on government at all and as I said earlier on, we are using money paid by enrollees to treat them, . . . As I said the other time, there is this NHIS counterpart funding, if you place N100 million on the table, NHIS gives us N200 million as the big father, the big brother to assist the agency. We plan to generate more money to empower the agency by reinvestment, there are windows of opportunities to reinvest and multiply the money. (A male, State government official)

Other study participants were of the opinion that, there may not be an adequate plan on how the programme is sustained at the initial stage, hence, an alternative source of funding for the scheme is necessary. It was also suggested that organisations and other players in the scheme who realize some profits in the scheme could be mandated to pay tax, which could be helpful for the maintenance of the scheme. Quoting one of the participants,

Even if there is enough money realized the government may divert it to something else. So, the major focus for financial sustainability is to establish other innovative ways of financing care and back it up with the law to make it difficult for any government interference with the fund, otherwise, the money could be diverted. (A male, Medical Doctor, NHIS).

Participants have not been able to conclude on how to go about enrolling beneficiaries. While some were of the opinion that it could start in some selected LGAs to serve as pilot schemes from where it expands to other areas of the state, others believed that the best strategy will be to commence registration of enrollees in all the LGAs within the state at the same time. An average period of between three to five years was suggested as achieving total population coverage in the state. According to some of them,

For me I think since the programme is just been implemented for the first time, though we anticipate some challenges, you can never tell, you see . . . how much these challenges will be and in what manner, for example, the health

facilities we have in the state are not adequate, we need to refurbish many of them. It is even worse in the rural areas with lack of health facilities in many of the rural settlements, that's why I am of the opinion that we should start small and expand gradually (male, financial expert and a hospital administrator from the private sector) And some others had this to say;

The best strategy is to implement the scheme and commence registration of enrollees in all the LGAs at the same time, I don't believe in testing it in some LGAs before it spreads to others. Let's start everywhere and solve the problems that surface together, you will see that in less than 5 years, all LGAs will be covered (A male medical practitioner from the private sector)

Legal backing for sustainability

Responding to the issue on legal backing for the establishment of the scheme, all the participants made mention of a law backing the scheme's establishment. It was made known that a bill establishing the Health Insurance Agency of Oyo State has been signed into law and operational. One of the participants, who was a state lawmaker said thus:

Yes, we have implemented the law. We first had to sensitize other honourable members to embrace it, back it up and sign the bill into law. We also encourage them to take the information to their constituencies. we are soliciting support for the scheme among our people, so the agreement is that, if they are going for any publicity in any constituency, a member of the health committee in the State House of Assembly must be part of the visiting team, so he can say something to sell the scheme and convince them like he did when they voted for him in recent past". (A male, state Assembly committee chairman on health).

Programme commencement

Participants said the State Supported schemes have not commenced. Some of the reasons given for the delay in take-off were getting the stage ready especially advertisement and selection of health care providers, HMOs, and delay in passing the 2017 budget. A study participant put it this way,

According to the plan, we expect it to kick off this March, but, I am not very sure because of the delay in the passage of this year's budget, it is one of the reasons for this. But I am sure, in fact, I do not doubt it, that at least by the month of May, it will kick off fully. The tender board is working on all these HMOs, health care providers. The staff have been screened and employed, so very soon we will kick-start it (A male, State Government Official)

Challenges militating against the implementation of the programme

Participants anticipated challenges in the process of scheme implementation. One of the likely areas where there could be challenges includes people's trust in the scheme and with funds management especially. According to them, most people might be hesitant in enrolling for the scheme for an illness that has not come. Participants were however of the opinion that much needs to be done selling the scheme to the potential beneficiaries. Quoting some of the interviewees:

One of the major challenges is trust, generally, we are in a nation, where the masses do not trust their leaders, generally the populace doubt too much. So, we need to make them see how it works and why they need to enrol. But we should build integrity first for that programme, especially in a situation where the financial reward will not be made to contributors as it happens in Esusu (A male, Financial Consultant, and private health facility Chief Medical Director).

Another interviewee had this to say;

Hmmm, it is everywhere, 'Ha, emi o fe sick o (I don't want to take ill)'. . .. 'I rarely go to the hospital'. 'Assuming I'm not sick, what happens? So, they will be using my money to treat other people?' It is a normal scene, but we are trying to make them understand how it works and the reason why they need to enrol. (A female, State government official)

Awareness and knowledge about the scheme among potential beneficiaries

Participants were of the opinion that the level of awareness of most of the people in the State about health insurance was generally low. As a result, they believed many people might not have adequate knowledge to inform their decision on the scheme in terms of the plan options available to them, mode of payment of premium, illnesses covered by each plan option, benefits of each plan option and care providers where health care services could be accessed. They pointed out that plans were underway to address these. Quoting one of the participants,

"*As at now, nothing, nobody is aware of anything, nobody is aware of anything going on. Addressing these challenges is left for the agency to do, that's why we tell them, go on air, they need*

to do that . . . do posters, public enlightenment, do rallies, sensitize people about it, go to schools, go to offices, tell them the advantages. Emphasis should include why there are different benefits packages, people may not understand why individuals receive different treatment for the same illness". (A male, a Medical Doctor in private practice).

Discussion

Majority of the participants in this study were of the opinion that the presence of the NHIS was not adequately noticed in the state, and therefore may not fulfil its objective of facilitating providing universal health coverage (UHC) for the intended target population. Although, regional branch office of the NHIS exists in all the state capitals including where the research was conducted, however, the level of activity of the NHIS and engagement of other stakeholders such as the HMOs, health care providers and community members that could have been responsible for the low level of activities and uptake of the scheme in the state could not be ascertained.

However, what has been widely reported in previous studies is the opposition of the sub-national governments such as the states in Nigeria as well as the labour unions to enrolment in the NHIS [19, 28]. Non- or poor acceptance of a national programme such as the NHIS by sub-national levels of government is possible because of the political structure and institution of Nigeria whereby the sub-national governments have the power of autonomy on certain areas of low policy politics such as the health sector, and thus rejection of a potentially beneficial social policy such as the NHIS initiated by the national level of governance in Nigeria [12, 13, 15, 18]. The opportunity of having a scheme close enough that could consider the contextual environment of the potential beneficiaries in its design was one of the reasons stated for the favourable disposition to SSHIP in the state.

Another reason stated was more about resources control. The desire for resource control has been cited in previous studies [13, 28] as a manifestation of aspiration for self-determination as much as it is allowed under the legal structure within which the component parts of an entity operates [18]. The reasons stated above for a favourable disposition to SSHIP could be leveraged upon as motivating factors for stakeholders in Oyo State in making the design and implementation of the scheme a work in progress to overcome emerging challenges during implementation for sustainable social policy.

There are many areas of similarities between the SSHIP and NHIS in design; the two share the many attributes inherent in the design of social health insurance. However, a major difference is that, while the NHIS is a voluntary scheme, SSHIP is mandatory. Studies have shown that achieving universal health coverage is more likely when a scheme is mandatory unlike when it is voluntary [29]. There is evidence that countries in sub-Saharan Africa (SSA) with mandatory health insurance schemes such as Ghana, Rwanda, and Kenya have higher population coverage than those with voluntary schemes [1, 19]. Thus, with appropriate decisions and strong political will and support from stakeholders in the health insurance industry, SSHIP in Oyo State might achieve better population coverage than did the NHIS.

It is not too clear at this stage how much individuals and families will contribute periodically under the stated premium platforms. Also, it cannot be categorically stated that the planned contribution mechanisms, especially for enrollees in the informal sector of the population, will be efficient. These challenges are a major issue for sustainable social health insurance schemes especially in developing countries of the SSA with a characteristically large and poor informal sector where individual and family incomes are difficult to assess, setting health insurance contributions and collecting it is difficult and willingness to pay regular contributions is low [30]. In these circumstances inefficient fund collection mechanisms runs a risk of higher administrative costs than the actual premium collected [31].

However, what was obvious was the recognition by the participants that premiums and frequencies of contributions across different socio-economic groups need to be different. There is conflicting evidence about the ability of individuals and households to contribute; while some claimed that the poorest in the communities do not have the financial capability [8, 10, 30], others had a contrary opinion [31]. However, more evidence is in support of the inability of the poorest to contribute [32]. Also, while some may find it easy to make a whole payment at once, others may not have the financial capability to do so. Inability to afford premium contributions in a scheme, especially among the poor, is one of the largely stated reasons for non-membership, and as such inequity of access to available health care.

This can be minimised to a large extent by the adoption of sliding-scale premium contributions to reflect differences in the financial abilities of various socio-economic classes [33]. However, the concern is the ability of the health insurance officials to handle

this as the managerial and administrative skills required for such are usually unavailable in many developing countries where the practice of health insurance is relatively new [33-35]. Subsidy from the government and donors is also a viable addition to augment the financial needs in health insurance schemes [1, 34, 35].

To make it easier for those whose incomes are low and irregular, majority of who are in the informal sector, instalment payment is a good strategy [10, 23], and that such should be targeted at a period when they are most likely to afford it, especially during and immediately after harvest periods for farmers [34]. It was also suggested that funding will be mainly limited to the ability of the Agency to raise funds. This stand seems overambitious and possibly out of reality. Experiences from Thailand, Costa Rica and Tanzania [16] suffice that government subsidy, either partial or full, is one of the most important sources of funds, in the absence of which the poorest in the population are left out of the scheme for the reason of inability to pay the required premium [39].

One of the strategies for achieving universal coverage faster is the adoption of family enrolment as opposed to individual enrolment method [6, 21]. As much as this is an appropriate plan, what must be borne in mind is the peculiar nature of the family types and structures in many African societies and in Nigeria especially. In many of these societies, polyandry is common, usually where a man could have as many as four wives or more with many children, and with possibly other dependents. This is a unique challenge that is peculiar to many SSA countries but alien to many countries in Europe that characteristically have well-established health care financing institutions.

Thus, determining benefit package and premium contribution pattern in these circumstances, as well as other challenges such as identifying the poor [40], amount of premium charged per group or per individuals in the family and modalities of the collection, should be strategically and clearly defined. Again, it was suggested that a few platforms will be adopted for enrolment purposes. One of these is the use of the electronic method, which in many instances is not reliable especially in the rural, hard to reach areas characterised by very poor social infrastructural facilities and where the majority of those in the informal sector of the population resides [6, 17, 41]. Registration in health care facilities may be a fair alternative, however, this may not yield the optimum for the reason of non-availability of healthcare facilities in many of the rural areas. Other alternatives that could be employed such as house to house registration will be counter-productive as administrative costs incurred in such exercise could outweigh fund generated by the scheme [42]. This is more likely the case in many of the Low to Middle-Income Countries (LMICs) and especially in the SSA (33). Managing a complex arrangement as presented here will be a daunting task. Nevertheless, hands-on training and learning from other climes that have well established social health insurance institutions and adapting such skills to evolving challenges could be a way out [7,33]. It is also suggested that investment in social infrastructure and establishment of health care facilities in the rural areas where necessary is desirable. The presence of health care facilities, in addition to serving as enrolment platforms, will double as healthcare service provision platforms to enable the achievement of the purpose of the scheme itself. In the absence of this, the scheme risk abandonment by those who need to make use of it.

Unlike the NHIS which is a national government establishment and characterised by inadequate involvement of representatives of potential beneficiaries especially the opinion moulders such as the organised labour union leaders, the design of the SSHIP in Oyo State involved these leaders. This is suggestive of likely support of the scheme. Having the support of these groups from inception and including them in the design and implementation of the scheme could foster the needed sense of ownership of the scheme, especially during its teething stages. There is evidence that community involvement in the design and implementation of schemes is a more effective strategy to facilitate the inclusion of the usually excluded marginalized poor [8]. This is much needed to ensure achievement of the scheme's goals and its sustainability.

It is encouraging that stakeholders in this scheme understood certain pertinent issues in the operationalisation of a health insurance scheme by asserting that the benefits package cannot afford to cover all ailments. However, as desirable as this understanding is, potential beneficiaries, should be made to understand this reality. Otherwise, disappointments and dissatisfaction with the scheme, which could discourage people from enrolment, are likely.

There were conflicting opinions about whether funds will be sourced from outside in addition to premium contributions by the enrollees. While some claimed that funds will be limited to internally generated revenue by the Agency in form of premium contributions made by the enrollees, others claimed

that provisions have been made to raise funds from the federal government (statutory NHIS support for SSHIP) and the state governments as start-off grants. However, a cause for concern is the current non-payment of salaries of workers for many months in many states in Nigeria, including Oyo State, which could be a constraint to enrolees' premium payment in the scheme.

As much as SSHIP is desirable for much-needed access to health care, the absence of regular sources of income, especially among the state civil servants, may constitute a hindrance to enrolment. Thus, there may be the presence of a willingness to participate and pay, but the ability to pay is absent. This challenge needs to be decisively addressed especially as there are indications that the state is eager to kick-start the scheme. It is appropriate that the Agency is well acquainted with global best practices, such as the reality of government funding support as a crucial aspect for the scheme's sustainability and to achieve the needed universal health coverage [16]. One of the alternatives suggested for financial sustainability of the scheme are plans to generate more funds by reinvesting some of the money available to the Agency. This may to some extent, enhance the self-sustained fiscal capacity of the Agency provided it is well managed. However, as earlier stated, financial support for the scheme by the government cannot be over-emphasized.

There has not been any consensus as to the modality of implementing the scheme; while some believed implementation should be gradual with a pilot test in selected LGAs, others were in support of a one-time, state-wide implementation. While it may not be stated categorically which of the two approaches is better, what is known is that no one was sure when the implementation of the scheme will commence. One major challenge for this is the State budget for the year that has not yet been passed. In addition to this, preliminary steps in the selection of HMOs, health care providers and advertising the scheme were said to be ongoing. Irrespective of when and the modality, what is more, important is the state of preparedness of the scheme and the contextual environment where it is being implemented. Stakeholders need to ensure this is well planned to avoid a major mishap that could have a long-lasting effect on the scheme.

Experiences from other schemes suggested achieving universal health coverage will take more than a decade of consistent implementation activities (43). A target of fewer than five years to achieve total population coverage by the Oyo State SSHIP, though is suggestive of the enthusiasm of the stakeholders to achieve the purpose of the scheme, however, it may not be in synchrony with reality; Germany and other Western European countries with almost total population coverage started over a century ago, and recently some of the Asian countries such as the Republic of Korea, adjudged to have a very short time period in achieving the same were able to do so in approximately a period of three decades.

To reinforce these plans and make the Agency survive undue interference from successive governments, a legal framework in the form of a bill was designed and accented to by the State's legislatures. The same has been signed into law as an Act establishing the Agency by the executive arm of government in the state. This is a welcome development for the scheme survival.

Previous studies stated certain common areas of challenges in the adoption and implementation of social health insurance schemes in LMICs. These include: low level of awareness and understanding of schemes, lack of trust with fund management, superstitious beliefs associated with prepayment schemes [1, 6, 47, 38], inability to differentiate contributions under social health insurance from other forms of contributory arrangements [45,46], and the need to continue with paying the premium even when it seems as if there is no health need to keep doing so.

It is a good development that stakeholders were aware of and mentioned these challenges. However, appropriate steps must be taken to address them in good time. One of the strategies to do this is through rigorous and sustained advocacy visits to the communities that could provide avenues for direct interaction and engagement. The success of similar schemes in countries such as Thailand, Cambodia, and India had been partly ascribed to these strategies [47]. Targeted awareness campaigns using different approaches had been advocated. In a study by Nyagero and colleagues in a rural area in Kenya, the use of road shows, and radio adverts were said to have increased awareness and understanding of social health insurance schemes among the elderly [48].

Adewole and colleagues in a study among market women in a southwest city of Nigeria could demonstrate the use of an IEC (Information-Education-Communication) material as a social marketing tool to improve the understanding of market women on the modus operandi of prepayment schemes, and to debunk certain superstitious beliefs associated with prepayment scheme for health [45].

It is also important that enrollees need to know the difference between contributions under this scheme and the contributions under *Esusu,* a form of reciprocal loans and savings microfinance institutions common among indigenous Africans where contributors take a turn to collect fund for business financing [46]. Failure to realise these differences and address it appropriately may deepen an already poor image of government policies with regards to funding management among potential beneficiaries.

Definitive steps must be taken to build the trust of the people especially with regards to fund management [1,44] and provision of good quality health service provision in the absence of which the demand for and uptake of schemes could experience setbacks [38] and undesirable exposure to poor quality health care [32]. This could lead to a gradual disenchantment with and an eventual collapse of the scheme.

As states in Nigeria are making efforts to implement SSHIP, 'inequity of access to health care and financial protection' [16] is inevitable arising from differential benefit packages for similar ailments, as well as unequal financial capabilities of the states implementing the scheme. It is suggested that a re-insurance (cross-subsidization) of the schemes across the states' SSHIP for a possible national pool [32,49] is instituted in the future. This will make the 'fragmented' schemes more viable and sustainable than otherwise and minimise likely inequities of access to health care [16, 32]. However, the type and structure of the political institution and governance in Nigeria as in other countries with similar federal presidential arrangements may hinder such an alliance [12, 15, 18].

Conclusion

Decentralisation of a national, centrally controlled health insurance scheme to the sub-national levels may provide the catalyst to achieving needed UHC especially in developing countries with limited experience in the health insurance industry. This may be a positive signal for the SSHIP, more so that it currently enjoys support from relevant stakeholders in the health sector, the health insurance industry, the labour union and the state lawmakers. Potential beneficiaries may also have more confidence in it than they had in the centralised NHIS because of its closeness to the people and therefore may achieve better than the NHIS. Efforts should be made to address the gaps identified in the design of the Oyo State SSHIP. The policy document itself should be a work-in-progress entity to enable stakeholders continuously address challenges as they emerge. However, low level of awareness and understanding of the scheme including the benefit package and modalities for premium contributions and cost-efficient platform for collection especially in the rural areas with scattered settlements, limited in number health care facilities with poor human and material resources, and very limited banking services are some of the anticipated challenges in this scheme. A bigger likely challenge is the sustainability of the scheme in the absence of an active government financial support. Findings in this study would have been more robust if it had incorporated the views of other stakeholders, such as the State Chairman of the Nigerian Labour Congress and members of the public who are potential enrollees and beneficiaries of the SSHIP. We accept this as a limitation.

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Frailty in the Ibadan study of aging- characterization and association with disability, quality of life and healthcare utilization

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Abstract

Objectives: Variability in the prevalence of frailty in older populations suggests a need for context-specific information about the phenotype. We characterized a frailty phenotype variant in community dwelling Yoruba Nigerians who were aged 60 years or over.

Methods: Cross-sectional analysis of the first of three follow-up waves in a five year prospective study of a household multistage sample of 1595 stroke- and dementia-free persons. We characterized frailty by relying on locally validated tools and the Cardiovascular Health Study (CHS) principle of 'vicious cycle of decline'. The association of frailty with disability, quality of life (QoL) and healthcare utilization was investigated using multivariate logistic regression analyses.

Results: We found a prevalence of 7.3% (95% C. I=5.9-9.0) for the full frail phenotype and 62.1% (95% C. I=59.9-64.3) for the prefrail phenotype. In fully adjusted logistic regression models, frail respondents had approximately two, five and eight times the odds of greater healthcare utilization (O. R=1.8, 95% C. I=1.2-2.7), disability (O. R=5.4, 95% C. I=3.2-9.2) and poor QoL (O. R=8.4, 95% C. I=4.8-14.6) respectively.

Conclusion: The prevalence of frailty in this population is similar to those reported in other surveys. The results suggest that with cohort specific modifications, the risk profile of frailty as originally conceptualised in North Americans is applicable to, and has suggestive evidence of validity in, this sub-Saharan African population.

Keywords: *Frailty syndrome; low income population; frailty index*

Résumé

Objectifs : La variabilité dans la prévalence de fragilité chez les populations âgées suggère un besoin d'information contextuelle-spécifique sur le phénotype. Nous avons caractérisé une variante du phénotype de fragilité chez des Yorouba Nigérians vivant en communauté qui étaient âgés de 60 ans ou plus.

Méthodes : Analyse transversale de la première des trois vagues de suivi d'une étude prospective de cinq ans sur un échantillon aléatoire à plusieurs degrés de ménages constitué de 1595 personnes sans AVC ni démence. Nous avons caractérisé la fragilité en nous basant sur des outils validés localement et sur le principe du 'cycle vicieux de déclin' de l'Étude sur la santé cardiovasculaire (ESC). L'association de la fragilité avec un handicap, la qualité de vie (QV) et l'utilisation des soins de santé a été étudiée en utilisant des analyses de régression logistique multivariée.

Résultats : Nous avons trouvé une prévalence de 7,3% (95% IC = 5,9 à 9,0) pour le phénotype complet fragile et de 62,1% (95% IC = 59,9 à 64,3) pour le phénotype prefragile. Dans les modèles de régression logistique entièrement ajustés, les répondants fragiles présentaient avec environ deux, cinq et huit fois plus de chances d'avoir une plus grande utilisation des soins de santé (OR = 1,8, 95% IC = 1,2-2,7), un handicap (OR = 5,4, 95 % IC = 3,2 à 9,2) et mauvaise qualité de vie (OR = 8,4, 95% IC= 4,8 à 14,6) respectivement.

Conclusion : La prévalence de fragilité dans cette population est similaire à celle rapportée dans d'autres enquêtes. Les résultats suggèrent qu'avec des modifications à cohorte-spécifiques, le profil de risque de fragilité tel que conçu initialement chez les Américains du Nord est applicable à, et offre des preuves évocatrices de validité dans, cette population d'Afrique subsaharienne.

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Mots-clés : *syndrome de fragilité ; population à faible revenu ; index de fragilité*

Introduction

Frailty in older adults is widely acknowledged as a determinant of their wellbeing [1]. Due to numerous definitions of the syndrome, including the Frailty Index (FI)[2] and Survey of Health Ageing and Retirement in Europe Frailty Index (SHARE-FI) [3], there is variability in reported prevalence estimates in diverse populations. Also, the question of whether to consider frailty as a one-dimensional diagnostic entity [4, 5] or a multidimensional construct [6] remains unanswered. Nevertheless, the phenotype perspective [4, 5, 7] (which considers disability as an outcome of frailty) appears to be the more common and most validated definitions of the syndrome [8].

Irrespective of definition, variability in the prevalence of frailty persists across countries and contexts. For example, recent meta-analytic studies of the phenotype suggest that frailty prevalence ranges from 7.4% in Japan [9] to about 10% in Europe and America [10]. Other studies from High Income Countries (HICs) [6, 11] report higher prevalence of frailty in persons living in low socio-economic neighbourhood and among minority ethnic groups.

Epidemiological studies of frailty phenotypes in Low- and Middle-Income Countries (LMICs) are few [12, 13], but growing. Notably, most LMICs studies of frailty have focused on Chinese and South American populations. One prior study [14] of rural South Africans who were aged 40 years or older found prevalence estimates of between 5.4% and 13.2% across nine different variants of the phenotype.

The wide variability in prevalence estimates of frailty phenotypes across definitions, methods of ascertainment, countries and contexts would suggest the need for context specific information. Such data may be derived by applying locally validated tools, ascertainment procedures and context-appropriate interpretations to the globally accepted concept of frailty as a 'vicious cycle of decline'.

In the present study, we aimed to: 1), characterise a frailty phenotype variant among Yoruba Nigerians by relying on the Cardiovascular Health Study (CHS) [7] principle of 'a vicious cycle of decline', and 2), provide evidence of validity of the phenotype by describing association with disability, poor quality of life (QoL) and healthcare utilization.

Methods

Sample selection and recruitment

The Ibadan Study of Ageing (ISA) is a stratified multistage cluster randomised sample derived from eight neighbouring states in predominantly Yoruba-speaking region of Nigeria, with a population of about 25 million people at the time of the study. The details of the selection procedure have been fully described [15, 16]. Up to five calls were made to contact the selected individuals; and there was no replacement for those who could not be contacted or who refused to participate in the study.

The survey was approved by the University of Ibadan/University College Hospital, Ibadan Joint Ethical Review Board. Participants were those who provided consent, mostly verbal (either because of illiteracy or by choice), before interviews were conducted. Baseline assessment were conducted on a total of 2149 respondents in 2003/2004.

The first of three follow-up waves was conducted in 2007. The present report is based on 1862 respondents who were followed-up in 2007. They represent 86.7% of the baseline sample.

Measures

In 2007, face to face interviews were carried out in the homes of participants to assess a range of domains. All instruments used in the ISA were translated into the local Yoruba language (using the iterative back-translation method) and subjected to cultural adaptation.

Operational definition of frailty and its indicators in the ISA.

The assessment of frailty in the ISA was based on published criteria [1, 5, 7, 8, 17] and informed by the specific features of the study protocol (Table 1).

1. As in some previous studies [5, 8, 14], weight loss was defined as Body Mass Index (BMI) of <18.5 kg/m^2.

2. Exhaustion was assessed with the relevant item in the depression module of the World Mental Health Survey version of the WHO Composite International Diagnostic Interview (CIDI) [18]. The item enquires whether respondent felt tired or low in energy nearly every day for several days or in the past two weeks even when they had not been working very hard.

3. Low physical activity was assessed using an item from the International Physical Activity Schedule [19]. Respondents were asked about whether they actively engaged in outdoor activities such as riding a bicycle or doing farm work in the past 30 days. Those who were not engaged in outdoor activities in the past 30 days were categorized as having low physical activity.

4. Slowness was defined, using previously validated gait speed categories in the ISA [20], as gait

speed ≥8.7 seconds for a 4-meter walk or ≥6.52 seconds for a 3-meter walk. Similar to many previous studies [1, 5, 8, 17, 21], we did not measure hand-grip strength as a specific index of muscle weakness.

We determined whether each frailty indicator was present by assigning scores on each of the four features (1= present, 0=absent). The sum of these scores was used in categorizing ISA participants into the different frailty phenotypes for the present study: Frail (3 or 4 components), Pre-frail (1 or 2 components), and Robust (0 components).

Participants with stroke and dementia were excluded in defining frailty as both conditions are frequently associated with motor or functional disability in older people and may preclude performance in some component tasks used for the definition. Stroke was ascertained by self-report of clinician diagnoses while dementia was diagnosed using a standardized two-staged clinical examination [22].

Measurement of associated factors

Functional Disability: The Katz index of independence in activities of daily living (Katz ADL) [23] was used to assess the ability of participants to perform ADL independently. We rated participants' functional status by the adequacy of performance of six functions: bathing, dressing, toileting, transferring, feeding and continence.

Instrumental activities of daily living (IADL) was evaluated by the ability of the participants to perform seven functions in the following areas: climbing a flight of stairs, reaching above the head to carry something weighing about 4.5 kg, stooping, gripping small objects with hands, shopping, and activities such as sweeping the floor with a broom or cutting grass.

Each of the activities in the two domains was rated: (1) can do without difficulty; (2) can do with some difficulty; (3) can do only with assistance; (4) unable to do activity. We classified as functionally disabled, any respondent with a rating of 3 or 4 on any item.

Quality of life (QoL): was measured using the WHO QoL instrument (WHOQoL-BREF). The measure contains a total of 26 questions arranged in four domains of physical health, psychological health, social relationships and environment. The domain scores are indicative of an individual's subjective perception of QoL in the corresponding domain. Higher scores denote higher QoL. The mean score of items within each domain is used to calculate the total domain score. In the present study, poor QoL was defined by a total domain score below the lowest quartile in the distribution.

Other baseline measurements

Participants were asked whether, in the past year, they had utilized a health facility for the care of any health condition/s. In the present study, healthcare utilization was defined as visit to a health care facility (out-patient, in-patient, or both) for any personal health concern.

Residence was classified based on the Nigerian census categorization at the time of study. Economic status was estimated using an asset based procedure relevant to developing countries [24]. Use of tobacco and alcohol was categorized, based on self-report, as ever having smoked or not, and ever used alcohol or not. Those who responded in the affirmative to ever using alcohol were further classified into regular (weekly use or more often) or occasional users (less often than weekly use). Social engagement was assessed using items derived from the WHO Disability Assessment Schedule, version 2 [25].

Data analyses

The sample from which frailty was determined in the ISA comprised of 1595 participants who were free of stroke and dementia out of the 1862 who completed full assessments in 2007. The demographic characteristics of those who survived, died, or were censored were compared using Pearson chi-square test, with a Rao and Scott correction [26] to account for the survey design.

Descriptive statistics such as means and standard deviations were used to summarize quantitative variables while frequencies and percentages were used for categorical variables.

Characteristics of the study sample were compared across frail, pre-frail, and robust participants using the chi-squared test or t-test for categorical or continuous variables, respectively. The analyses took account of the stratified multistage sampling procedure and the associated clustering by applying weights as appropriate. We made adjustment for differences between the sample and the total Nigerian population by applying post-stratifications to the target sex and age range.

Subsequently, we conducted logistic regression analyses to explore the cross-sectional association of frailty with disability, healthcare utilization and QoL. We first conducted an unadjusted analysis. Next, we conducted step-wise adjustments (in three models) for factors that might have significantly affected the risk of being frail in our bivariate analyses. In model I, we adjusted for the significant demographic characteristics (age and gender). In model II, we added significant economic

characteristics (economic and marital statuses) to model I, while in model III we added the significant lifestyle factor (alcohol use) to model II.

The results of adjusted analyses are presented as odds ratios (OR's) with 95% confidence intervals (C. I's). All C. I's are adjusted for design effects. All analyses were conducted using STATA version 13.0 [27]. The survey commands in Stata were used to account for the study sampling scheme. A significance level of 0.05 was used throughout the analyses.

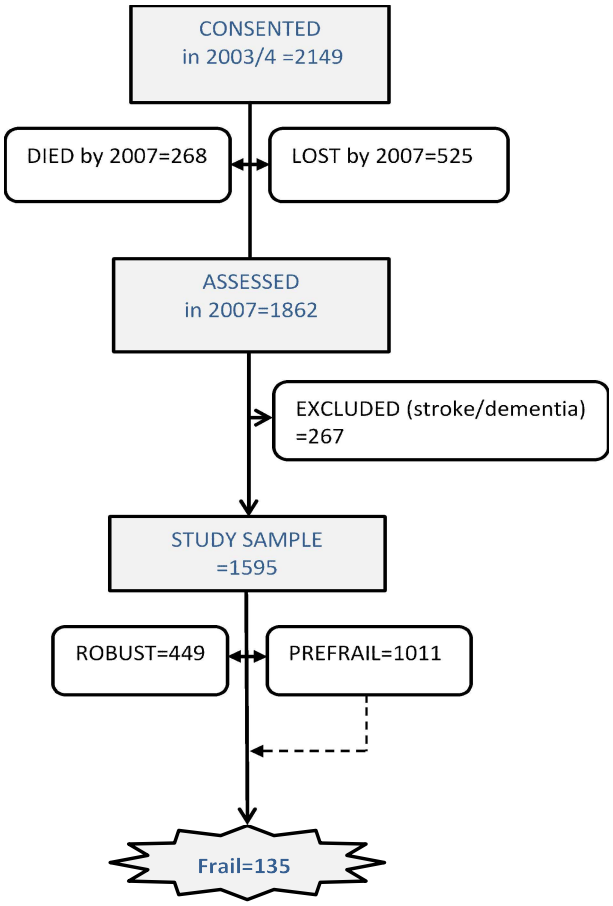

Fig.1: Flow chart of the frailty sample in the Ibadan study of ageing

Results

A total of 525 participants (24.4% of the 2003/4 sample) were lost to follow-up by 2007 (Figure 1). Respondents who were lost to follow-up were more likely to be separated and belong in lower socio-economic positions (Table 2). The mean age of the 2007 sample was 74.8 (± 8.8) years (range= 66 to 84 years). The sample characteristics and frailty indicators are shown in Table 3.

Prevalence of frailty in the ISA

Of the 1595 respondents, 135 (7.3%, 95% C. I=5.9-9.0) were classified as frail while 1011 (62.1%, 95% C. I=59.9-64.3) were pre-frail (Table 4). Table 3 also shows that frail participants were more likely to be older, separated women who belonged in a low economic status and had poor physical functioning and QoL.

Association of frailty phenotypes with adverse health outcomes

Table 4 summarizes the bivariate and multivariable associations of the three phenotypes with adverse health outcomes. In general, there was a dose-response relationship between the number of frailty components in an individual respondent and the risk of adverse health outcomes (Table 5).

Discussion

In this sample of community-dwelling older Nigerians we found a prevalence of 7.3% for the full frail phenotype and 62.1% for the intermediate (prefrail) phenotype at risk of becoming frail. The full frail and prefrail phenotypes were associated with greater odds for poor physical functioning, QoL and use of health care. The odds for adverse health outcomes increased as participants moved from prefrail to the full frail phenotypes.

The prevalence and sizes of associations of our frailty phenotype variants with adverse health outcomes suggest that, with cohort-specific modifications, the risk profile of frailty as conceptualised in older adults from the United States [4, 5, 7] is applicable and valid for community dwelling older adults from SSA. Minor variations in the findings of surveys conducted in different contexts may be due to differences in social, economic and cultural factors affecting understanding, interpretation and reporting of some defining components of the frailty phenotype described in the CHS. As an example, high burden of undernutrition and disease [28] in socio-economically deprived settings may contribute to a higher prevalence of weight loss in studies conducted in such settings, while socio-cultural roles defined by gender in some African communities [29] may affect respondents' understanding and interpretation of some aspects of outdoor physical activities.

Substantial overlaps can also be discerned between the findings of the present study and those conducted in other LMICs [1, 12-14]. Similarities in prevalence and in associated risk factors for adverse health outcomes in studies conducted in

Table 1: Cohort-specific definitions of frailty in the Cardiovascular Health Study, Women's Health Study and Ibadan Study of Ageing

Defining components	Cardiovascular Health Study (N=5317)†	Women's Health Study (N=1002)‡	Ibadan Study of Ageing (N=1595)§
Weight loss	Self-reported weight loss >10 pounds, unintentionally in the past year	BMI <18.5 or e"10% weight loss over the previous H"5 years	BMI<18.5
Exhaustion	*Self-report of any of:* -Low usual energy level (≤3 on a scale of 0-10) -Felt unusually tired in the last month -Felt unusually weak in the past month	*Self-report of either:* -Felt everything I did was an effort in the last week -Could not get going in the last week	Self-report of feeling tired or low in energy low in nearly every day for several days or in the past two weeks even when they had not been workingvery hard.
Low physical activity	Minnesota Leisure time Activity Questionnaire-Short version	Minnesota Leisure time Activity Questionnaire	International Physical Activity Schedule-Short version
Slowness	4 m walk: Speed ≤4.57/7 for a height of ≤159 cm Speed ≤4.57/6 for a height>159 cm	4.57 m walk: Time ≥7 for a height ≤159 Time ≥6 for a height >159	≥8.70 seconds to complete a 4 m ≥6.52 seconds for a 3-meter walk
walk or Weakness	Grip strength	Grip strength	Grip strength not measured in the
ISA			
Overall frailty status (%)			
Robust	46.4	33.2	30.6 (95% C. I=28.3-33.1)
Pre-frail	53.3	55.2	62.1 (95% C. I=59.9-64.3)
Frail	6.9	11.6	7.3 (95% C. I=5.9-9.0)

Notes: †Community-dwelling men and women who were 65 years or older, ‡Comprised the most disabled one-third of community dwelling women aged 70-79 years, §Community-dwelling men and women who were 60 years or older .

Table 2: Characteristics of Ibadan study of ageing participants who were followed up from 2003/4 to 2007

Characteristics	Survived N=1862 (%)	Died N=268 (%)	Lost N=525 (%)	Design based F statistic	p-value
Age group, years					
60-64	346 (19.6)	23 (15.3)	91 (19.2)	1.40	0.216
65-69	395 (23.3)	36 (17.6)	113 (23.1)		
70-74	410 (26.0)	54 (27.5)	107 (26.1)		
75-79	359 (20.0)	53 (20.0)	107 (19.8)		
80+	352 (11.2)	102 (19.7)	107 (11.8)		
Gender					
Male	750 (49.3)	132 (56.8)	234 (56.0)	2.93	0.065
Female	1112(50.7)	136 (43.2)	291 (41.0)		
Residence					
Urban	517 (28.0)	80 (33.4)	153 (29.0)	0.45	0.729
Semi-urban	752 (40.5)	100 (37.7)	191 (39.6)		
Rural	593 (31.6)	88 (28.9)	290 (32.6)		
Education, years					
>13	96 (7.8)	28 (8.0)	42 (8.8)	0.81	0.521
7-12	173 (13.7)	33 (12.1)	60 (10.7)		
1-6	329 (24.6)	74 (31.5)	130 (26.3)		
0	758 (53.9)	133 (48.4)	293 (54.3)		
Economic status					
High	203 (13.6)	28 (14.8)	46 (11.7)	4.31	<0.001
High-average	511 (31.3)	53 (28.0)	112 (25.9)		
Low-average	684 (35.4)	82 (25.0)	177 (35.1)		
Low	464 (19.7)	105 (32.3)	190 (27.4)		
Marital status					
Separated†	780 (32.7)	129 (34.6)	283 (41.2)	4.26	0.019
Married	1082 (67.3)	139 (65.4)	242 (58.8)		

†*Separated by death or divorce*

LMICs provide important evidence of reliability for the frailty phenotype variant characterised in the present study.

Due to the unique features of the present study, we have reasons to believe that the 7.3% prevalence of the full frail phenotype reported here, though broadly in agreement with the estimates in the original CHS study [7], is likely to be an underestimation. First, our sample comprised person who were 60 years or older at the time of survey. The reported prevalence of frailty in the literature has tended to increase with the age of the respective survey samples [5]. As an example, we found in the present study that frail respondents were more likely to be older on average than robust persons, being generally over 80 years of age.

Second, considering all previous criteria for defining frailty, we have relied on some of the most restrictive indices. For weight loss, as an example, we used a BMI of less than 18.5 Kg/m^2. Even though the weight loss index in the present study is a popular indicator of undernutrition [28] and may reflect both the historical and empirical realities of the frailty phenotype [30], we think that our reliance on a BMI of less than 18.5 Kg/m^2 may have led to an underestimation of weight loss in our sample. This is because some participants who recorded BMI greater than 18.5 Kg/m^2, may in fact have lost weight unintentionally from a higher weight category. Conversely, self-report of weight loss in the elderly is subject to information bias, especially in relation to the quantitative estimation of the extent of loss.

Third, in our bid to improve the specificity of our definition of frailty in the ISA, we excluded persons with probable dementia and stroke. It is reasonable to expect respondents with stroke or dementia to have motor or functional disability which may confound the classification of respondents as having slowness of movement or low physical activity. Many previous characterizations of frailty have failed to exclude possible causes of slowness of movement or low physical activities [8].

Fourth, the original frailty phenotype-variant proposed in the CHS [7] relied on five defining

Table 3: Characteristics and defining components of frailty in the Ibadan Study of Ageing

Characteristics	Total sample N=1595	Weight loss N=217	Exhaustion N=748	Slowness N=269	Low physical activity N=588
Age group, years					
60-69	467 (30.5)	47 (21.8)	216 (29.2)	53 (24.2)	111 (19.6)
70-79	682 (49.6)	93 (50.2)	326 (51.1)	106 (44.2)	245 (51.1)
80+	446 (19.9)	77 (28.0)	206 (19.8)	110 (31.7)	232 (29.3)
Gender					
Female	942 (50.4)	113 (43.6)	512 (59.8)	174 (54.7)	359 (51.9)
Male	653 (49.6)	104 (56.4)	236 (40.2)	95 (45.3)	229 (48.1)
Residence					
Urban	609 (38.1)	85 (37.8)	271 (35.1)	103 (40.2)	205 (35.2)
Semi-urban	548 (34.6)	72 (33.1)	276 (36.8)	89 (31.8)	221 (36.5)
Rural	438 (27.3)	60 (29.2)	201 (28.1)	77 (28.0)	162 (28.4)
Education, years					
0	633 (54.1)	107 (66.0)	299 (53.7)	117 (57.0)	258 (53.4)
1-6	275 (24.8)	34 (17.4)	135 (25.6)	50 (26.3)	108 (25.0)
≥7	224 (21.1)	29 (16.7)	106 (20.8)	30 (16.7)	94 (21.6)
Economic status					
Low	313 (16.4)	63 (26.6)	145 (17.4)	57 (19.0)	111 (17.0)
Low average	612 (36.8)	86 (40.0)	305 (38.4)	115 (40.8)	251 (41.9)
Higher	670 (46.8)	68 (33.6)	298 (44.1)	97 (40.1)	226 (41.1)
Marital status					
Separated†	657 (32.7)	102 (36.9)	373 (40.2)	134 (37.1)	294 (40.0)
Currently married	938 (67.5)	115 (63.1)	375 (59.8)	135 (62.9)	294(60.0)
Alcohol use					
Never	948 (57.3)	123 (52.6)	480 (61.5)	183 (71.2)	365 (60.0)
Occasional	441 (28.9)	69 (33.8)	192 (27.9)	67 (22.6)	174 (31.4)
Regular‡	183 (13.8)	24 (13.6)	69 (10.7)	17 (6.2)	46 (8.9)
Tobacco smoking					
Never	987 (62.4)	122 (55.6)	491 (65.7)	173 (64.6)	343 (58.0)
Past	448 (29.7)	67 (32.9)	186 (26.5)	70 (27.3)	185 (33.1)
Current	143 (7.9)	27 (11.5)	57 (7.1)	24 (8.1)	56 (8.8)
Social engagement					
Good	1538 (98.4)	203 (95.9)	720 (97.1)	257 (97.6)	559 (96.9)
Poor	41 (1.9)	11 (4.1)	21 (2.1)	10 (2.4)	28 (3.1)
Physical functioning					
Poor	280 (15.0)	49 (20.0)	143 (16.8)	74 (24.1)	192 (31.1)
Good	1315 (85.0)	168 (80.0)	605 (83.2)	195 (75.9)	396 (68.9)
Use of Healthcare					
Yes	752 (50.4)	95 (45.5)	365 (51.8)	132 (53.3)	289 (54.4)
No	827 (49.7)	119 (54.5)	376 (48.2)	134 (46.7)	297 (45.6)
Quality of Life					
Poor	323 (18.7)	52 (18.4)	194 (24.2)	68 (24.3)	214 (37.7)
Good	1215 (81.3)	158 (81.6)	534 (75.8)	192 (75.7)	362 (62.3)

Notes: ‡Regular use of alcohol= ≥ weekly use of a regular measure of alcoholic beverage, Poor physical functioning= Impairment in Activities of Daily Living (ADL)/Instrumental ADL, Poor quality of life= WHO-QoLBREF total domain score in the lowest quartile of the sample distribution. Social engagement=having regular social contacts/participation in family and community activities, †Separated by death or divorce

components. However, as hand-grip strength was not assessed in the ISA, we have relied on four CHS proposed frailty-defining components. The use of a limited number of defining components for the phenotype may reduce the sensitivity of the relevant cohort-defined frailty. In this way, an unintended but systematic underestimation of the burden of frailty in the studied population may result. Nonetheless, the use of four defining components for the frailty phenotypes has been previously proposed for surveys

Table 4: Sample characteristics and frailty status in the Ibadan Study of ageing

Characteristics	Robust N=449 (%)	Pre-frail N=1011 (%)	Frail N=135 (%)	p-value
Mean age (SD), years	73.0 (8.2)	75.6 (9.0)	78.9 (9.8)	<0.001
Female gender	231 (43.9)	612 (52.3)	99 (61.7)	0.008
Rural place of residence	116 (22.9)	288 (30.1)	34 (22.3)	0.075
No formal Education	162 (52.8)	402 (51.4)	69 (65.1)	0.258
Low economic status	78 (13.6)	207 (17.0)	20 (23.6)	0.011
Separated (death/divorce)	129 (23.4)	441 (34.8)	87 (51.7)	<0.001
Regular alcohol use	66 (18.1)	111 (12.9)	6 (4.0)	0.008
Current tobacco smoking	35 (6.7)	94 (8.2)	14 (10.6)	0.799
Poor social engagement	3 (0.6)	31 (2.5)	7 (2.7)	0.063
Poor physical functioning	30 (5.0)	202 (17.8)	48 (33.5)	<0.001
Use of Healthcare	193 (45.6)	488 (52.1)	71 (55.6)	0.121
Poor quality of life	24 (4.3)	249 (23.8)	50 (35.3)	0.001

Note: Regular use of alcohol= e" weekly use of a regular measure of alcoholic beverage, Poor physical functioning= Impairment in Activities of Daily Living (ADL)/Instrumental ADL, Poor quality of life= WHO-QoLBREF total domain score in the lowest quartile of the sample distribution.

without protocol inclusions for hand-grip strength [1, 5, 8, 17, 21]. Previous findings [31, 32] suggesting that the effect of hand-grip strength on disability and other adverse health outcomes were attenuated (to non-significant thresholds) by the other four CHS frailty-defining components provide additional support for surveys to rely on four components as a meaningful way to characterize frailty.

Where four defining components have been used because of non-inclusion of hand-grip strength, some surveys have attempted to improve sensitivity of cohort-defined frailty phenotype-variant by relying on an alternative interpretation of the CHS frailty-phenotype construct. For example, the requirement for frail respondents to meet criteria for only two (instead of three) defining components have been proposed [1].

Within constraints of the listed caveats, we believe that the findings of this study provide important information that could inform the future research about the nature of frailty among elderly populations in SSA.

Acknowledgments
We would like to thank the data collection team for their work.

Table 5: Cross-sectional association of frailty with disability, poor quality of life, and healthcare utilization

	Poor physical functioning (N=280)			Use of healthcare (N=752)			Poor quality of life (N=323)		
Frailty status	n (%)	O.R (95% C.I)	P-value	n (%)	O.R (95% C.I)	P-value	n (%)	O.R (95% C.I)	P-values
Robust	30 (5.0)	Reference	Reference	193 (45.6)	Reference	Reference	24 (4.3)	Reference	Reference
Pre-frail	202 (17.8)	3.5 (2.3-5.2)†	<0.001	488 (52.1)	1.2 (1.0-1.5)†	0.083	249 (23.8)	5.6 (3.6-8.7)†	<0.001
Model I		3.1 (2.1-4.7)	<0.001		1.3 (1.1-1.7)	0.019		5.2 (3.3-8.0)	<0.001
Model II		3.0 (2.0-4.5)	<0.001		1.3 (1.1-1.7)	0.013		5.2 (3.3-8.0)	<0.001
Model III		2.9 (1.9-4.4)	<0.001		1.4 (1.1-1.7)	0.012		5.1 (3.3-8.0)	<0.001
Frail	48 (33.5)	7.7 (4.6-12.9)†	<0.001	71 (55.6)	1.5 (1.0-2.2)†	0.049	50 (35.3)	10.1 (6.0-17.9)†	<0.001
Model I		6.1 (3.6-10.3)	<0.001		1.8 (1.2-2.6)	0.006		8.8 (5.1-15.2)	<0.001
Model II		5.7 (3.3-9.6)	<0.001		1.8 (1.2-2.7)	0.005		8.7 (5.0-15.2)	<0.001
Model III		5.4 (3.2-9.2)	<0.001		1.8 (1.2-2.7)	0.004		8.4 (4.8-14.6)	<0.001

†*Unadjusted model, Model I=Adjusted for significant demographic factors (age and gender), Model II= Adjusted for significant demographic and economic factors (economic and marital statuses), Model III=Adjusted for significant demographic, economic and lifestyle factors (Alcohol use)*

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Cephalometric values of sickle cell anaemia individuals in a Nigerian population.

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Abstract
Objective: To establish cephalometric values in HbS individuals and compare with those of HbA individuals.
Methods: Lateral cephalometric radiographs were taken for HbS and HbA participants and hard tissue tracings obtained manually on a 0.003 inch thick cellulose acetate tracing paper over a light viewing box.
Results: Sixty HbS and sixty HbA participants were recruited for the study. In group 1 (HbS) 29 (48.3%) of the participants were males, 31 (51.7%) females while in group 2 (HbA) 27 (45.0%) were males and 33 (55.0%) females. The mean age of the participants was 21.55 ± 2.55 years for the HbS group and 22.15 ± 2.52 years for the HbA group. The mean SNA angle measured for the HbS participants was 85.66 ± 4.93 while SNB angle was 80.56 ± 4.41^0. The ANB angle ranged between -3 and 10^0. The HbS group had a mean ANB value of 5.10 ± 3.32^0 as compared to 3.93 ± 1.63^0 for the HbA group. Significant differences were observed between the mean SNB and ANB values in the HbS and HbA groups. The mean SNB for HbS was lower than that of HbA participants while mean ANB was higher.

Keywords: *Sickle cell anaemia, cephalometric radiograph, jaw protrusion*

Résumé
Objectif : Pour établir les valeurs céphalométriques chez les individus HbS et les comparer à celles des individus HbA.
Méthodes Des radiographies céphalométriques latérales ont été prises pour les participants HbS et HbA et les tracés de tissus durs ont été obtenus manuellement sur un papier calque en acétate de cellulose à 0,003 pouce d'épaisseur sur une boîte d'observation lumineuse.
Résultats : Soixante participants HbS et soixante participants HbA ont été recrutés pour l'étude. Dans le groupe 1 (HbS), 29 (48,3%) des participants étaient des hommes, 31 (51,7%) des femmes, tandis que dans le groupe 2 (HbA), 27 (45,0%) étaient des hommes et 33 (55,0%) des femmes. L'âge moyen des participants était de 21,55 ± 2,55 ans pour le groupe HbS et de 22,15 ± 2,52 ans pour le groupe HbA. L'angle moyen du SNA mesuré pour les participants à l'HbS était de 85,66 ± 4,93 tandis que l'angle du SNB était de 80,56 ± 4,41^0. L'angle ANB variait entre -3 et 10 ^{0}. Le groupe HbS présentait une valeur moyenne d'ANB de 5,10 ± 3,32^0 par rapport à 3,93 ± 1,63^0 pour le groupe HbA**.** Des différences significatives ont été observées entre les valeurs moyennes de SNB et d'ANB dans les groupes HbS et HbA. La moyenne du SNB pour l'HbS était inférieur à celui des participants de l'HbA, tandis que la moyenne d'ANB était plus élevé.

Mots - clés : *falciforme anémie, radiographie céphalométrique, saillie de la mâchoire*

Introduction

Sickle cell disease (SCD) is a group of blood disorders which have in common a tendency for red blood cells to sickle (or distort into a crescent shape) under conditions of low oxygen tension [1]. It is a generic term for the family of haemoglobin (Hb) disorders having in common the inheritance of the sickle cell beta-globin gene (HbS) from at least one parent. Sickle cell anaemia results from the inheritance of the haemoglobin S gene from both parents, resulting in the homozygous state (HbS) [2]. It is a hereditary and familial haemolytic disease, the most common genetic disorder amongst black people and one of the major chronic non-communicable diseases affecting children [3].It is the most common worldwide symptomatic Haemoglobinopathy [4] and has an incidence of about 3% in Nigeria [5].

The sickle cell haemoglobin formed as a result of this disorder is destroyed more rapidly than normal red blood cells. The resulting anaemia from erythrocyte destruction leads to compensatory mechanisms associated with hyperplasia and expansion of bone marrow of long bones [6]. Sickle cell anaemia is known to affect hard tissues of the body, the dental structures inclusive. The mandible

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and the maxilla, just like the rest of the bony structures of the body, play a role in the haemopoiesis.

Sickle cell anaemia has been reported to have an effect on the bones of the jaw.To investigate the degree of severity of this effect on the jaw bones, lateral cephalometric radiograph, which is a tool used in the assessment of jaw relationship in orthodontics, can be employed. This radiograph is a standardized true lateral radiograph which provides both research and clinical tools for study of malocclusion and underlying skeletal disproportion and can also be used to investigate the effect of sickle cell anaemia on the jaws. This tool has been used to establish norms for different races and ethnicity in individuals with HbA and has been found to be very useful in treatment planning and clinical practice in general.

Nigeria has the highest burden of sickle cell disorder in the whole world [7] and the burden is increasing with increase in overall population [8]. The survival of sickle cell anaemia patients with access to good care is also steadily improving because of general improvement in health care delivery [1,7,9,10]. A substantial proportion of patients with sickle cell anaemia have severe malocclusions and this may be a reflection of the degree of craniofacial abnormalities found in them [11]. These malocclusions may have functional and psychosocial effects such as poor self-esteem [12].

Previous studies have been carried out on cephalometric values in sickle cell anaemia in other populations and these have shown that the degree of severity of the disease varies among races [13]. The only study found in literature carried out on cephalometric findings in sickle cell anaemia patients in this environment was 27 years ago [14].As a result of the high burden of SCA in Nigeria [7], a revalidation of cephalometric measurements in HbS individuals is necessary. Also, with the increasing awareness of orthodontic treatment in recent times, there is an increase probability that these individuals will present for the management of malocclusion.

Materials and methods

The study was carried out at the Haematology and the Orthodontic clinic of a tertiary health care facility in the South Western region of Nigeria.The study population comprised of a total of 120 participants divided into two groups of 60 HbS individuals (previously diagnosed with sickle cell anaemia by haemoglobin electrophoresis) and 60 HbA individuals attending the orthodontic clinic. Both groups were matched for age and gender.The control group was sent to the hematology clinic for confirmation of their genotype by haemoglobin electrophoresis. Ethical approval (UI/EC/14/0106) was obtained from the University of Ibadan/ University College Hospital Ethical Review board. Written informed consent was obtained from all participants.

The inclusion criteria included for group 1 was 18-25 years old confirmed sickle cell anaemia patients with no other known systemic disorder who are Nigerian by origin. For group 2, inclusion criteria was 18- 25 years old confirmed HbA individuals (with haemoglobin electrophoresis) who are Nigerians by origin with Angles class 1 malocclusion on skeletal pattern 1.

Procedure

Each consecutive individual that met the inclusion criteria was comfortably seated on a chair and their oral cavity was examined for eligibility and occlusal presentation (Angle's Class I molar relationship) with the use of gloved hands, dental mirror and dental probe.

During exposure of the participants for radiographs, theywere required to wear a protective lead lined apron after which the lateral cephalometric radiograph was taken using an analogue Pan-Blue-Oris machine (Blue-X Imaging S.R.L BLD XP PAN CEPH METRIC 71680000700: S/No 2402kk0164 ASSAGO, ITALY) with participants' head held in a cephalostat, looking forward with the Frankfort horizontal plane parallel to the floor, ear rods placed in both ears and the teeth in complete intercuspation. The distance from mid-sagittal plane of each participant to the source of radiation and the film was maintained at 150cm and 15cm respectively. Hard tissue tracings were obtained manually on a 0.003 inch thick cellulose acetate tracing paper and a sharpened 2H pencil over a light viewing box.

The following angles were measured

- Sella-Nasion-A-point angle (SNA): evaluates the antero-posterior position of the maxilla relative to the anterior cranial base.
- Sella-Nasion-B-point angle (SNB): evaluates the antero-posterior position of the mandible relative to the anterior cranial base.
- A-point-Nasion-B-point angle (ANB): indicates the magnitude of the skeletal jaw discrepancy.
- Upper incisors to Nasion-A point line (UiNA): establishes the relative protrusion of the maxillary dentition.
- Lower incisor and chin to Nasion-B point line (LiNB): establishes the relative protrusion of the mandibular dentition.

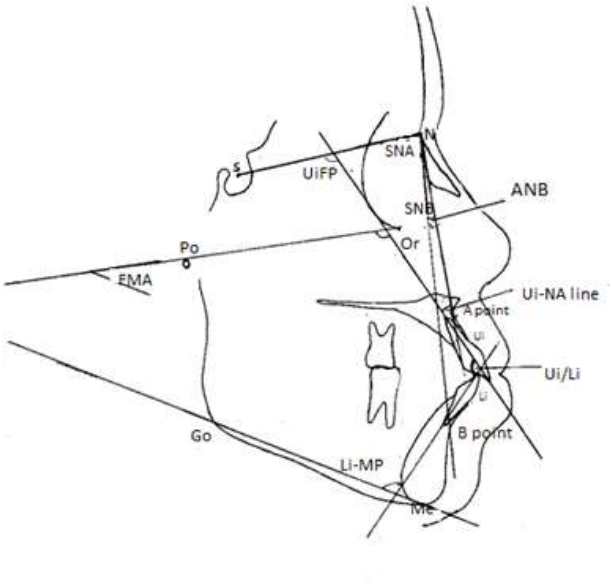

Fig.1: Angles measured on lateral cephalometric radiograph

- Frankfort-mandibular plane angle (FMA): establishes the degree of inclination of the mandible to the Frankfort horizontal plane
- Upper incisor to Frankfort plane (UiFP): establishes the relative proclination of the upper incisors in relation to the Frankfort plane
- Lower incisor to mandibular plane (LiMP): establishes the relative proclination of the lower incisors in relation to the mandibular plane.
- Upper incisor to lower incisor (Ui/Li): establishes the relationship of the upper central incisor to the lower central incisor.

Each measurement was taken at least twice and the average of the measurements recorded.

Data analysis

The collected data were analyzed using the Statistical Package for Social Sciences (SPSS Inc. Chicago IL) version 22. Frequency distribution of variables was generated and measures of central tendency calculated to summarize the numerical data. The data generated were presented as tables. The differences in means of cephalometric values of HbS patients and HbA patients were assessed using Student t-test.

Results

In group 1, 29 (48.3%) of the participants were males, 31 (51.7%) females while in group 2, 27 (45.0%) were males and 33 (55.0%) females. The mean age of the participants was 21.55 ± 2.55 years for the HbS group and 22.15 ± 2.52 years for the HbA group (Table 1).

The minimum SNA angle measured was 73.50º while the maximum was 100.00º. The mean SNA and SNB angle were 85.66 ± 4.93º and 80.56 ± 4.41º respectively.Comparison of the mean SNA angle in both groups, it was observed to be higher in HbA than HbS with a mean difference of -0.72º (t = -0.75, p= 0.46).The SNB values for HbS and HbA revealed a mean difference of -2.18º which was statistically significant (t = -2.47, p= 0.02). The ANB angle ranged between -3 and 10º with a mean value of 5.10 ± 3.32º.The mean difference in ANB value was found to be statistically significant 1.17º (t = 2.45, p= 0.02). In addition, the mean UiNA, LiNB and FMA measured 26.75 ± 6.77º, 38.63 ± 5.74º and 28.71 ± 5.84º respectively.The mean differences between the two groups for the UiNA (-0.99) and LiNB (2.03) were not statistically significant with p values of 0.44 and 0.08 respectively. The FMA value measures ranges between 16 – 46 degrees with a mean value of 28.71±5.84º

Discussion

The mean SNA angle for HbS participants in this study was found to be within the standard deviation for this variable in a Nigeria norm [15]. The interpretation of this is that maxillary protrusion which is a common feature among HbS individuals was found to be absent. A similar finding had been reported by Maia *et al* [16] in a study to characterize the craniofacial features of HbS patients in Brazil where they found the average value for SNA to be within the standard deviation for the variable in Brazilians. The possible reason for this might be connected to increased awareness of this disorder and the willingness of HbS individuals to accept treatment. More so, this current study population is hospital based and they receive treatment on regular

Table 1: Mean age and gender of participants by genotype.

	HbS	HbA	p value
Mean age ± SD (years)	21.55 ± 2.55	22.15 ± 2.52	0.20[#]
Gender Female n (%)Male n (%)	31 (51.7%)29 (48.3%)	33 (55%)27 (45%)	0.71[##]

SD: Standard deviation; [#] Student t-test; [##] Chi square test

Table 2. Comparison of mean cephalometric values of HbS and HbA participants.

Angles	HbS Mean (SD)º	HbA Mean (SD)º	Mean difference	*t* value	p value
SNA	85.66 (4.93)	86.38 (5.55)	-0.72	-0.75	0.46
SNB	80.56 (4.41)	82.74 (5.25)	-2.18	-2.47	0.02*
ANB	5.10 (3.32)	3.93 (1.63)	1.17	2.45	0.02*
UiNA	26.75 (6.77)	27.75 (7.35)	-0.99	-0.77	0.44
LiNB	38.63 (5.74)	36.59 (6.84)	2.03	1.76	0.08
UiFP	120.59 (6.85)	119.26 (9.00)	1.33	0.91	0.36
LiMP	102.33 (8.11)	101.87 (7.42)	0.47	0.33	0.74
Ui/Li	109.16 (8.70)	110.08 (11.44)	-0.92	-0.49	0.62
FMA	28.71 (5.84)	27.53 (5.12)	1.18	1.17	0.24

basis hence there is the likelihood of a reduction in the participation of jaw bones in haemopoiesis. Comparison of the mean SNA between HbS and HbA participants in this study showed a lower value for the HbS participants but the mean difference was not statistically significant. Similar findings had been reported by Adekile *et al* [14] who found the SNA value to be higher in HbA than in HbS individuals though this difference is not statistically significant [16]. Also, Brown and Sebes [17] in their study of lateral cephalometric radiographs of fifty HbS and twenty five HbA individuals found a similar results. Contrasting findings were however reported by Altemus and Epps[18] where the mean SNA value was higher in the HbS group than the HbA group, though the difference was not significant.Improvement in healthcare in recent times which include early diagnosis of sickle cell disease, more consistent follow-up from childhood leading to long survival rates [7,10] may be responsible for the lack of significant maxillary protrusion in HbS individuals in this study. The improvement in healthcare leads to reduction in the frequency of crises which eventually reduces the need for compensatory hyperplasia of the bones due to chronic hemolysis.

Concerning the mean SNB, the value recorded in this study was significantly lower in the HbS group than the HbA group thus, presenting a mandibular retrusion in relation to the cranial base in the HbS group. Similarly, Adekile et al [14]in a study observed that the mean SNB value was higher in HbA than in HbS individuals but the mean difference was not statistically significant. Furthermore, Bandeen [19] observed that craniofacial dimensions were reduced in sickle cell disease and subjects presented with small mandible. The reason for this could be the result of vaso-occlusive crises common in the acute phase of bone involvement in sickle cell anaemia [20,21]which results in compromised blood supply to the mandible, and hence hypoplasia of the mandible [14].

The ANB angle represents the antero-posterior relationship of the maxilla to the mandible and indicates the magnitude of skeletal jaw discrepancy. The mean ANB was significantly greater in the HbS than in HbA group. Adekile et al [14] also found the mean ANB of HbS individuals to be greater than that of the HbA though not statistically significant. Similar findings were observed by Pithon et al [22] who found a statistically significant difference in ANB values between the HbS, HbAS and HbA group in their studied population. Likewise, Altemus and Epps[18] found the ANB angle to be significantly greater in HbS than HbA. The degree of skeletal discrepancy observed in this study is due to the lower value of mean SNB as compared to the close to normal SNA value in the HbS group.

The significantly reduced SNB with consequent increase in ANB in the sickle cell anaemia patients require special consideration during treatment planning in orthodontics. When these patients present with retrusion of the mandible, the treatment should be aimed at bringing the mandible forward as much as possible in order to correct the skeletal discrepancy.

The UiNA and LiNB angles indicate the degree of proclination of the upper and lower incisors relative to the NA line and NB line respectively. The mean UiNA angle in this study was greater in the HbA group than HbS group though not statistically significant. This is similar to the measurements results (HbS 21.5º, HbA 23.0º) in a study by Altemus et al [18] in North American black children with sickle cell disease. Pithon et al [22] however noticed a statistically significant difference in UiNA values (HbS 20.5 ± 7.3º, HbA 26.7 ± 4.8º) in Brazilians with the HbA participants having a higher value. The

UiNA value in this current study is lower though not statistically significant when compared with that of HbA. This lower values noticed in the HbS group could be attributed to mandibular retrusion, hence a need for the maxillary incisors to compensate by retroclination for functional occlusal reasons.

The mean LiNB angle was greater in HbS group as compared with HbA group but not significant. Similar findings were reported by Altemus et al [18] and Pithon et al [22]. This higher LiNB angle value in HbS participants in this study can be ascribed to dental compensation for the retruded mandible.

The FMA angle which is a measurement of the facial height and a relationship between the Frankfort horizontal plane and the mandibular plane was larger in HbS than HbA participants. A steeper mandibular plane observe in the HbS group may have being responsible for this. Similar findings were noted by Licciardello et al [13] and Bandeen [19] in the HbS populations they studied at different times. The increase in FMA indicates an increased tendency towards open bite in the HbS individuals and this has being documented by a study in literature [23]. The increase in FMA has been attributed to hyperdivergence of the face in sickle cell anaemia [19].

Conclusion

The cephalometric findings showed that there was a significant difference between the mean SNB and ANB values in the HbS group compared to the HbA. The mean SNB was lower in HbS compared to HbA thereby increasing the mean ANB value. Therefore, during treatment, attempt at correction should be directed towards correcting the retrognathic mandible especially in HbS individuals under good care for the sickle cell condition since all the HbS sample were drawn from the hematology clinic.

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Reversal of tooth eruption sequence: beliefs and perceptions

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Abstract

Background: Among some Nigerians, eruption of the maxillary primary incisors before their mandibular counterparts is considered a taboo. Data regarding the perceptions of residents of Igbo Ora to reversal of eruption sequence appear non-existent.

Aims and objectives **:** The aim of this study is to assess the attitudes and beliefs of some adults of Igbo Ora to reversal of eruption sequence of primary incisors

*Design of study***:** A cross-sectional study was conducted among community dwelling females aged 18 years and older in Igbo Ora, Southwestern Nigeria

*Materials and methods***.** A house to house survey was conducted among all willing adult females available at the time of the study. Data for the study was collected with an interviewer administered questionnaire in the Yoruba Language. Data collected were analyzed with SPSS version 21. Frequencies, means and proportions were generated and test of association between categorical variables was done using Chi Square statistics.

Results: There were 229 participants with a mean age of 34.6 (SD = 12.6) years and majority (34.1%) had secondary school education . Reversal of eruption sequence was attributed to child being evil (47.6%) and mother exposed to other evil children (4.8%). About 56.3% of respondents believe that reversed eruption sequence has a negative effect on the child, including the ability to place irrevocable curses on people. A perceived consequence of having a child with reversed tooth eruption sequence on the family was fear of the child by other family members (21.8%). Beliefs about reversed sequence of eruption of primary anterior teeth being a normal variation increased with educational qualification (p = 0.001).

*Conclusion***:** The study has revealed gross fallacies regarding reversal of eruption sequence in children in Igbo Ora. Health education intervention should be given to them particularly targeting mothers and the less educated.

Keywords *Eruption, teeth, reversal, taboo*

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Résumé

Contexte : Chez certains Nigérians, l'éruption des incisives primaires maxillaires avant leurs homologues mandibulaires est considérée comme un sujet tabou. Les données concernant les perceptions des résidents d'Igbo Ora sur l'inversion de la séquence d'éruption semblent inexistantes.

Buts et objectifs **:** Le but de cette étude est d'évaluer les attitudes et les croyances de certains adultes d'Igbo Ora à l'inversion de la séquence d'éruption des incisives primaires.

Plan d'étude **:** Une étude transversale a été menée parmi des femmes de 18 ans et plus vivant dans la communauté d'Igbo Ora, dans le sud-ouest du Nigéria.

Matériels et méthodes : Une enquête porte à porte a été menée auprès de toutes les femmes adultes consentantes disponibles au moment de l'étude. Les données de l'étude ont été recueillies à l'aide d'un questionnaire administré par un enquêteur en langue yoruba. Les données collectées ont été analysées avec SPSS version 21. Des fréquences, des moyennes et des proportions ont été générées et un test d'association entre variables qualitatives a été réalisé à l'aide de statistiques Chi Carré.

Résultats: Il y avait 229 participants avec un âge moyen de 34,6 (SD = 12,6) ans et la majorité (34,1 %) avaient fait des études secondaires. L'inversion de la séquence d'éruption a été attribuée à être un enfant maléfique (47,6%) et à une mère exposée à d'autres enfants maléfiques (4,8%). Environ 56,3% des personnes interrogées pensent que la séquence inversée des éruptions a un effet négatif sur l'enfant, notamment en ce qui concerne la possibilité de lancer des malédictions irrévocables à des personnes. Une conséquence perçue d'avoir un enfant avec une séquence d'éruption de dent inversée sur la famille était la peur de l'enfant de la part des autres membres de la famille (21,8%). Les croyances selon lesquelles la séquence inversée d'éruption des dents antérieures primaires était une variation normale augmentaient avec le diplôme éducatif (p = 0,001).

Conclusion **:** L'étude a révélé des fausses idées concernant l'inversion de la séquence d'éruption chez les enfants d'Igbo Ora. Une intervention d'éducation pour la santé devrait leur être ciblée, en particulier pour les mères et les moins instruits.

Mots-clés *Eruption, dents, inversion, tabou*

Introduction

Tooth eruption in children is an important milestone in the Nigerian culture as parents, neighbors and friends eagerly await eruption of baby's first teeth. Literature reveals that the primary mandibular incisors usually erupt before their maxillary counterparts[1-3]. In some instances however, the primary maxillary incisors have erupted ahead of the mandibular ones reversing the order of eruption [4,5].

Prevalence rates of reversal of eruption sequence of primary incisors in infants appear scarce. In a Nigerian study, 3.1% of mothers claimed that their children erupted the maxillary primary incisors prior to the mandibular counterparts [5].

The eruption of maxillary primary incisors before the mandibular ones have sometimes been unacceptable in certain cultures. Among the Marakwet of Kenya [6], some tribes in Zambia [7], Benin republic [8], and the Hammer of Ethiopia [9] eruption of upper teeth before the lowers have been viewed with disdain. Amid some Nigerians tribes, it is considered a taboo and affected children are deemed evil: believed to possess mysterious powers[10-14]. An earlier study on eruption sequence in infants among Yoruba rural dwellers in southwestern Nigeria revealed that 70.4% of the community members regarded eruption of upper primary incisors before the lowers as a sign of the affected child being evil [4], Consequently, as affected children grow, they are stigmatized , suffer humiliation and immense emotional trauma [4,12].

Data regarding the perceptions of Nigerians in remote areas of Igbo Ora, a rural farming community in Ibarapa to reversal of eruption sequence in infants appear nonexistent. Hence this study, aims to investigate their beliefs, attitudes and practices towards reversal of eruption sequence of primary incisors in children.

It is expected that the results of this study will reveal knowledge gaps, which will lead to development of health education tools/programmes to address such misconceptions.

Materials and Methods

This cross-sectional study was conducted among community dwelling females aged 18 years and older in Igbo Ora, Southwestern Nigeria. Igbo Ora is the headquarters of Ibarapa Central Local Government Area in Oyo State and administratively consists of seven wards [15]. The town is bordered by six other Ibarapa communities with typical characteristics of rural settlements and the local language of this community is Yoruba [15].

Ethical approval for the study was obtained from the Oyo State Ethics Review Board.

A minimum sample size of 166 was calculated for the study using a sample size calculation formula for cross sectional study [16] at a power of 90%, a degree of error of 5% and prevalence rate of 12.3% obtained from a previous study [12].

Participants for the study were selected using a cluster random sampling technique. Two wards were randomly selected from a list of seven wards within this community by balloting using sealed envelopes. Within the two selected clusters, a house to house survey was conducted, all females who satisfied the inclusion criteria were approached for the study.

Permission and approval was obtained from the head of each household before approaching the females. The purpose of the study was explained to each of the participants and consent sought before interviewing them. Females that were 18 years or older who have been residing in the community for at least one year were recruited for the study while those that were ill or did not consent to participate or those in whom communication was impossible were excluded from the study.

Data for the study was collected with an interviewer administered questionnaire which was translated into Yoruba Language and back translated to English by independent individuals versed in both languages. Ambiguous questions were modified appropriately. The questionnaire was divided into three sections: Section A comprised of sociodemographic characteristics of the participants, Section B; beliefs about reversed tooth eruption and Section C assessed advice the respondents will give mothers of children with reversed sequence of tooth eruption. The questionnaire consisted of both open and close ended questions. The close ended questions had responses obtained from literature review on similar issue, while open ended questions were included so as to capture extensively the opinions and beliefs of the participants. The questionnaire was pretested among females in another cluster not included in the study so as to validate and ascertain that the questionnaire actually addressed what it set out to measure. Ambiguous questions were removed and appropriate modification was made before the final study. The research assistants employed for this study received a one day training on the proper technique of administration of the questionnaires. Data was collected over a period of four weeks

Data collected were analyzed with SPSS version 21. Frequencies, means and proportions were generated and test of association between categorical variables was done using Chi Square statistics. To reduce the number of empty cells for cross tabulation and analyses, age was dichotomized around the mean age as < 35years and ≥ 35years. Likewise, perceptions of the study participants about reversed eruption of tooth sequence in a child was also re-constructed into two categories as being "normal variation" in a category and other views into the second category named "others". Statistical level of significance was set at $p<0.05$.

Results

There were 229 participants with a mean age of 34.6 (SD = 12.6) years and only a few 19.2% of the participants had no formal education (Table 1).

Table 1: Demography of study participants

Variable	Frequency	%
Age group (years)		
≤20	27	11.8
21-30	77	33.6
31-40	66	28.8
41-50	31	13.6
>50	28	12.2
Educational qualification		
No formal education	44	19.2
Primary	65	28.4
Secondary	78	34.1
Post-secondary	42	18.3
Tertiary	0	0
Tribe		
Yoruba	222	96.9
Hausa	5	2.2
Ibo	2	0.9
Religion		
Christian	57	24.9
Muslim	159	69.4
Tradition	1	0.4
Others	12	5.3

The majority 192 (83.8%) had seen or heard of a child with reversed sequence of tooth eruption.

Ninety-four (41.0 %) respondents would be alarmed on seeing such a child (Table 2). Attributed reasons to reversed sequence of tooth eruption in children include; child being evil 109 (47.6%), mother's exposure to a child with reversed sequence of tooth eruption during pregnancy 11 (4.8%), mother had contravened laid down cultural rules and traditions 6 (2.6%) while 93 (40.6%) believed it as a normal variation but may have consequences (Table 2). More than half of the respondents 129 (56.3%) believed that a child with reversed eruption sequence may suffer adverse consequences as a result and 66 (51.2%) of them affirmed that it included the ability of child to place permanent curses on others (Table 2). Perceived consequences of having a child with reversed tooth eruption sequence on the family mentioned by respondents were; fear of the child by other family members as the child is believed to be evil 50 (21.8%) (Table 2).

Respondents will advise mothers of affected children to hide/get rid of them (28.4 %) and extract the teeth (22.3%) (Table 2). .

A higher proportion 90 (91.8%) of older women (aged 35years or older) were found to have seen children with reversed sequence of tooth eruption when compared with those younger than 35years ($p = 0.004$).

No statistical significance was found with educational qualification and having seen a child with reversed sequence of eruption (Table 3).

Analysis of the perception of participants about reversed eruption sequence and their sociodemographic characteristics (Table 4) showed that beliefs about reversed sequence of eruption as being a normal variation increased with educational qualification with the highest proportion (76.2%) noted

Table 2: Beliefs and perceptions of respondents about reversal of tooth eruption sequence
Multiple responses

Variable n = 229	N	%
Initial reaction on seeing a child with reversed sequence of tooth eruption		
Surprised	94	41.0
Suspect it's an evil child	51	22.3
Will not be surprised as they had seen such before	84	36.7
Reasons why children erupt the upper incisors before lower ones		
Evil children	109	47.6
Mother contravened cultural taboos	6	2.6
Mother exposed to other evil children	11	4.8
Mother touching the child's gum before tooth erupts	1	0.4
It is a normal variation	93	40.6
No idea	9	4.0
Effect of reversed sequence of tooth eruption on the child		
Negative consequences	129	56.3
None	100	43.7
Perceived negative effect of reversed sequence of tooth eruption(n=129)		
Places permanent curse on family and other people	66	51.2
Engages in strange/abnormal/dangerous things	47	36.4
Dull	2	1.6
Combination of all the options above	14	10.9
Consequences of reversed sequence of tooth eruption on the family		
Child feared by others members of the family	50	21.8
Source of embarrassment	49	21.4
A source of curse on the family	26	11.4
Abomination	19	8.3
Combination of the above	10	4.4
None	82	35.8
No idea	3	1.3
Advice to the mother of a child with reversed sequence of tooth eruption		
Hide the child/get rid of the child	65	28.4
Extract the tooth	51	22.3
Appease gods with sacrifice to reverse the eruption sequence, then extract tooth	15	6.6
Leave child alone (do nothing)	94	41.0
No idea	4	1.7

among those with post-secondary education (p = 0.001).

A greater proportion of those with lower educational levels will be surprised at seeing children with such teeth and will suspect affected children are evil as compared to respondents with post – secondary education (p=0.001) (Table 5).

Discussion

This study reveals gross misconceptions regarding reversal of eruption sequence of primary incisor teeth in Igbo Ora. This is hazardous and may affect the child's physical, psychological and social wellbeing in the future. Over four fifths of the respondents had seen/ heard of a child with reversed sequence of tooth eruption. However, about two fifths would be astounded at seeing such a child. This may be due to the fact that it is a deviation from the acceptable cultural norm that lower anterior incisors should erupt first. In addition, none of the respondents mentioned ever having a child with reversed sequence of tooth eruption. This may either be due to the relatively low prevalence of the condition or the cultural norm associated with owning up to having such children because of the associated consequential stigmatization that may be suffered if others in the community get to know about it.

Many (47.6%) of the respondents were convinced that affected children erupt their upper teeth before the lower ones because they are evil. 'Evil children' in this context implies that these children are witches/sorcerers possessing supernatural powers. Reports by Aderinokun and Oyejide (1991) [4] and Uchegbue (2010) [11] are in congruence with this report. Other African cultures such as Baribar of Benin [8] and Hamar of Ethiopia [9] share this

Table 3: Socio demographic characteristics, having seen a child with reversed sequence of tooth eruption and perceptions about a child with reversed sequence of tooth eruption

Variable	Seen a child with reversed sequence of tooth eruption Yes n (%)	No n (%)	X^2	P- value
Age (years)				
<35	102 (77.9)	29 (22.1)	8.081	0.004*
≥35	90 (91.8)	8 (8.2)		
Total	192 (83.8)	37 (16.2)		
Educational qualification				
None	38 (86.4)	6 (13.6)	0.528	0.913
Primary	54 (83.1)	11 (16.9)		
Secondary	64 (82.1)	14 (17.9)		
Post-secondary	36 (85.7)	6 (14.3)		
Total	192 (83.8)	37 (16.2)		

**Statistically significant*

Table 4: Socio demographic characteristics and perceptions about a child with reversed sequence of tooth eruption

Variable	Normal variationn (%)	Others n (%)	X^2	P value
Age (years)				
<35	51 (38.9)	80 (66.1)	0.549	0.588
≥35	42 (42.9)	56 (57.1)		
Total	93 (40.6)	136 (59.4)		
Educational qualification				
None	14 (31.8)	30 (68.2)	27.026	<0.001*
Primary	21 (32.3)	44 (67.7)		
Secondary	26 (33.3)	52 (66.7)		
Post-secondary	32 (76.2)	10 (23.8)		
Total	93 (40.6)	136 (59.4)		

**Statistically significant*

Table 5: Socio demographic characteristics and reaction on seeing a child with reversed sequence of tooth eruption

Variable	Reactions on seeing a child with reversed sequence of tooth eruption			X^2	P-value
	Surprised n (%)	Suspect child is evil n (%)	Reassure mother n (%)		
Age (years)					
<35	51 (38.9)	33 (25.2)	47 (35.9)	1.560	0.458
≥35	43 (43.9)	18 (18.4)	37 (37.8)		
Total	94 (41.0)	51 (22.3)	84 (36.7)		
Educational qualification					
None	19 (43.2)	12 (27.3)	13 (29.5)	23.883	0.001*
Primary	31 (47.7)	14 (21.5)	20 (30.8)		
Secondary	36 (46.2)	20 (25.6)	22 (28.2)		
Post-secondary	8 (19.1)	5 (11.9)	29 (69.0)		
Total	94 (41.0)	51 (22.3)	84 (36.7)		

**Statistically significant*

same belief. Some of the respondents alluded this condition to the fact that mothers of affected children had come in contact with other children with a similar condition during pregnancy, while others alleged it to retributive justice as it is believed that their mothers had contravened some cultural norms of their communities. This reveals a great degree of ignorance. The consequences of designating a child as evil in the Nigerian society is associated with discrimination and general avoidance of such a child by the society which could culminate in emotional instability later in the child's life[4]. Mothers' touching gum pads of their babies prior to tooth eruption was another factor believed to be responsible for such a reversal.

It is worthy of note that only about two fifths of the respondents were of the opinion that reversal of eruption sequence was just only a natural occurrence.

Over half, believed that reversed eruption sequence leads to negative consequences in the child's life. This include the supernatural ability to place irreversible / lifelong curses on individuals and display of bizarre behavior. Participants stated that in neighborhoods and communities' other children avoid playing with such children as they are believed to transmit an aura of ill luck and perceived as a bad omen and in local markets community members avoid buying wares from their mothers thus creating great misery.

The study has revealed that the family unit, an important place for care and solace of the child is gravely affected by the prevailing condition of the child. A fifth of the respondents affirmed that the child becomes a source of intense fear and dread by family members. This is due to the child being perceived as evil, believed to possess strange powers and capability to pronounce irrevocable curses on people. Furthermore, some of the respondents regarded these children as a source of a ill luck and were deemed as abominations to their families. This results in avoidance of such children by neighbors, relatives and friends further contributing to physical isolation, and psychological and emotional stress which may even progress into adulthood. Many of the respondents (21.4%) adjudged these children as a huge family embarrassment. The family is thus under intense emotional pressure. Consequently, they may dodge social relationships, spend energy in concealing the family's "problem", or relocate to another area leading to social isolation [17,18]

Generally, in the Yoruba culture in South Western Nigeria, children who erupt the upper teeth before the lowers are highly stigmatized and disparagingly called *omo eleyin oke* meaning "upper teeth child". Unwholesome and scornful comments are made about them, and they are often sneered and jeered at, thus suffering from intense emotional trauma as they grow [14]. This may affect their self-esteem, academic achievement and prospects for marriage in the future [4,19]. This may explain why over a quarter of the participants would advise mothers that such children should be hidden/gotten rid of. This is cruel and disheartening and is in congruence with other studies [4,12] and anecdotal reports [20]. Sometimes affected children are poisoned with some local herbs and left to die [13]. Over two fifths would want such teeth extracted and since the child is believed to be endowed with supernatural powers such extractions are preferably done by the quacks in the community. Sacrifices to appease the gods prior to the tooth extractions were considered crucial by some of the respondents. Quacks forcefully and traumatically remove teeth with unsterile crude instruments and consequences of patronizing them include high probability of child contacting bacterial and viral infections such as Human Immunodeficiency Virus and hepatitis [21-22].

Beliefs about reversed sequence of eruption as being a normal variation increased with educational qualification. The less educated respondents were more deeply entrenched in the myths and misconceptions associated with reversed tooth eruption

Conclusion

The study has revealed gross fallacies regarding reversal of eruption sequence in children among the studied population. In view of these findings, oral health education to this community will be highly beneficial as this will deliver affected individuals from needless stress, anxiety /fear and save the lives of some children who would otherwise have suffered infanticide. Health education intervention should be given to rural societies particularly targeting pregnant women, nursing mothers, elderly women (who are the grandmothers and mother in law), mothers, and the less educated.

Limitations of the study

A cluster random sampling technique was employed and two wards were selected from seven within this community. Sampling of a greater number of wards would have given a more representative sample of the inhabitants of Igbo Ora.

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An assessment of the impact of acrylic removable partial dentures (RPDs) on the quality of life of partially edentulous patients in a Nigerian Teaching Hospital.

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Abstract

Background: There is a regular demand for replacement of lost teeth, which is an indication that loss of teeth has negative impact on the affected individuals. The impact of prosthetic rehabilitation with acrylic RPDs is not clear yet in our environment.

Objective: To assess the impact of acrylic RPDs on the quality of life of edentulous patients.

Patients and method: A prospective study was carried out using the OHIP questionnaire to assess the effects of acrylic RPDs on the quality of life of partially edentulous patients. Data collected was analysed using SPSS version 19 software and Chi-square test was used to assess the impact of acrylic denture on the quality of life of the patients. Level of statistical significance was set at $p \leq 0.05$.

Results: The majority, 59.6% of the patients had maxillary RPDs, while 19.2% had a combination of upper and lower RPDs. The greatest impact of partial edentulousness on oral functions was on self-consciousness with a score of 17, which reduced to 9 following rehabilitation with acrylic RPDs. Two patients had the worst severity of impact (31 -40 scores) without RPDs while none had the worst severity of impact after the insertion of the RPDs. There was a significant difference between the severity (p=0.004) and extent of impact (p=0.000) when the values before was compared with that after the use of dentures.

Conclusion: The use of acrylic RPDs significantly reduced the severity and extent of impact of edentulousness on quality of life of partially edentulous patient, and thereby improved their overall wellbeing.

Key words: *Acrylic removable denture, Quality of life, Partially edentulous Patients*

Résumé

Contexte : Il y a une demande régulière de remplacement des dents perdues, ce qui indique que la perte de dents a des effets négatifs sur les personnes touchées. L'impact de la réhabilitation prothétique avec les RPDs acrylique n'est pas encore clair dans notre environnement.

Objectif : Pour évaluer l'impact des RPDs acrylique sur la qualité de vie des patients édentés.

Patients et méthode : Une étude prospective a été réalisée à l'aide du questionnaire OHIP afin d'évaluer les effets des RPDs acrylique sur la qualité de vie des patients partiellement édentés. Les données recueillies ont été analysées à l'aide du logiciel SPSS version 19 et un test de chi carré a été utilisé pour évaluer l'impact de la prothèse acrylique sur la qualité de vie des patients. Le niveau de signification statistique a été fixé à p d" 0,05.

Résultats : La majorité, 59,6% des patients étaient atteints des RPDs maxillaire, tandis que 19,2% présentaient une combinaison des RPDs supérieurs et inférieurs. Le plus grand impact de l'édentement partiel sur les fonctions buccales était sur la conscience de soi, avec un score de 17, qui a réduit à 9 après la réhabilitation avec des RPDs acrylique. Deux patients avaient l'impact plus grave (scores de 31 - 40) sans RPDs, tandis qu'aucun n'avait d'impact plus grave après l'insertion des RPDs. Il y avait une différence significative entre la sévérité (p = 0,004) et l'étendue de l'impact (p = 0,000) lorsque les valeurs antérieures étaient comparées à celles après l'utilisation d'une prothèse dentaire.

Conclusion : L'utilisation des RPDs acryliques a considérablement réduit la gravité et l'ampleur de l'impact de l'édentement sur la qualité de vie des patients partiellement édentés et a ainsi amélioré leur bien-être général.

Mots-clés : *Prothèse amovible en acrylique, qualité de vie, patients partiellement édentés*

Introduction

Partial edentulism is a state of the dental arch in which one or more, but not all natural teeth are missing. Generally, it is a pathological sequel of caries, periodontal diseases, trauma, neoplasm and cystic lesions of the jaws [1,2]. Partial edentulism presents

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with various challenges such as: difficulty in chewing, altered speech, changes in facial appearance and temporo-mandibular disorders [2]. In addition, it leads to lack of confidence and social problems, which may adversely affect the quality of life and lead to psychological disturbance [3]. It is referred to as "the final marker of disease burden for oral health" [4]

Acrylic removable partial denture (RPD) is one of the options for the management of partially edentulous patients. Other options include: metallic partial dentures, over dentures, tooth and implant supported fixed dentures [5]. Acrylic partial denture has the following favourable characteristics: it is affordable, reversible, yet gives satisfactory aesthetics. In addition, acrylic denture is easy to process and repair, and requires no special apparatus for its fabrication [6, 7]. These advantages particularly the favourable costs of acrylic dentures make it the most common option in the management of tooth loss in Nigeria [8]

Acrylic dentures however, are mucosa borne and show low resistance to fatigue, hence cannot withstand heavy occlusal load [9]. This limits their effectiveness in restoration of masticatory function in partially edentulous patient. It can also act as gum stripper, causing inflammatory reaction in the gingivae, sometimes with pain and swelling particularly when left unattended to [10, 11]. In addition, it can cause residual ridge resorption [9]. These disadvantages can have a negative impact on the quality of life of the patient. Despite these shortcomings, acrylic denture still remains the most utilized method of addressing the negative impact of tooth loss in our country [8].

Currently, there is little information on the effects of acrylic RPDs on the quality of life of acrylic denture wearers in Nigeria despite being the most frequently used method of replacing missing teeth. This study was therefore, designed to assess the impact of acrylic RPDs on the quality of life of partially edentulous patients. This will provide a record of the effectiveness of this treatment option in the management of edentulous patients in our environment since quality of life assessment is a reliable tool to measure treatment outcome.

Patients and method

This prospective clinical study was conducted at the Prosthetic out-patient clinic of a Nigerian Teaching Hospital. Ethical approval was obtained from the Institutional Review Committee, and informed consent to examine and carry out the study was obtained from each participant before the commencement of the study.

Patients aged 16 years or more with one or more missing teeth in the upper or lower arch requiring RPDs were recruited into the study. Other inclusion criteria were patients who had lost their teeth for $\geq$3 months with no history of prosthetic replacement and gave assurance of their availability through the period of the study. Individuals with systemic conditions such as cardiovascular diseases, uncontrolled diabetes mellitus, psychiatric disorder or neurological defects were all excluded from the study. In addition, patients with poor periodontal health of standing teeth were excluded. The recruitment and assessment of the participants was done over a period of one year.

Oral health impact (OHIP) questionnaire developed by Slades and Spencer [12] was administered to each patient by one of the researchers who have been previously trained on how to administer the questionnaire to assess the impact of missing teeth on the quality of life of the patient before placement of denture. Then acrylic denture was fabricated for each patient following standard procedure and post insertion instructions were given verbally and in writing at the point of insertion of the dentures. After the initial recall visits, the patients were recalled after using the denture for a period of three months for reassessment with the questionnaire.

The questionnaire consisted of two parts; the first part asked about patient's age, gender, occupation, the missing teeth and the second part assessed the oral health impact of the patient using the oral health impact questionnaire (OHIP-14). The OHIP-14 questionnaire [12] consists of 14 questions subdivided into seven areas. Responses to each of the questions were recorded using a 5-point Likert scale: 0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often and 4 = very often. Total OHIP score was calculated for each subject by adding the score for each question, and the mean score for each patient calculated by dividing the total score by fourteen. The prevalence, extent and severity of oral health impact were calculated as suggested by Slade et al., [13]. Prevalence is the percentage of respondents reporting 1 or more "fairly often" or "very often". Extent is the number of items reported "fairly often" or "very often" while severity is the sum of the scores for the 14 items (Total OHIP scores). The OHIP questionnaire had been validated and found reliable in our environment [14].

Data analysis

Data analysis was done using IBM SPSS Software Version 19 (SPSS, Chicago, IL). Descriptive statistics were represented as percentage, means and standard deviations. Differences between values obtained before and after wearing of dentures were compared using Chi-square test and independent t-test was used to assess the influence of age and gender on the impact of denture on the respondent quality of life. The level of statistical significance was set at $p \leq 0.05$.

Results

Fifty-two partially edentulous patients participated fully in the study, which included 31(59.6%) males and 21(40.4%) females. Their age ranged from 18 to 80 with a mean age of 43.7 (±10.57) years. Over half of the respondents, 27(51.9%) were in the age group 20 – 40 years. The majority, 31(59.6%) of the respondents had maxillary denture alone while 11(19.2%) had both maxillary and mandibular dentures. When the position of the teeth replaced

Table 1: Distribution of the acrylic dentures used by the respondents according to their characteristics

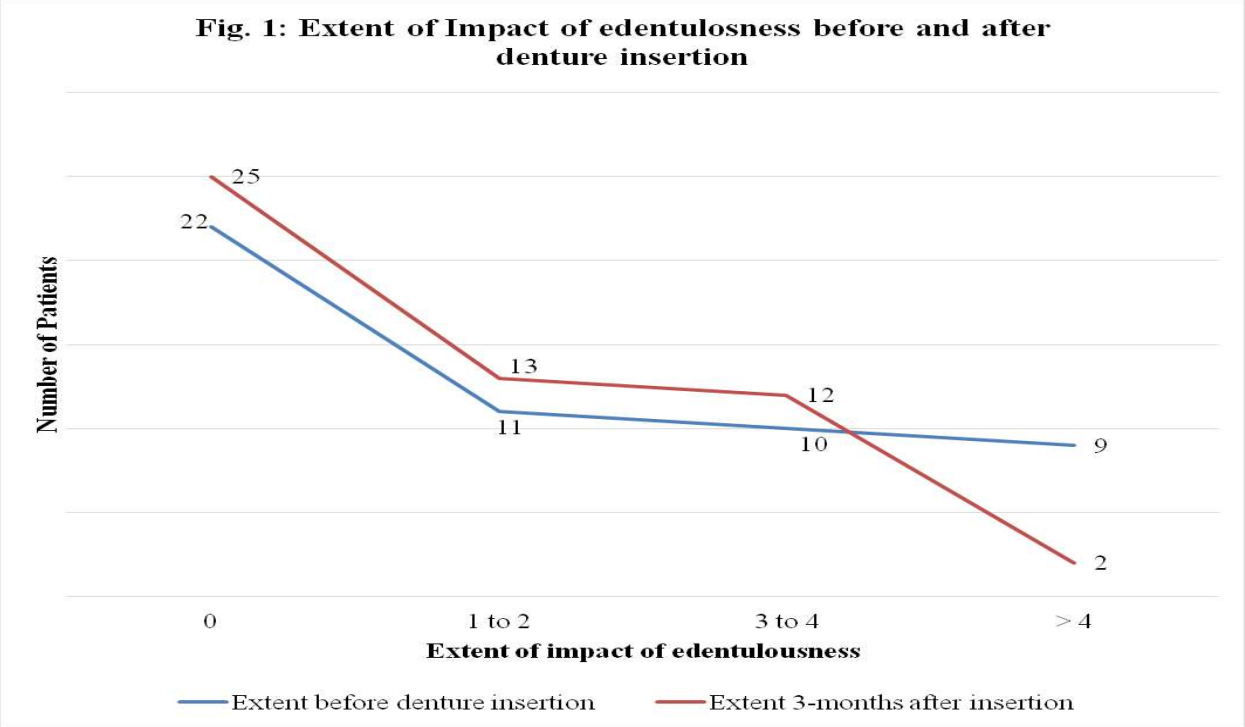
Characteristics of denture		n	%
Types of denture based on location on the arch	Maxillary	31	59.6
	Mandibular	11	21.2
	Maxillary and mandibular	10	19.2
	Total	52	100
Types of denture based on position of teeth replaced	Anterior teeth	37	71.2
	Posterior teeth	5	9.6
	Combination	10	19.2
	Total	52	100
Types of denture based on number of teeth replaced	1 – 2 teeth	30	57.7
	2 -4 teeth	9	17.3
	> 4 teeth	13	25.0
	Total	52	100

Table 2: The distribution of items with very and fairly often responses by the patient before and after wearing of denture

		No of patients with Very/ Fairly often Responses before the use of denture	No of patients with Very/ Fairly often Responses after fitting of denture
a)	**Have you had trouble pronouncing any words because of your dentures**	11 (21.5%)	7 (13.5%)
b)	**Has your sense of taste been affected because of your denture**	4 (7.7%)	5 (9.6%)
c)	Have you had painful aching anywhere in your mouth?	5 (9.6%)	5 (9.6%)
d)	Have you found it uncomfortable to eat any food?	14 (26.9%)	12 (23.1%)
e)	Have you been self-conscious because of your denture?	17 (32.7%)	9 (17.3%)
f)	Have you felt tense because of your denture?	9 (17.3%)	7 (5.8%)
g)	Has your diet been unsatisfactory because of your denture?	6 (11.5%)	3 (5.8%)
h)	Have you had to interrupt meals because of your denture?	6 (11.5%)	4 (7.7%)
i)	Have you found it difficult to relax because of your denture?	5 (9.6%)	3 (5.8%)
j)	Have you been embarrassed because of your teeth	12 (23.1%)	5 (9.6%)
k)	Have you been a bit irritable with other people because of your denture?	6 (11.5%)	4 (7.7%)
l)	Have you had difficulty doing your usual jobs (or attending school) because of problems with your denture?	4 (7.7%)	2 (3.8%)
m)	Have you found life less satisfying because of your denture?	2 (3.8%)	1 (1.9%)
n)	Have you been unable to perform the usual functions because of your dentures?	5 (9.6%)	2 (3.8%)

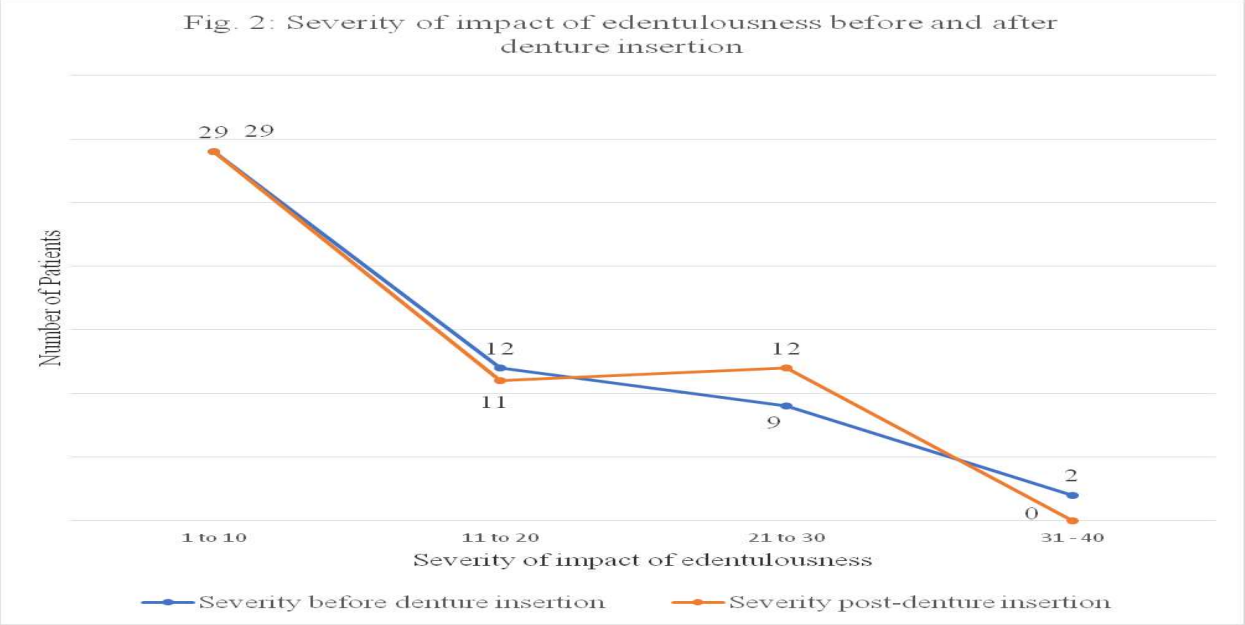
was considered, many of the respondents, 37(71.2%) replaced their anterior teeth, while only few 5(9.6%) replaced the posterior teeth. Majority of them 30 (57.7%) replaced one or two teeth (Table 1).

of missing teeth 12 (23.1%) and speech problems 11 (21.5%). Following prosthetic rehabilitation, notable improvement was recorded in the areas of feeling embarrassed because of missing teeth where the



The response of the participants to the quality of life questionnaire items assessed before and after prosthetic rehabilitation is shown in table 2. The quality

number of respondents dropped from 12 (23.1%) to 5 (9.6%), self consciousness where the number dropped from 17 (32.7%), to 9 (17.3%) and speech



of life areas with the highest number of responses before prosthetic rehabilitation were: feeling of self consciousness 17 (32.7%), difficulty in eating some food items 14 (26.9%), feeling embarrassed because

difficulty where the number dropped from 11 (21.5%) to 7 (5.8%) respectively. The least impact was recorded in the area of eating difficulty where the number only dropped from 14 (26.9%) to 12 (23.1%).

The prevalence of impact of partial edentulism on quality of life before wearing of denture was 55.8% and this was reduced to 50.0% after wearing of denture for three months. The extent of impact of the edentulous state of respondents reduced following insertion of the RPDs. Twenty-two patients had scores of zero extent without denture while twenty-five had zero extent after insertion of dentures. Nine patients had a score of greater than four extents before insertion of denture while only two patients had a score of greater than 4 three months after insertion of dentures (Fig 1). There was only a slight improvement on the severity of impact of partial edentulousness following insertion of the RPDs. Twenty-nine patients had the least level of severity of impact (1-10 scores) before and after wearing dentures, while two patients reported having the worst severity of impact (31 -40 scores) without RPDs and none reported the worst severity of impact after the insertion of the RPDs (Fig 2).

For data analysis, respondents were grouped into two before and after placement of denture based on their extent of impact as 0 and $\geq$ 1 extent. There was a statistically significant difference (p=0.000) when the extent of impact of edentulous state of the respondents was compared before and after the insertion of the denture. Also, the respondents were grouped into two before and after wearing of denture for analysis based on severity of impact. There was a statistically significant difference (p=0.004) when the severity of impact of edentulous state of the respondents was compared before and after the insertion of the denture (Table 3). The distribution of the respondents based on the domain of OHIP showed that the mean score was lower for each of the domains following the insertion of denture with the exception of physical pain domain, in which the mean score after insertion of denture was higher than that before the insertion of denture. The most significant difference reported by the respondents was in the area of social disability with a mean of 1.40 without denture and 0.99 after inserting denture (Table 4).

The mean sum-OHIP score decreased after wearing of denture from 13.43 to 11.61 among patients below 65 years old while the mean sum-OHIP score increased from 5.100 to 8.400 after wearing of denture among patients who were 65 years old and above. Independent t-test shows a statistically significant difference between the mean sum-OHIP scores for patients below 65 years and those that were 65 years and above before wearing of denture (p = 0.00). The mean sum-OHIP scores were slightly higher for females than males both before and after wearing of denture while the mean sum-OHIP scores decreased after wearing of

Table 3: Comparison of extent and severity of impact of edentulism on quality of life of patients before and after placement of denture

Impact on quality of life	Patients before denture insertion		Patients after denture insertion		Chi-square test
Severity of impact	n	%	n	%	0.004
$\leq$ 14	29	55.8	32	61.5	
> 14	23	44.2	20	38.5	
Extent of impact	Without denture		With denture		
0 extent	22		25		0.000
1-10 extent	30		27		

Table 4: Distribution of OHIP scores according to domains before and after the use of denture by the patients.

	Before placement of denture		After placement of denture	
OHIP DOMAINS	Mean	SD	Mean	SD
Functional limitation	1.73	2.06	1.62	1.94
Physical pain	2.06	2.09	2.19	2.00
Psychological discomfort	2.35	2.47	2.02	2.16
Physical disability	1.77	2.13	1.44	2.04
Psychological disability	1.64	2.29	1.40	1.86
Social disability	1.40	2.14	0.99	1.21
Handicap	1.15	1.78	0.83	1.46

denture in both the female and male respondents. Independent t- test however, shows no statistically significant differences (Table 5).

Table 5: Distribution of mean sum -OHIP values in relation to age and gender of the patients

Age group and gender of patients		N	Before wearing of denture Mean sum of OHIP	S.D	P	After wearing of denture Mean sum of OHIP	S.D	P
Age	< 65 yrs	42	13.432	10.897	0.00	11.609	8.882	
	≥ 65 yrs	10	5.100	3.957		8.400	8.909	0.249
Gender	Male	31	11.936	11.347	0.941	10.645	9.344	
	Female	21	11.714	8.866		10.905	8.514	0.919

Discussion

In this study, maxillary anterior teeth were the most commonly replaced with denture, which is in agreement with previous studies by Olusile and Esan [15], and Arigbede and Taiwo [16] who reported that upper central and lateral incisors were the teeth most demanded for. It had also been reported that 38. 5% of dentures demanded for in our environment were for replacement of maxillary anterior teeth and it was stated that the reason for the predominant maxillary anterior teeth replacement could be due to the aesthetic importance of these teeth which makes patients to promptly attempt to replace them [17].

The results of the study suggested that acrylic removable partial denture improved the oral health quality of life of the patients. This is in agreement with the findings of previous studies that reported improvement in quality of life of patients following insertion of RPDs [18, 19]. The prevalence of impact of partial edentulism (number of individuals with very/ fairly often responses) and the extent of impact (number of items reporting very/fairly often) was reportedly higher before insertion than after insertion of denture. This is contrary to the findings by Shekhawal *et al* of a slight decrease in prevalence (68.0% to 66.0%) but marked increase in extent of impact (17.8% to 41.2%) following the use of acrylic RPDs [20].

The decrease in prevalence and extent in this study implies that RPDs improved the quality of life of respondents by reducing the impact of their lost teeth. This improvement could be due to the fact that the majority of the respondents were more concerned about their appearance in the public, which was the reason why anterior teeth were replaced more than posterior teeth. So, it is possible that once the missing teeth are replaced, their morale is boosted even in the absence of their natural teeth. The same trend was noticed with the severity of impact of the partial edentulous state which reduced in all respondents following insertion of the RPDs. This is also contrary to the findings by Shekhawal *et al* in which the severity of impact increased following insertion of RPD [20]. Literature on impact of acrylic denture on quality of life of patient is scarce in this environment, so adequate comparison with other studies on the prevalence, extent and severity of impact could not be done. From these results the authors wish to promote the use of RPDs in rehabilitation of partial edentulous mouth and as a viable option especially in patients with missing anterior teeth.

When the OHIP domains were considered, there were improvements in all the domains except the physical pain domain contrary to the result of the study by Barreto et al., where the seven dimensions of its domains decreased after three months of wearing acrylic dentures [21]. This suggests that RPDs improved the various domains of OHIP. It wasn't clear why there was no improvement in the physical pain domain in our study. The fact that the greatest improvement was recorded with psychological disability confirms our view that majority of the respondents were possibly psychologically affected by the lost of their teeth, which drastically improved following the insertion of RPDs. This is in agreement with Jones *et al*., [22] who reported that dentures could improve facial appearance and social interactions of individuals, which enhanced self-esteem and thus contribute to psychological well-being. This is also in agreement with the report of improved appearance, psychological and social behaviour of an ectodermal dysplasia patient rehabilitated with acrylic RPD in our environment [19].

In this study, age and gender were analysed to determine whether they influenced the results of the use of denture in relation to patients' quality of life and it was observed that patients with age 65 years and above show better quality of life (lower mean sum-OHIP) than patients with age below 65 years before fitting of removable partial denture. This is in agreement with the hypothesis of Hagglin et al., [23] that older patients had a better acceptance of their state of oral health than younger patients. After the placement of denture, the older patients had a diminished quality of life. This could be because it is more difficult for older individuals to adapt to denture as wearing RPD demands emotional and functional adjustments [24]. The disproportionate distribution between the two age groups could also be contributory. The gender of the patients, however, has no influence on the result. Barreto et al., [21] reported similar findings as they observed no effect of gender as it relates to impact of denture on oral health related quality of life. Also, John et al., [25] reported no influence of age and gender on the impact of denture but the type of prosthesis, whether removable or fixed was found to influence the quality of life of partial edentulous patients.

Conclusion

The use of acrylic RPDs reduced the prevalence, severity and extent of impact of missing teeth on quality of life of partially edentulous patients and thereby improved their overall wellbeing, especially in patients who were less than 65years in age. Although acrylic RPD remains a valuable solution for partially edentulous patients, the authors suggest a more critical assessment of the elderly before prescribing acrylic RPDs for them.

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Changing trend of transitional cell carcinoma of the bladder in Ile-Ife, South Western Nigeria

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Abstract

Background: Recent studies from other parts of the world have reported a rising pattern of transitional cell carcinoma (TCC) amongst other histologic variants of bladder cancer.

Objective: To report the changing trend of TCC in our practice at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria.

Materials and methods: A retrospective review of clinical and pathological records of all bladder cancer cases managed between January 2006 and December 2015 in our hospital was done. Cases of TCC were identified, extracted and analyzed.

Results: A total of 38 histologically confirmed bladder cancers were seen during the study period. TCC accounted for 61% (23), Squamous cell carcinoma 16% (6), Adenocarcinoma 13% (5), while secondary bladder tumour from prostate cancer accounted for 10% (4).

Of the patients with TCC, mean age was 60 years ±13.4SD while the male to female ratio was 4:1. Ninety-five percent of them presented with haematuria. Risk factors identified in 57% of patients included smoking (43%) and industrial exposure to carcinogens (14%). Only 26% (6) of the TCC cases were non-muscle invasive while the remaining 74% (17) were muscle invasive. Eighty-seven percent (20) of the patients were treated while 13% (3) defaulted further treatment in our hospital after diagnosis. Among those treated in our centre, 30% (7) have had complete treatment with surgery and or chemotherapy and are presently on follow-up. Two patients (9%) have died, while 6 (26%) are still on treatment with intravesical chemotherapy. The remaining 8 patients (35%) have been lost to follow-up.

Conclusion: TCC is rising in proportion amongst other types of bladder cancer. It is the commonest bladder cancer seen associated with cigarette smoking and industrial exposure to carcinogens**.**

Keywords: *Transitional cell carcinoma (TCC), Changing trend, Ile-Ife, Nigeria.*

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Résumé

Contexte : Des études récentes dans d'autres parties du monde ont révélé une tendance à la hausse du carcinome à cellules transitionnelles (CCT) parmi d'autres variantes histologiques du cancer de la vessie.

Objectif : Pour rendre compte de la tendance changeante du CCT dans notre pratique au Complexe Hospitalier d'Enseignement Universitaire de l'Université Obafemi Awolowo (OAUTHC), Ile-Ife, Nigéria.

Matériels et méthodes : Un examen rétrospectif des dossiers cliniques et pathologiques de tous les cas de cancer de la vessie traités entre janvier 2006 et décembre 2015 dans notre hôpital a été effectué. Les cas de CCT ont été identifiés, extraits et analysés.

Résultats : Un total de 38 cancers de la vessie histologiquement confirmés a été observé au cours de la période de l'étude. Le CCT représentait 61% (23), le carcinome épidermoïde 16% (6), l'adénocarcinome 13% (5), tandis que les tumeurs de la vessie secondaires du cancer de la prostate représentaient 10% (4).

Parmi les patients atteints de CCT, l'âge moyen était de 60 ans ± 13,4 ans tandis que le rapport hommes-femmes était de 4 : 1. Quatre-vingt-quinze pour cent d'entre eux ont présenté une hématurie. Des facteurs de risque ont été identifiés chez 57% des patients et incluent le tabagisme (43%) et l'exposition industrielle aux carcinogènes (14%). Seuls 26% (6) des cas de CCT étaient non invasifs sur le muscle, alors que les 74% (17) restants étaient invasifs. Quatre-vingt-sept pour cent (20) des patients ont été traités, tandis que 13% (3) ont abandonné le traitement dans notre hôpital après le diagnostic. Parmi les personnes traitées dans notre centre, 30% (7) ont subi un traitement complet par chirurgie ou chimiothérapie et font actuellement l'objet d'un suivi. Deux patients (9%) sont décédés, tandis que 6 (26%) suivent toujours un traitement de chimiothérapie intra-vésicale. Les 8 patients restants (35%) ont été perdus de vue.

Conclusion : Le CCT augmente proportionnellement aux autres types de cancer de la vessie. Il s'agit du cancer de la vessie le plus courant associé au tabagisme et à l'exposition industrielle aux carcinogènes**.**

Mots-clés : *Carcinome à cellules transitionnelles (CCT), Évolution de la tendance, Ile-Ife, Nigeria.*

Introduction

Carcinoma of the bladder is the second commonest urological malignancy following prostate cancer in Nigeria [1,2]. It accounts for 6.2% of all cancer cases and the fourth most common in men [3]. Worldwide, transitional cell carcinoma (TCC) is the predominantly found histological type of bladder cancer most especially in the developed world were urbanization and industrialization have been postulated to play a major role [3]. Squamous cell carcinoma (SCC) of the bladder on the other hand was found to be commoner in the developing world, in areas exposed to schistosomiasis [1,4,5]. Earlier in the twenty first century, studies found SCC to be the commonest histological type of bladder cancer, however there appears to be a changing trend in recent times with a rising incidence of TCC of the bladder [2,6,7].

This report aims to show the changing pattern of bladder cancer in a tertiary center in South-west Nigeria.

Materials and method

A retrospective review of bladder cancer cases managed between Jan 2006 and Dec 2015 at Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife was done. Information extracted from clinical, pathological and cancer registry records and subsequently analyzed using Microsoft Excel 2016 included the demographic characteristic of the patients, bladder cancer histologic type, risk factors, ultrasound and cystoscopic findings, pathologic extent of invasion, type of treatment offered, and outcome.

Results

During the study period, there were 38 histologically confirmed bladder cancer cases. Transitional cell carcinoma accounted for 61% (23), squamous cell carcinoma 16% (6), adenocarcinoma 13% (5), while secondary bladder tumour from prostate cancer accounted for 10% (4). The mean age of the patients was 60±13.4SD with a range of 39-85 years. The male to female ratio was 4:1. Civil service accounted for 43% (10), 13% (3) patients were paint factory workers, other occupation are as shown in the Table 1. Ninety-five percent (22) of the patients presented with haematuria, 52% (12) with irritative lower tract symptoms, 21% (4) with fever, 36% (8) with weight loss, while 30% (7) had palpable abdominal mass at presentation. Risk factors identified in 57% (13) of all the patients with TCC included smoking in 43% (10), while 14% (3) were paint factory workers. Only 26% (6) of TCC were non-muscle invasive while the remaining 74% (17) were muscle invasive. Eighty-seven (20) of the patients with TCC were treated while 13% (3) defaulted further treatment in our hospital after diagnosis. Among those treated in our centre, 30% (7) have had complete treatment with surgery and or chemotherapy and are presently

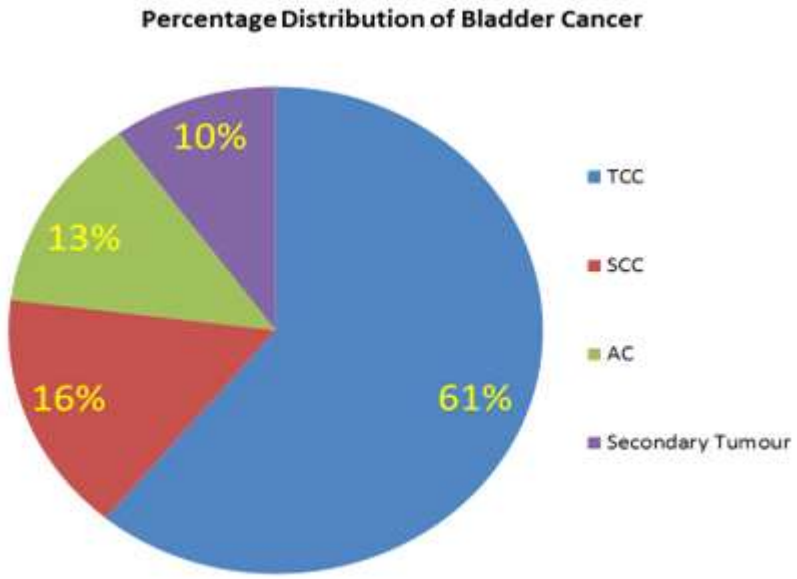

Fig. 1

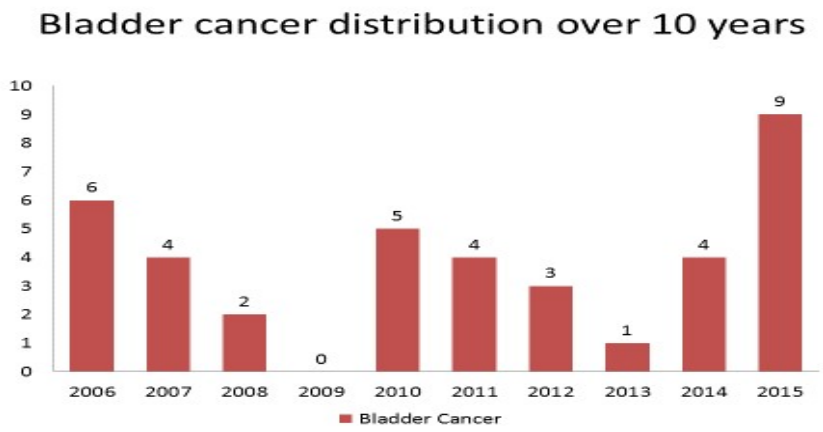

Fig. 2

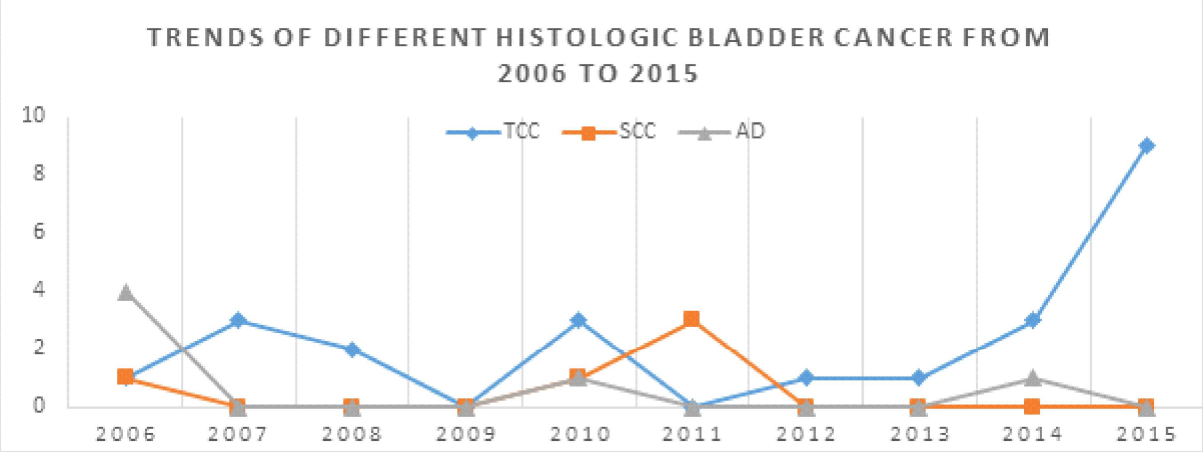

Fig. 3

Table 1:

Occupation

Occupation	n(%)
Civil Service	10(43)
Paint factory work	3(13)
Trading	4(18)
Driving	3(13)
Farming	3(13)

Table 2:

Presentation

Presentation	n(%)
Haematuria	22(95)
Irrtative LUTS	12(52)
Fever	4(21)
Weight loss	8(36)
Palpable suprapubic mass	7(30)

on follow-up. Two patients (9%) died, while 6 (26%) are still on treatment with intravesical chemotherapy. The remaining 8 patients (35%) have been lost to follow-up.

Table 3:

Outcome	
– Alive and on follow-up	7 (30%)
– Still on treatment	6 (26%)
– Died	2 (9%)
– Defaulted	8 (35%)

Discussion:

There were three peak incidence of bladder cancer observed during the study duration, with the highest being in 2015. Adenocarcinima and SCC respectively were majorly responsible for the two earlier peaks while TCC was not only responsible for the peak in 2015 but the sole histologic type seen throughout the year. Thus, our study has shown that TCC is currently on the increase as compared to other histologic types of bladder cancer.

TCC accounted for 61% of all bladder cancer cases in this study. Anunobi *et al* [8] in Lagos and Goonewardena *et al* [9] in Sri Lanka respectively reported that TCC accounted for 61% and 93.4% of all bladder cases in their studies. Similar observations on TCC has been documented in some other parts of Nigeria, as well as China, and in most of the series it has been attributed to environmental exposure to carcinogens from smoking, as well as increasing industrialization and urbanization [10-12]. In fact, similar surge in TCC is also being experienced in some schistosomiasis endemic regions where SCC used to be the most predominant bladder cancer [13]. This has been linked to increasing smoking habit, and growing industrialization and urbanization.

The mean age in our study was 60±13.4SD. Similarly, Anunobi *et al* [8] in their study done in Lagos, Nigeria, found a mean age of 59 years, while Lam KY *et al* found a mean age of 69 years in their study done among Chinese [11]. Hence, these are in tandem with the fact that the incidence of TCC is higher among older people due to latent period of exposure to carcinogen [12,14].

We found a male preponderance of TCC with sex ratio of 4:1 in our study. A male-female ratio of 5:1 had been reported in Lagos, Nigeria, while a study in Sri Lanka also showed male preponderance with a sex ratio of 6:1. Therefore, similarity in all these findings may be suggesting sex-linked etiological factors [9,15,16]. In these regions, cigarette smoking is commoner among men than women [17]. Also, many of the industrial workers are males as many females may be made full-time housewives and therefore not be permitted to work [18]. In this study, smoking accounted for 43% of identified risk factors. El-Mawla *et al* [16] in Egypt and Kunze *et al* [19] in Germany also found smoking, which accounted for over 50% of cases, as the single most common risk factor in their studies.

Thirteen percent (13%) of patients with bladder cancer were paint factory workers, hence they could have been exposed to carcinogens in the paint [20,21]. Similar studies in literature have coated different relative risks for paint exposure as a risk factor for TCC of the bladder [22,23].

The most common presentation was haematuria found in 95% (22) of the TCC patients in this study. Similarly, haematuria was the presenting symptom of urothelial malignancy in 90% of cases in Sri Lanka [9,24]. Similar finding has been documented in other studies [24-26]. This means haematuria as a predominant presentation of TCC of the bladder has no racial or regional preference. In this present series, the finding of predominantly muscle-invasive carcinoma (74% Vs 26%) of the bladder was due to late presentation which is usually the pattern in developing countries. About half of all bladder cancers in Sri Lanka were found to be muscle invasive [25]. Similar results have been documented in many developing countries [16,27]. In contrast, only approximately 20% of newly diagnosed bladder cancers in developed countries have muscle invasion at initial presentation [25]. This difference could be attributed to the established screening programmes, early presentation, early diagnosis, and prompt intervention which are known with developed nations.

Intravesical immuno- and chemotherapy, surgery, and systemic chemotherapy are all critical elements in our management of patients with TCC of the bladder. Majority of the patients presented with advanced and inoperable tumours. Hence, it is needful to state that 87% of the patients accepted treatment of which 52% had intravesical and systemic

chemotherapy with 30% of them had complete treatment and are being followed up in our outpatient clinic with regular abdominopelvic ultrasound scan coupled with surveillance cystoscopy. Twenty-six percent of the patients are still presently on treatment. One of the 2 patients who had TURBT and one of the 2 patients who had radical cystectomy died during the course of follow-up as a result of medical conditions not related to surgery. Careful selection of patients for specific treatment option is of paramount importance in a low resource centre like ours whereby patients also present late with advanced tumours.

Conclusion

TCC is rising in proportion amongst other types of bladder cancer. It is the commonest bladder cancer seen associated with cigarette smoking and industrial exposure to carcinogens. The cessation of smoking and primary prevention need to be emphasized.

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Evaluation of the possible mechanisms involved in the anti-inflammatory and anti-nociceptive properties of Jobelyn® in laboratory rodents

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Abstract

Background: Jobelyn (JB)® is a product derived from Sorghum bicolor. For several centuries, the people of Southwestern part of Nigeria have used this plant in its raw form to treat and cure many diseases. Previous studies have suggested JB efficacy in the treatment of pain, hence, the need for the exploration of its probable mechanism of its action. This study was undertaken to evaluate the mechanism of action through which JB exerts its anti-nociceptive and anti-inflammatory activities in rodents.

Materials and methods: The administration of naloxone, prazosin and atropine (1 mg/kg, intraperitoneally) to groups of mice using acetic acid-induced abdominal writhing and formalin-induced paw licking tests were done to investigate the anti-nociceptive mechanism of action of JB. Animals were divided into six groups comprising of six mice in each experiment; two groups were orally administered normal saline (1ml/200g b.w) and indomethacin (2 mg/kg) respectively, while the remaining four groups were pre-treated intraperitoneally with the blockers followed by administration of JB (100 mg/kg). Hematoxylin and Eosin (H&E) staining and immunohistochemical analysis of rat paw tissues in carrageenan-induced hind paw edema in rats was used to analyze the level of inflammation.

Results: Atropine significantly reversed the anti-nociceptive effects of Jobelyn® (100mg/kg) when compared with Jobelyn® in acetic acid-induced abdominal writhing test. In the formalin-induced paw licking test, the pre-treatment with the blockers showed no significance when compared with Jobelyn® group. Jobelyn (10, 50, 100, and 200mg/kg) given orally, produced a significant inhibition of acute inflammation induced by carrageenan in rat paws, from which 100 mg/kg JB shows higher activity. The results from H&E staining and immunohistochemical analysis showed that JB considerably reduced the infiltration of inflammatory cells in the paw tissues.

Conclusions: Jobelyn® has both analgesic and anti-inflammatory property, and its analgesic effect may be mediated through the cholinergic system.

Keywords: *Cholinergic system; Opioidergic system; Jobelyn; Pain; Inflammation.*

Résumé

Contexte : Jobelyn (JB) ® est un produit dérivé du Sorgho bicolore. Pendant plusieurs siècles, les habitants du sud-ouest du Nigéria ont utilisé cette plante sous sa forme brute pour traiter et soigner de nombreuses maladies. Des études antérieures ont suggéré l'efficacité de JB dans le traitement de la douleur, d'où la nécessité d'explorer son mécanisme probable d'action. Cette étude visait à évaluer le mécanisme d'action par lequel JB exerce ses activités anti-nociceptives et anti-inflammatoires chez les rongeurs.

Matériels et méthodes : L'administration de naloxone, de prazosine et d'atropine (1 mg / kg, par voie intrapéritonéale) à des groupes de souris utilisant des tests d'aberration abdominale induite par l'acide acétique et de léchage de la patte au formol a été réalisée afin d'étudier le mécanisme anti-nociceptif de l'action de JB. Les animaux ont été divisés en six groupes comprenant six souris dans chaque expérience ; deux groupes ont reçu par voie orale une solution saline normale (1 ml / 200 g de poids) et de l'indométacine (2 mg / kg), tandis que les quatre groupes restants ont été prétraités par voie intrapéritonéale avec les inhibiteurs, puis par l'administration de JB (100 mg / kg). La coloration à l'hématoxyline et à l'éosine (H & E) et l'analyse immunohistochimique des tissus de la patte de rat dans l'œdème de la patte postérieure induite par le carraghénane chez le rat ont été utilisés pour analyser le niveau d'inflammation.

Résultats : L'atropine a significativement inversé les effets anti-nociceptifs de Jobelyn ® (100 mg / kg) par rapport au Jobelyn ® dans le test de résistance abdominale induit par l'acide acétique. Dans le test de léchage de pattes induit par le formol, le prétraitement avec les inhibiteurs n'a montré aucune

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signification par rapport au groupe Jobelyn ®. Jobelyn (10, 50, 100 et 200 mg / kg) administré par voie orale a provoqué une inhibition significative de l'inflammation aiguë induite par le carraghénane dans les pattes de rat, à partir de laquelle 100 mg / kg de JB présentaient une activité supérieure. Les résultats de la coloration H & E et de l'analyse immunohistochimique ont montré que le JB réduisait considérablement l'infiltration de cellules inflammatoires dans les tissus de la patte.
Conclusions : Jobelyn ® possède à la fois des propriétés analgésiques et anti-inflammatoires et son effet analgésique peut être véhiculé par le système cholinergique.

Mots-clés: *Système cholinergique; Système opioïdergique ; Jobelyn ; Douleur ; Inflammation.*

Introduction

Inflammation is considered an immunological defense mechanism that is elicited in response to mechanical injuries, burns, microbial infections, allergens and other noxious stimuli [1]. It also establishes memory that enables the host to build up a quicker and more exact response on an upcoming encounter, which leads ultimately to the restoration of tissue structure and function [2, 3].

Inflammation and pain are usually managed with non-steroidal anti-inflammatory drugs (NSAIDs) [4]. However, in chronic pain conditions, NSAIDs are used for a prolonged time which ultimately leads to severe toxicities including gastric and renal adverse effects [5]. Many natural products are being used in traditional medical systems and practices to treat pain and inflammation symptoms [6]. The search for new analgesics and anti-inflammatory agents is currently the subject of intense drug company interest. However, the possibility of getting such drugs with no or ignorable side effects, being also affordable, will help ignite hope in the lives of a great number of the population.

Jobelyn (JB)® is an African sorghum-based food supplement and one of the fastest selling herbal medicines in Nigeria with most pharmaceutical outlet being used as the distribution channels. It is available as a powdered preparation formulated into capsule and suspensions. It has been reported to possess anti-nociceptive and anti-inflammatory activities [7, 8], but the exact mechanism is yet to be elucidated. Hence, this research investigated the probable mechanisms through which JB exert its anti-nociceptive and anti-inflammatory actions, exploring the adrenergic, cholinergic and opioidergic systems.

Materials and methods

Chemicals and reagents

The chemicals and reagents include: carrageenan, indomethacin, acetic acid, formalin, atropine, prazosin, naloxone hydrochloride dehydrate (Sigma Chemical Company), normal saline, distilled water (obtained from our laboratory), and Jobelyn® (Health Forever Products Ltd, Lagos, Nigeria) were used in this study. The drugs were dissolved in normal saline before administration. The doses of 10, 50, 100 and 200 mg/kg of JB used in the study were selected based on the results obtained from preliminary investigations.

Experimental animals

Swiss mice weighing (25-30g) and Wistar rats weighing (150-170g) were used for this study. They were purchased, housed and bred at the Pre-Clinical Animal House, Faculty of Basic Medical Sciences, College of Medicine, University of Ibadan, Ibadan, Nigeria where this study was carried out. Animals were housed in cages under a 12-hour light/12-hour dark cycle (8:00 a.m. - 8:00 p.m.) at 27±5°C and 50%–65% relative humidity environment. They were acclimatized for 2 weeks with unrestricted access to food and water before the experiment. All the experimental protocols complied with the Principle of Laboratory Animal Care (NIH publication No. 85-23) guidelines [9].

In vivo anti-nociceptive and anti-inflammatory test of Jobelyn®

Acetic-acid induced writhing test in mice

This test was carried out using the modified method [10] with slight modification. Animals were pre-treated for 7 days before the experiment. Jobelyn® (10, 50, 100 and 200 mg/kg, p.o.), indomethacin (2 mg/kg, p.o.) and normal saline (10 mg/kg, p.o.) were administered for 6 days, followed by a 16 hour fast till the 7th day. One hour after pre-treatment on the 7th day with JB, indomethacin and the vehicle, mice were given intraperitoneal injection of 0.2ml of 3% acetic acid solution to induce characteristic writhing. The number of writhing occurring post-injection was recorded. Indomethacin (2 mg/kg) was used as a standard drug. Naloxone (1 mg/kg, i.p), prazosin (1 mg/kg, i.p), and atropine (1 mg/kg, i.p), were administered to separate groups of animals for the mechanisms of action of antinociception.

Formalin-Induced Paw licking test in mice

The formalin test [11] was used according to the modifications of the test for mice by [12, 13]. Animals were pre-treated as stated above. Jobelyn

(100 mg/kg, p.o.), indomethacin (2 mg/kg, p.o) and normal saline (1ml/200g, b.w, p.o.) were administered to the animals. Sixty minutes after the administration of JB, indomethacin or normal saline on the 7th day, 20µl of 1% formalin was injected just under the skin of the dorsal surface of the right hind paw using a micro syringe. The time the mice spent licking the injected area was recorded for 0–5 min (early phase) and 15–30 min (late phase) post-formalin injection. Nociceptive behavior was quantified by counting the incidents of spontaneous biting/licking of the injected paw [14]. Three separate groups were also pre-treated with naloxone (1 mg/kg, i.p), prazosin (1 mg/kg, i.p), and atropine (1 mg/kg, i.p) 30 mins before administration of JB (100 mg/kg), followed by formalin administration 60 mins later.

Carrageenan-induced paw edema in rats

Anti-inflammatory activity was evaluated on the basis of inhibition of carrageenan-induced rat hind paw edema [15, 16]. Six groups of six rats each were used in this experiment. Four groups received JB (10, 50, 100 and 200mg/kg, p.o). The remaining two groups received indomethacin (2mg/kg, p.o) and normal saline (1ml/200g, b.w, p.o) as positive and negative controls, respectively. Animals were pre-treated 7 days with the drugs before the administration of carrageenan. A dose of 0.05 ml of 1% freshly prepared carrageenan suspension in normal saline was injected into the sub-plantar surface of the left hind paw of each rat, 60 minutes after the oral administration of the test substances, the standard and the vehicle. The volumes of injected paws were measured before and at 0, 1, 2, 3, 4, 5 and 24 hr after the injection of carrageenan using plethysmometer (Ugo Basile, Italy). Twenty- four hours after carrageenan injection, the rats were sacrificed by cervical dislocation and the soft paw tissues were excised for H&E staining, histological and immunohistochemical analyses.

Mechanisms of action of Jobelyn®

To investigate the probable mechanism through which *Jobelyn® (JB)* inhibits formalin-induced nociception and acetic acid-induced abdominal writhing tests, animals were divided into six groups each comprising of six mice in each experiment; two groups were orally administered normal saline (10mg/kg) and indomethacin (2 mg/kg) respectively, while the remaining four groups were pre-treated intraperitoneally with 1 mg/kg body weight of naloxone (a non-selective opioid receptor antagonist), atropine (an adrenergic receptor antagonist) and prazosin (a cholinergic receptor antagonist). After 30 minutes, the animals received *JB* (100 mg/kg, p.o.). The nociceptive response to the formalin intraplantar injection (20 µL of 1% formalin) and the number of writhes in acetic acid-induced abdominal writhing test was recorded 60 mins after administration of *JB*.

Immunohistochemistry

Immunohistochemistry of COX-2 was carried out according to the method of Salvemini and co-worker (1995). Slides of samples were de-paraffinized in xylene twice for 5 minutes each. The slides were later transferred to 100% alcohol twice for 3 minutes each. They were then passed through 95% alcohol (twice) and 70% alcohol (once), respectively for 3 minutes each. They were later rinsed with wash buffer twice for two minutes each.

Antigen retrieval was performed to unmask the antigenic epitope. The method used was the citrate and EDTA buffer method. This was done by pouring 300ml of 10mM citrate pH 6.0/EDTA pH 9.0 buffer into the staining container and incubated at 95-100^{0}C for 5 minutes. The slides were arranged in a staining hanger and dipped into the pre-heated buffer and incubated for 10-20 minutes in the water bath. Then the staining container was removed to room temperature and the slides were allowed to cool for 20 minutes. Then, the slides were rinsed with wash buffer twice for 5 minutes each.

Blocking buffer [3% hydrogen peroxide (H_20_2)] into the sections of the slides and incubated in a humidified chamber at room temperature for 15 minutes. The blocking buffer was then drained off from the slides and the slides were washed in wash buffer.

130µl of appropriately diluted primary antibody was applied to the sections of the slides and incubated in a humidified chamber at room temperature for an hour. The slides were washed again with wash buffer twice for 5 minutes each.

130µl of appropriately diluted biotinylated secondary antibody was applied to the sections of the slides and incubated in a humidified chamber at room temperature for 30 minutes. The slides were later washed with wash buffer twice for 5 minutes each.

130µl of appropriately diluted Sav-HRP conjugates were applied to the sections on the slides and incubated in a humidified chamber at room temperature for 30 minutes and kept protected from sunlight. The slides were later washed with wash buffer twice for 5 minutes each.

130µl DAB substrate solution was applied to the sections of the slides to reveal the colour of the antibody staining. The colour was allowed to develop for about 5 minutes so that the desired colour intensity would be reached. The slides were then washed in phosphate buffer solution (PBS) three times for 2 minutes each.

The slides were then counterstained by immersion of slides in Hematoxylin for about 20 seconds. The slides were then rinsed in running tap water for 10 minutes. The tissue slides were then dehydrated through alcohol 4 times of different concentrations each (95%, 95%, 100% and 100%), 5 minutes each. The tissue slides were cleared in coverslips and xylene using mounting solution. The mounted slides were stored at room temperature. The colour of the antibody staining in the tissue sections were then observed under microscopy.

Statistical analysis

Data were expressed as Mean ± Standard Error of Mean (SEM) and analyzed by One-way analysis of variance (ANOVA), followed by Newman-Keul's multiple comparison post-hoc test using Prism Software Version 5 (GraphPad Software Inc., San Diego, CA, USA). $P<0.05$ was considered significant.

Results

Effect of Jobelyn® on acetic acid-induced abdominal writhing in mice

The effect of Jobelyn® on acetic acid-induced abdominal writhing in mice is shown in figure 1. The pre-treatment of animals with naloxone and prazosin each did not significantly decrease or increase the number of writhes produced by Jobelyn. However, the pre-treatment of mice with atropine significantly ($p<0.001$) increased the number of writhing activities of Jobelyn.

Effect of Jobelyn® on formalin-induced paw licking test in mice

The mechanism of action of the anti-nociceptive activity of Jobelyn® on formalin-induced paw licking test is shown in figure 2 below. The result shows that the blockers (naloxone, atropine and prazosin) have no significant difference when compared with Jobelyn®.

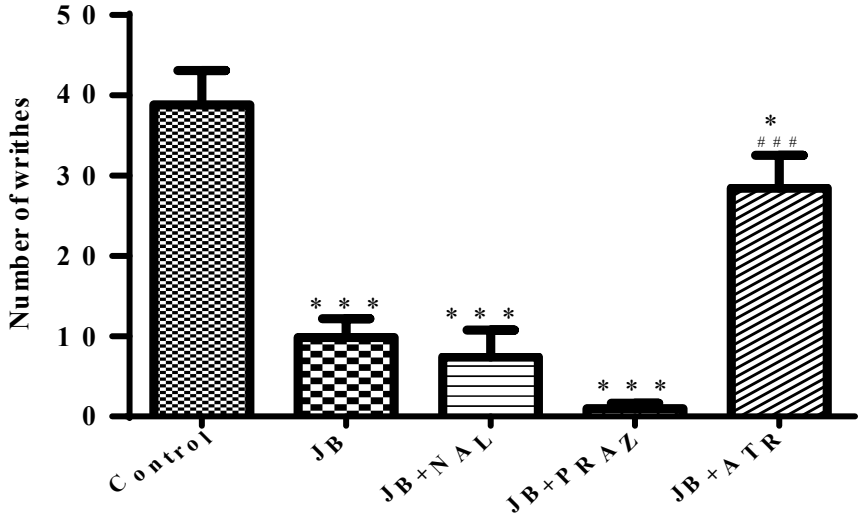

Figure 1: Effects of pre-treatment of opioid, adrenergic and cholinergic receptor blockers on the anti-nociceptive effect of Jobelyn® (100mg/kg) on acetic acid-induced abdominal writhing test in mice. Data is expressed as Mean ± SEM (n=5). Comparisons were made using One-way ANOVA followed by Newman-Keul's multiple comparison tests. *P<0.05, ***P<0.001 compared with the control group; ###P<0.001 compared to JB group. JB- Jobelyn®; NAL-Naloxone; PRAZ- Prazosin; ATR-atropine.

Histological analyses of rat paw tissues in carrageenan-induced hind paw edema in rats

Samples of paw tissue from each experimental group were examined by Hematoxylin and Eosin (H&E) staining. The injection of carrageenan into the paw of rats recruits inflammatory cells to the site of injection. However, the infiltration of inflammatory cells was significantly decreased with pre-treatment

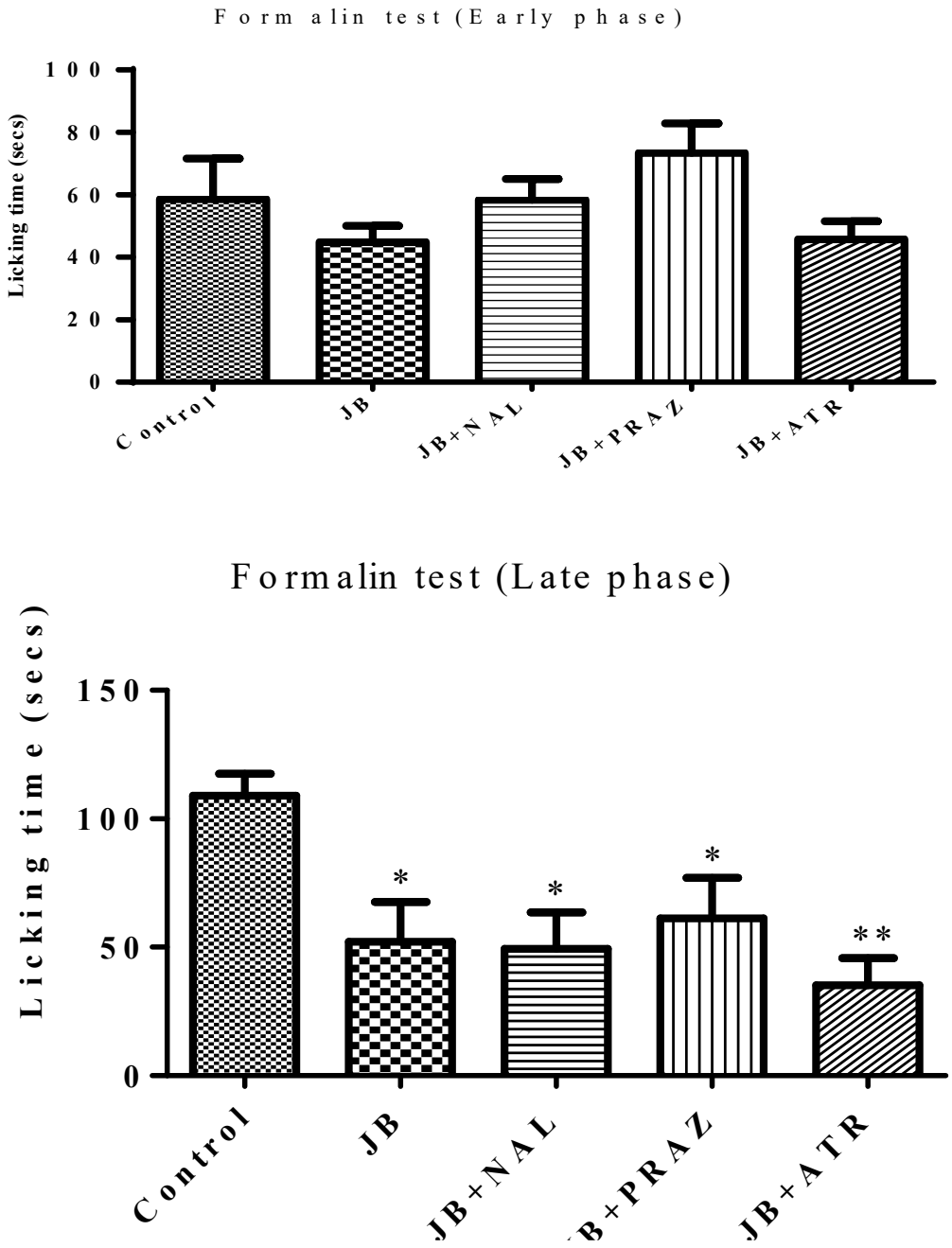

Fig.2: Effects of pre-treatment of opioid, adrenergic and cholinergic receptor blockers on the anti-nociceptive effect of Jobelyn (100mg/kg) in formalin-induced paw licking test in mice. Data is expressed as Mean ± SEM (n=5). Comparison was made using One-way ANOVA followed by Newman-Keul's multiple comparison tests. *P<0.05, **P<0.01 compared with the control group. JB- Jobelyn®; NAL- Naloxone; PRA- Prazosin; ATR- atropine.

of Jobelyn® (10, 50, 100 and 200 mg/kg) and indomethacin (2mg/kg), for 7 days.

Immuno-histochemical analyses of rat paw tissues in carrageenan-induced hind paw edema in rats.

Plate 2 shows the photomicrographs of the immunohistochemistry COX-2 from the samples of paw tissues from each experimental group.

Discussion

This study evaluated the pharmacological mechanism by which Jobelyn® exerts its anti-nociceptive and anti-inflammatory activities by investigating the involvement of opioidergic, adrenergic and cholinergic pathways. The anti-edematogenic and anti-nociceptive effects were analyzed using different agents including, acetic acid,

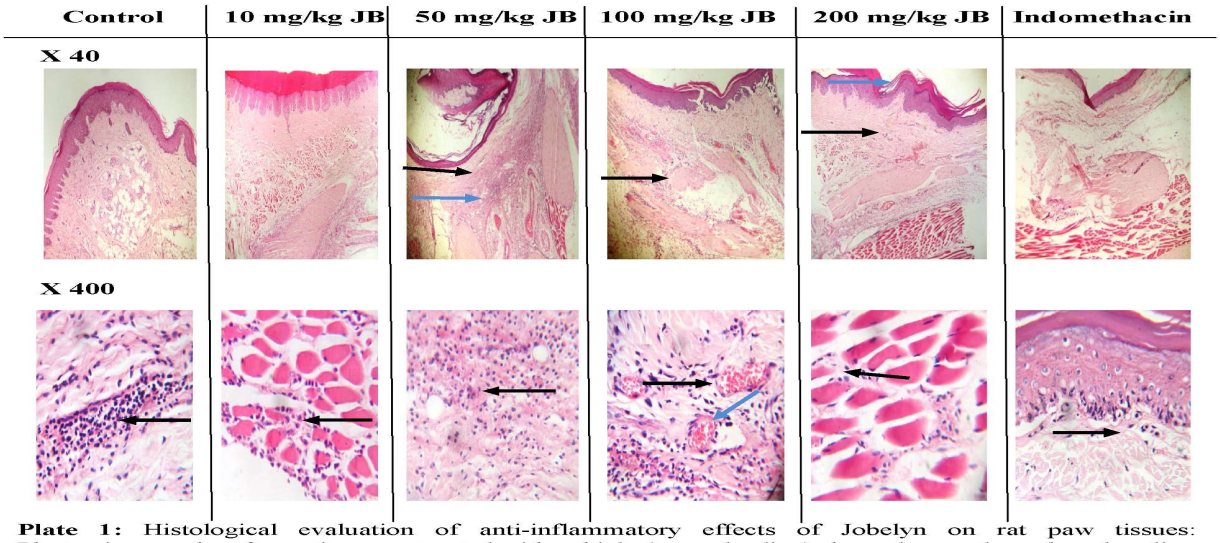

Plate 1: Histological evaluation of anti-inflammatory effects of Jobelyn on rat paw tissues: Photomicrographs of paw tissue pretreated with vehicle (normal saline) showed normal rough and scaling appearance of epidermal layer and moderate chronic inflammation (slender arrow) of subcutaneous layer (X40 and X400). Normal epidermal layer and moderate inflammatory infiltrates into muscle (slender arrow) and subcutis layers (black arrow) was observed in group pretreated with 10 mg/kg JB. Groups pretreated with 50 mg/kg JB showed chronically diffused inflammatory cells in the dermal layer (black arrow), mild angiogenesis with congestion (blue arrow) of blood vessels and the muscle layer is severely infiltrated by inflammatory cells (slender arrow). The paw tissue of 100 mg/kg JB showed moderate inflammatory infiltrates to subcutis (black arrow) and muscle layer (blue arrow). 200 mg/kg JB showed rough and scaling appearance of epidermal layer (blue arrow), mild angiogenesis (black arrow) and mild inflammation (slender arrow) of attached smooth muscle. Photomicrographs of paw tissue showed mild inflammation (slender arrow) of dermal layer, moderate inflammation (black arrow) of attached smooth muscle and moderate inflammation of subcutis layer.

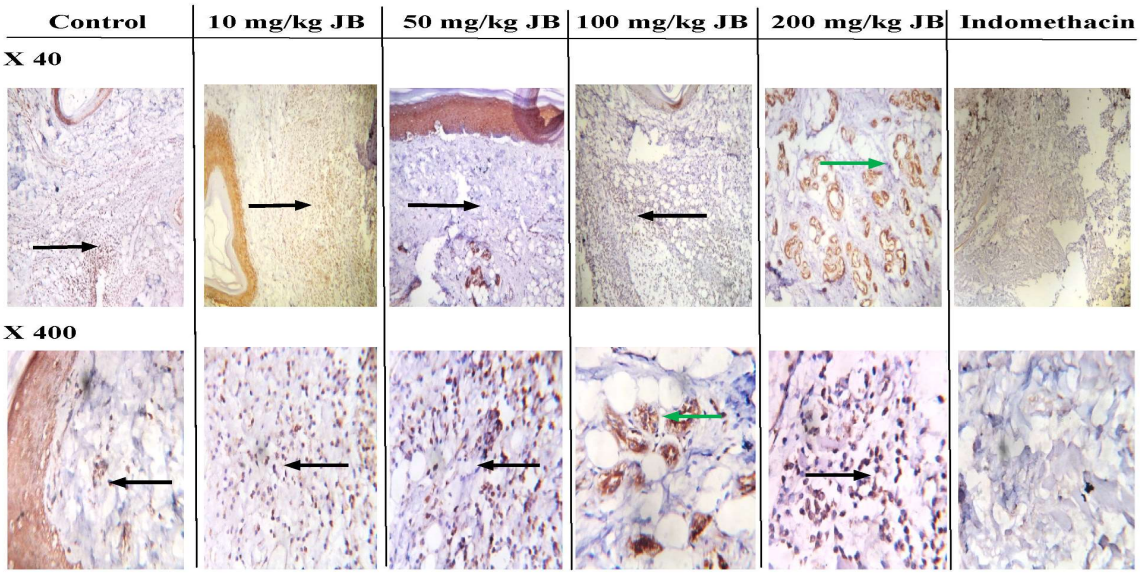

Plate 2: Immuno-histological evaluation of rat paw tissue: Photomicrographs of skin Immunohistochemistry COX 2 pretreated with normal saline showed Strongly COX positive cells (+++); Mildly COX positive cells (+) with group pretreated with 10mg/kg JB; Moderately COX positive cells (++) in 50 mg/kg JB group. Group pretreated with 100 mg/kg and 200 mg/kg JB showed Moderately (++) and strongly COX positive cells (+++) with the presence of blood vessels respectively. The Photomicrographs of skin Immunohistochemistry COX 2 in Indomethacin group was Negative.

formalin and carrageenan in acetic acid-induced writhing, formalin-induced paw licking and carrageenan-induced hind paw edema models.

The acetic acid-induced writhing test is used for screening peripheral anti-nociceptive effects of test compounds, and it is considered to be a visceral pain model where the stimulation of nociceptive neurons by liberation of mediators such as histamine, serotonin, cytokines, and eicosanoids in the peritoneal fluid, produces writhing responses related to the

development of peripheral inflammation. Pain transmission is a complex mechanism that involves interaction of peripheral and central structures, and different modulatory pathways [17]. It stimulates central pain by the activation of mitogen-activated protein (MAP) kinases and microglia in the spinal cord [18, 19]. It also modulates central pain via a number of complex processes including opiate, dopaminergic, descending noradrenergic and serotonergic systems [20]. The mechanism of action of Jobelyn® in acetic acid-induced test revealed the involvement of the cholinergic system in the analgesic effect of Jobelyn® which showed that pre-treatment of mice with atropine, a cholinergic receptor antagonist; significantly reversed Jobelyn®.

The formalin test was selected for this study, since it is more specific and it is possible to identify two distinct phases of nociception [21, 22] and it also reflects different pathological processes and it allows the elucidation of the possible mechanism involved in analgesia. In this study, formalin was observed to elicit biphasic pain episodes, the first phase (neurogenic pain) and second phase (inflammatory pain). The neurogenic pain is centrally mediated and it is attributed to the direct stimulation of the nociceptive primary afferent fibers. The inflammatory pain is peripherally mediated and it is due to peripheral release of chemical pain mediators that sensitize or activate nociceptors. The peripherally acting analgesic drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) are only effective against inflammatory pain produced by formalin. In contrast, the centrally acting analgesic drugs such as opioids inhibit both the neurogenic and inflammatory pains caused by formalin [23]. The result obtained in the formalin-induced paw licking model was able to ameliorate the pain sensation induced by formalin and shows higher potency in suppressing the inflammatory pain associated with the second phase due to its strong anti-inflammatory activity [8]. Jobelyn® co-administered with the blockers (naloxone, prazosin and atropine) in this model showed no significant antagonistic effect in both early and late phases.

Pain is a hallmark of inflammation process. So, the evaluation of the activity induced by Jobelyn® in inflammatory pain is an interesting point to be evaluated. Inflammation is a complex process, which is mostly associated with pain and involves several events, such as increase of vascular permeability, increase of granulocytes and mononuclear cells migration, as well as the granulomatous tissue proliferation. Anti-inflammatory compounds or agents can act on many steps of pathophysiological process. It is possible for a compound to block the biosynthesis of pro-inflammatory mediators by direct interaction with a key enzyme (e.g. inhibition of COX-2) or by decreasing enzyme expression (e.g. steroidal anti-inflammatory compounds) or by reducing substrate levels (e.g. decrease of arachidonic acid releasing prostaglandins). In addition, a compound can either act by inhibiting the release of pre-formed stored mediators (e.g. histamine release) or by blocking mediator-receptor interaction on target cells (e.g. histamine receptor antagonists). An anti-inflammatory compound may also act through immune-stimulation (e.g. maturation of myeloid cells or stimulation of phagocytosis) that in turn promotes an increase removal of the insulting signal molecules, which results in a less aggressive inflammatory response to allergen challenge [24].

Carrageenan-induced hind paw edema in rat is an experimental animal model for acute inflammation and it includes three distinct phases. The release of histamine and serotonin in the first phase (0-2 hour), kinins in the second phase (2-3 hour) and prostaglandin in the third phase (3-4 hour) [25]. The late phase is sustained by prostaglandin release [26]. So, the present study employed the use of carrageenan-induced paw edema model, which is the most widely used primary test for the screening of new anti-inflammatory agents [16]. From the result obtained from the anti-nociceptive experiment above, the level of significance of Jobelyn® was determined to be effective at 100 mg/kg. The result from the carrageenan-induced paw edema test was found to significantly decrease the edema by inhibiting the mediators of acute inflammation.

Histological study indicated that carrageenan-induced inflammation is linked to intense edema characterised by increased migration and infiltration of inflammatory polymorphonuclear leukocyte (PMN) cells, mainly neutrophils, in the inflamed paw tissues [13]. From our result, it was observed that Jobelyn® significantly decreases the severe edema formation and the elevated level of cellular infiltration in rat paw tissues. This study indicates that carrageenan affects the muscle contraction function and causes edematous muscle, thus, resulting to muscle weakness. However, this myotis symptoms observed in carrageenan-induced paw edema was significantly inhibited by the administration of Jobelyn®, thus, showing a normal musculature or muscle architecture [15].

Conclusion

In conclusion, the results of this study suggest that cholinergic and adrenergic pathways may be involved in the anti-nociceptive activity of Jobelyn®. Also, Jobelyn® down-regulated COX-2 expression in the inflamed paw of rat, indicating inhibition of prostaglandin biosynthesis and playing a vital role in its anti-inflammatory activity.

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Sociodemographic determinants of childhood male circumcision by traditional practitioners in a rural Nigerian town

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Abstract
Introduction: Circumcision, often associated with adverse effects, is performed by medical personnel and traditional circumcisers in Africa, with higher complication rate when performed by the latter. The aim of the study was to evaluate the sociodemographic determinants of seeking for male circumcision in childhood by a traditional practitioner.
*Materials and methods***:** This was a cross-sectional study conducted in Igbo Ora, a rural community, in Southwest Nigeria between April and September 2017. One mother was selected from each enumerated household using multi-staged sampling technique and information obtained with interviewer-administered questionnaires.
Results: A total of 317 participants were recruited with a median age of 40.0 years. The majority were Yoruba (290, 91.5%), Muslims (198, 62.5%) and unskilled workers (244, (77.0%). All had one or more sons circumcised; the last was by: doctors (28, 8.8%), nurses (214, 67.5%) or traditional circumcisers (75, 23.7%). A traditional circumciser was more often involved when mother was Yoruba, less educated, unskilled worker, baby delivered at government hospital/home, when circumcision was done long ago or has multiple sons ($p < 0.001$). The determinants of involvement of a traditional circumciser were: tribe (OR = 20.83, 95% CI: 2.42, 166.67, p = 0.006), education (OR = 34.48, 95% CI: 8.20, 142.86, $p < 0.001$), occupational class (OR = 8.11, 95% CI: 1.32, 49.80, p = 0.024) and how recent circumcision was (OR = 2.96, 95% CI: 1.41, 6.24, p = 0.004).
Conclusion: Tribe, education and occupational class are factors that determine patronage of traditional circumcisers.

Keywords: *Circumcision; predictors; rural; sociodemographic determinants; traditional*

Résumé
Introduction: La circoncision, souvent associée à des effets indésirables, est pratiquée par le personnel médical et les exciseurs traditionnels en Afrique, avec un taux de complication plus élevé lorsqu'elle est réalisée par ce dernier. Le but de l'étude était d'évaluer les déterminants sociodémographiques de la recherche de la circoncision masculine dans l'enfance chez un praticien traditionnel.
Matériels et méthodes **:** Il s'agit d'une étude transversale menée entre avril et septembre 2017 dans la communauté rurale d'Igbo Ora, dans le sud - ouest du Nigéria. Une mère a été sélectionnée dans chaque ménage énuméré en utilisant la technique d'échantillonnage en plusieurs étapes et l'informations obtenues à l'aide de questionnaires administrés par intervieweurs.
Résultats : Un total de 317 participants a été recruté avec un âge médian de 40,0 ans. La majorité était composée de Yoruba (290 ; 91,5%), de musulmans (198 ; 62,5%) et de travailleurs non qualifiés (244 ; 77,0%). Tous avaient un ou plusieurs fils circoncis, le plus moins par : les médecins (28, 8,8%), les infirmières (214, 67,5%) ou les exciseurs traditionnels (75, 23,7%). Les exciseurs traditionnels étaient plus souvent impliqués lorsque la mère était yoruba, travailleuse non qualifiée, peu instruites, et accouchées à l'hôpital du gouvernement / à la maison, lorsque l'excision était pratiquée il y a longtemps ou a plusieurs fils ($p < 0,001$). Les déterminants de l'implication d'un exciseur traditionnel étaient : la tribu (OR = 20,83, IC 95%: 2,42, 166,67, p = 0,006), éducation (OR = 34,48, IC 95%: 8,20, 142,86, $p < 0,001$), classe professionnelle (OR = 8,11, IC 95%: 1,32, 49,80, p = 0,024) et comment récente était la circoncision (OR = 2,96, IC 95%: 1,41, 6,24, p = 0,004).
Conclusion : La tribu, l'éducation et la classe professionnelle sont des facteurs qui déterminent le patronage des exciseurs traditionnels.

Mots - clés: *circoncision ; prédicteurs ; rural; déterminants sociodémographiques ; traditionnel*

Introduction

Male circumcision is one of the most often performed surgical procedures worldwide [1]. The procedure dates back to centuries and it is undertaken by surgically trained as well as untrained personnel. Circumcision, which had been associated with some controversies on account of its safety and benefits

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compared to retaining the prepucial skin, has gained more support with the evidence that it offers some protection against the HIV pandemic in high prevalence regions of Africa [2-4].

There are still concerns about the safety of the procedure because of serious complications reported in 0.2% to 33.7% [5-8]. These adverse events include post circumcision bleeding, redundant prepuce, urethrocutaneous fistula and glanular amputation among others [7,9,10]. The prevalence of complications is reported to be higher when performed at older ages [7,11] and when performed by less well trained individuals or traditional practitioners [7,12-14].

With renewed interest in circumcision and recommendations that neonatal age is perhaps the best time to perform the procedure [1,8], there are concerns about the morbidity that may be associated with the procedure. Training of personnel in terms of technique, instrumentation and perioperative care has been the main focus of advocacy for safe circumcision [6,7]. This, largely targeted at the medically trained practitioners, may not be enough to eradicate the morbidities. Behavioural changes and sociobiological models that identify the clients of traditional circumcisers would be an additional avenue to the preventive aspect. Identifying sociodemographic factors, which can predict parents that are likely to seek for circumcision performed by a traditional circumciser, will be useful for primary prevention. Parental education about choices to make, questions to ask the circumcisers and the perioperative plan may then be adequately addressed once the target personnel is known. The aim of the study was, thus, to evaluate the socio-demographic determinants of seeking for circumcision at the hands of traditional practitioners.

Materials and methods

This was a cross-sectional study conducted in a rural community, Igbo Ora, in South-western Nigeria between April and September 2017. Following institutional review board approval from the Oyo State Ethics Review Committee, multi-staged sampling technique was used to recruit participants. A minimum sample size of 289 participants was calculated based on a prevalence of male childhood circumcision by traditional practitioners of 25% obtained in a nearby rural town, a precision (d) of 5% and a power of 90%. The first stage involved selection of three out of the seven officially recognized wards by balloting using sealed envelopes. The second stage involved selection of 100 households in each ward, with each household consecutively visited and only one mother recruited from that household once the family had a son. Households where the mothers were not available at the time of the survey were skipped and the next household approached until the minimum required was reached.

Information was obtained from consenting participants using structured interviewer-administered questionnaires, which was translated into the local language – Yoruba. The Yoruba version of the questionnaire was back translated into English language and a linguistic expert made adjustments to the final version, which was validated in a rural community in a nearby town. The questionnaire contained items on the sociodemographic characteristics of the respondents, family sizes and ages of children, circumcision status of their sons, where the circumcision was done and the circumciser. Occupational status was recorded and recoded into three: skilled workers, unskilled workers i.e. traders and artisans and dependants [15]. Information was also obtained on antenatal care, details provided about male circumcision during pregnancy and by the circumciser and care of the circumcised phallus. Mothers who were not able to converse in either English language or Yoruba language were excluded from the study.

Data were entered into a computer and statistical analysis performed using SPSS version 21 (IBM; Armonk, New York). Univariate statistical analysis was done and results summarised as medians and ranges for continuous variables and percentages, ratios and proportions for categorical variables. Tests of association between categorical variables were conducted with Chi square statistic. For the purpose of cross-tabulation, age was dichotomized according to the median age. Variables that were significant at 20% during bivariate analysis were pooled into a multivariate logistic regression model to determine predictors of seeking for male childhood circumcision from a traditional practitioner. The p value for statistical significance was set at < 0.05.

Results

A total of 317 participants were recruited. The median age of the participants was 40.0 years (range of 16 to 86 years). The majority (290, 91.5%) were Yoruba, 198 (62.5%) were Muslims, 244 (77.0%) were unskilled workers and 242 (76.3%) had 12 years or less of education (Table 1).

The number of sons in each family was one to seven (median of two sons). A total of 93 (29.3%)

Table 1: Sociodemographic characteristics of the participants

Variables	Categories	Number	Percentage
Age (years)	≤40	168	53.0
	>40	149	47.0
Tribe	Yoruba	290	91.5
	Igbo	5	1.6
	Hausa/Fulani	22	6.9
Religion	Islam	198	62.5
	Christianity	117	36.9
	Others	2	0.6
Occupational class	Skilled workers	62	19.6
	Unskilled workers	244	77.0
	Dependants	11	3.5
Educational status	None	60	18.9
	Primary school	42	13.2
	Secondary school	140	44.2
	Technical post-secondary	48	15.1
	University	27	8.5
	Total	317	100.0

participants had three or more sons. The last son in the family was delivered at a Government hospital (187, 59.0%), private clinic (117, 36.9%) or at home (13, 4.1%).

All the participants had one or more sons circumcised. The circumcision of the youngest son was done at a median age of six weeks (range from one week to four years). The circumcision of the youngest son was done by: doctors (28, 8.8%), nurses (214, 67.5%) or traditional circumcisers (75, 23.7%). The majority (259, 81.7%) did not receive any counselling about male circumcision from health care workers during antenatal care. The parents were told to come back three to thirty days after the circumcision (median duration of three days).

Table 2: Association between sociodemographic characteristics of the participants and personnel that did the circumcision

Variable	Circumciser:				X^2	p value
	Doctor No (%)	Nurse No (%)	Traditional No (%)	Total No (%)		
Age (years)						
≤40	14 (8.3)	129 (76.8)	25 (14.9)	168 (100.0)	16.300	<0.001*
>40	14 (9.4)	85 (57.0)	50 (33.6)	149 (100.0)		
Tribe						
Yoruba	20 (6.9)	196 (67.6)	74 (25.5)	290 (100.0)	19.423	<0.001*
Others	8 (29.6)	18 (66.7)	1 (3.7)	27 (100.0)		
Religion						
Christianity	15 (12.8)	77 (65.8)	25 (21.4)	117 (100.0)	3.829	0.147
Islam & Others	13 (6.5)	137 (68.5)	50 (25.0)	200 (100.0)		
Occupational class						
Skilled workers	8 (12.9)	50 (80.6)	4 (6.5)	62 (100.0)	15.412	0.004*
Unskilled workers	18 (7.4)	159 (65.2)	67 (27.5)	244 (100.0)		
Dependants	2 (18.2)	5 (45.5)	4 (36.4)	11 (100.0)		
Educational status						
None	3 (5.0)	26 (43.3)	31 (51.7)	60 (100.0)	42.055	<0.001*
Primary/secondary	14 (7.7)	128 (70.3)	40 (22.0)	182 (100.0)		
Tertiary education	11 (14.7)	60 (80.0)	4 (5.3)	75 (100.0)		
Total	28 (8.8)	214 (67.5)	75 (23.7)	317 (100.0)		

**Statistically significant*

Table 3: Association between place of delivery and the number of boys in the family and personnel that did the circumcision.

Variable	Circumciser: Doctor No (%)	Nurse No (%)	Traditional No (%)	Total No (%)	X^2	p value
Place of delivery						
General hospital#	24 (12.8)	108 (57.8)	55 (29.4)	187 (100.0)	28.645	<0.001*
Private clinic	4 (3.4)	99 (84.6%)	14 (12.0)	117 (100.0)		
At home	0 (0.0)	7 (53.8)	6 (46.2)	13 (100.0)		
Number of boys						
1 or 2	20 (8.9)	165 (73.7)	39 (17.4)	224 (100.0)	16.890	<0.001*
≥3	8 (8.6)	49 (52.7)	36 (38.7)	93 (100.0)		
Total	28 (8.8)	214 (67.5)	75 (23.7)	317 (100.0)		

*# - Included all government run hospitals and health centres; * - statistically significant*

Table 4: Logistic regression analysis of relationship between socio-demographic variables and circumcision by a traditional practitioner

Variable	Categories of variable	OR	95% CI	p value
Age	> 40 years	2.96	1.41 – 6.24	0.004*
	≤ 40 years			
Tribe	Yoruba	20.83	2.42 – 166.67	0.006*
	Others			
Religion	Islam	1.00	0.52 – 1.94	0.998
	Christianity			
Occupational class	Dependants	8.11	1.32 – 49.80	0.024*
	Unskilled workers	3.72	0.80 – 17.23	0.093
	Skilled workers			
Educational status	None	34.48	8.20 – 142.86	<0.001*
	Primary/secondary	8.06	2.23 – 29.41	0.001*
	Tertiary			
Place of delivery	Home	3.55	0.76 – 16.52	0.106
	General hospital	1.28	0.30 – 5.49	0.739
	Private clinic			
Number of boys	≥3	1.19	0.57 – 2.49	0.636
	1 or 2			

**Statistically significant; reference category on logistic regression = traditional circumciser*

The proportion of sons of older respondents who had circumcisions done by traditional practitioners was higher than that of sons of respondents aged 40 years or less (33.6 vs. 14.9%, $p < 0.001$). A higher proportion of boys from Yoruba families were circumcised by a traditional practitioner than boys from other ethnic groups (25.5% vs. 3.7%, $p < 0.001$). Higher proportions of sons of dependants (36.4%) or unskilled workers (27.5%) were circumcised by traditional practitioners compared to sons of skilled workers (6.5%), $p = 0.004$. The proportions of sons of participants with 12 or fewer years of education (22.0%) or had who no formal education (51.7%) circumcised by traditional practitioners were higher than that of sons of mothers who had tertiary level of education (5.3%), $p < 0.001$. There was no significant association between the religious beliefs of participants and the choice of circumciser (Table 2).

The proportions of boys delivered at government hospitals (29.4%) or at home (46.2%) whom traditional practitioners circumcised were

higher than the proportion of boys delivered in private clinics (12.0%) who had the procedure done by traditional circumcisers, $p < 0.001$. The proportion of boys from families with three or more sons (38.7%) who were circumcised by a traditional practitioner was higher than the proportion of boys from families with fewer sons and whom traditional practitioners circumcised (17.4%), $p < 0.001$ (Table 3).

Sons of older mothers i.e. procedure performed chronologically much earlier were nearly three times more likely to have been circumcised by traditional practitioners compared to sons of younger mothers i.e. procedure performed much more recently (OR = 2.96, 95% CI: 1.41, 6.24, p = 0.004). Yoruba sons were 21 times as likely as sons of mothers from other ethnic groups to have had the procedure done by traditional circumcisers (OR = 20.83, 95% CI: 2.42, 166.67, p = 0.006). The odd of being circumcised by traditional practitioners was eight times higher for children of dependants than those of skilled workers (OR = 8.11, 95% CI: 1.32, 49.80, p = 0.024). Sons of uneducated mothers were also 34 times more likely than sons of those who had tertiary education to have had circumcisions done by traditional practitioners (OR = 34.48, 95% CI: 8.20, 142.86, $p < 0.001$). Religious beliefs of participants, the place of delivery of the last son and the number of sons in the family were not significant predictors of seeking for circumcision from traditional practitioners (Table 4).

Discussion

This cross-sectional study was conducted in a rural community to explore the sociodemographic factors that would be helpful in preventive health education targeted at reducing the complications of circumcision – a procedure that is ubiquitously performed in many parts of the world. A rural community was selected because of the possibility that traditional circumcisers will be more often encountered there than in more urban settings, which may have more qualified healthcare professionals working therein. The participants involved in the study were largely Yoruba, unskilled workers – mainly traders and artisans and the majority had 12 years or less of formal education. These are characteristic of rural communities in South-western Nigeria. The study design allowed information to be obtained easily on the aims and objectives in a snapshot fashion. A major limitation of the study, however, was recall bias, which might have arisen in the information provided by older participants whose most recent encounters could have occurred many years previously.

Circumcision of sons was reported in all the families surveyed in this study. This reflects the general pattern of behaviour in this part of Africa, where male circumcision is widely practiced [5,6]. The procedure of male circumcision in Africa had, hitherto, been largely influenced by religion and cultural practices with a much higher prevalence of male circumcision reported in Northern/Western African countries than in Eastern/Southern Africa [16]. In Nigeria, the influence of religion on male circumcision has resulted in most families circumcising their sons.

The median age at circumcision in this study was six weeks. All the sons had been circumcised by the age of four years. Abdur-Rahman *et al*. [17] reported similar ages at circumcision in a hospital-based study in North-Central Nigeria. The practice of neonatal or early childhood circumcision appears to be culturally influenced. Most Yoruba parents in the region circumcise their sons about the time of the naming ceremony [18] and over 90% of the participants in this study belonged to that ethnic group. Mothers who are civil servants would want the circumcision wound healed before resumption from maternity leave at about 8 to 12 weeks post-partum in the region [5]. Furthermore, the later the circumcision is performed, the more worried the parents get about cleaning the prepuce and pain control during the procedure.

A traditional circumciser performed the (last) male circumcision in 23.7% of cases. Healthcare professionals – largely nurses, did the overwhelming majority of circumcisions. This could be due to the presence of a few general and cottage hospitals, health centres and public health facilities in the town, such that the modern health care option was not unusual among the population. The proportion of male circumcision performed by traditional practitioners in this study was much higher than 9% obtained from the same region of the country but in an urban setting a few years previously [6]. Traditional circumcisers are more likely to practice in rural or semi-urban settings than in urban ones because of the wider gap in accessing orthodox medical care in rural communities. Traditional practitioners, in this series, were involved with childhood circumcision rather than circumcision done later as a rite of passage into adulthood. The latter is not routine cultural practice in South-western Nigeria.

Over 80% of the participants did not receive any counselling about male circumcision during antenatal care. This was in spite of over 95% of the mothers delivering their babies in a hospital. This is

in contrast to 83.5% of parents, in a study conducted in New York, who were counselled about circumcision of their sons [19]. In that study, the parents were informed of the advantages and disadvantages of the procedure and 50% of parents had decided to go ahead with circumcision even before the child was delivered [19]. Appropriate counselling of mothers, especially those expecting boys, about circumcision and care of the wound is a form of public health education to improve the outcome of circumcision.

Chronology was a significant factor influencing the choice of circumcision in this study, as older mothers were more likely than younger ones to have visited traditional circumcisers. In essence, circumcisions performed more recently were less likely to have been performed by traditional practitioners compared to those performed earlier. This may suggest a gradual reduction in patronage of traditional circumcisers. Ethnicity was another significant factor influencing the choice of circumcision; Yoruba mothers were more likely to engage traditional circumcisers than mothers from other ethnic groups. This is in keeping with the influence of culture and tradition over circumcision in our society [20,21]. This effect likely overtakes religious beliefs, as there was no significant relationship between the religious beliefs of the mothers and seeking for circumcision by a traditional practitioner. In a prospective study conducted on requests for circumcisions in Nnewi, South-Eastern Nigeria, 200 (59.3%) of 337 requests were for cultural reasons compared to 122 (36.2%) for religious reasons [21]. Culture also played a predominant role, regardless of the religious beliefs of the parents, in driving circumcision in other studies from the same country [5,6,20].

Educational level and occupational status were significant predictors of seeking for circumcision at a traditional circumciser's workshop. Participants who were less educated, unskilled workers or dependants were more likely to engage traditional circumcisers. Delivery at home or at a government hospital, which may be associated with a lower social status, rather than giving birth at a private clinic was also associated with circumcision of sons by a traditional practitioner. Low social class with associated poorer educational status, larger family sizes and less skilled occupations are features that predominate in rural communities in developing countries [22,23]. These factors are also implicated in driving patronage of traditional circumcisers. It is therefore, imperative to target mothers in this group during community health education programmes or antenatal care to provide information about circumcision options, techniques and care of the wound.

In conclusion, tribe, education and occupational class are factors that determine patronage of traditional circumcisers. Public health awareness targeted at identified groups can help improve safety of circumcision.

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Referral practices of trained Traditional Birth Attendants in selected Local Government Areas of Ibadan, Nigeria.

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Abstract

Background: Traditional birth attendants (TBAs) represent an important component of the healthcare system and are present at 50% of deliveries in developing countries. Despite the training given to TBAs by significant organisations on timely referrals, maternal deaths attributed to delay in referrals persists. The aim of this study was to assess the reported referral practices of trained TBAs in Ibadan.

Methods: A cross-sectional study was conducted among trained TBAs in Ibadan North and Lagelu Local Government Areas of Ibadan, Oyo state utilising mixed methods. A total of 114 trained TBAs were randomly selected and completed a questionnaire. Eight TBA leaders were interviewed using a key informant interview guide. The quantitative data was analysed using the Statistical package for social sciences (SPSS) version 22 and t-test at $\alpha = 0.05$.The qualitative data was analysed with NVivo version 12.

Results: Findings revealed that 61.4% of the TBAs had good referral practices. The leading perceived factors influencing the referral practices of the TBAs was rejection of referral by the pregnant women, cost and attitude of health care workers. A strong theme that emerged during the KIIs indicated that referral decisions were made by the TBAs although that did not guarantee compliance. There was no significant difference in the referral practice of TBAs located at semi urban or urban area ($t=0.429$, $p=0.669$).

Conclusion: There is need to subsidise cost of health care for pregnant women, improve attitude of health care workers and to target the pregnant women when developing policies on referral.

Keywords: *Traditional birth attendants, Health Personnel, Referral, Pregnant women, Delivery, Health Facilities*

Résumé

Contexte : Les accoucheuses traditionnelles représentent un élément important du système de santé et sont présentes dans 50% des accouchements dans les pays en développement. En dépit de la formation donnée aux accoucheuses traditionnelles par des organisations importantes sur la référence en temps voulu, les décès maternels attribués à un retard de référence persistent. Le but de cette étude était d'évaluer les pratiques de référence signalés des accoucheuses traditionnelles formées à Ibadan.

Méthodes : Une étude transversale a été menée parmi les accoucheuses traditionnelles formées dans les communes d'Ibadan North et de Lagelu à Ibadan, État d'Oyo, à l'aide de méthodes mixtes. Un total de 114 accoucheuses traditionnelles formées a été sélectionné au hasard et elles ont rempli un questionnaire. Huit dirigeantes d'accoucheuses traditionnelles ont été interrogés à l'aide d'un guide d'entrevue avec informateur clé (KII). Les données quantitatives ont été analysées à l'aide du logiciel SPSS (Statistical package for social sciences) version 22 et le test t à $\alpha = 0,05$. Les données qualitatives ont été analysées à l'aide de NVivo version 12.

Résultats : Les résultats ont révélé que 61,4% des accoucheuses traditionnelles avaient de bonnes pratiques en matière de référence. Les principaux facteurs qui ont influencé les pratiques de référence des accoucheuses traditionnelles ont été le refus de la référence par les femmes enceintes, le coût et l'attitude des agents de santé. Un thème fort qui a émergé au cours des KII indiquait que les décisions de référence étaient prises par les accoucheuses traditionnelles, bien que cela ne garantisse pas la conformité. Il n'y avait pas de différence significative dans la pratique de référence des accoucheuses traditionnelles situées dans des communes semi-urbaines ou urbaines ($t = 0,429$, $p = 0,669$).

Conclusion : Il est nécessaire de subventionner le coût des soins de santé pour les femmes enceintes, d'améliorer l'attitude des agents de santé et de cibler les femmes enceintes lors de l'élaboration de politiques sur la référence.

Mots-clés : *Accoucheuses traditionnelles, personnel de santé, référence, femmes enceintes, accouchement, établissements de santé*

Introduction

The importance of effective and timely referrals in an obstetric emergency is related to the unpredictability of pregnancy complications and their potential to progress rapidly to become severe

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and life threatening [1]. Prompt access to facility-based skilled birth attendance and emergency obstetric care have been considered as one of the primary ways that the challenge of maternal mortality and morbidity can be tackled [2]. Tabatabaie, Moudi and Vedadhir [3] reiterated that one factor identified to contribute to high maternal mortality in developing countries is a delay in accessing Emergency Obstetric care services (EmOC) when life-threatening complications arise during childbirth.

The use of unskilled birth attendants such as Traditional Birth Attendants (TBAs) has contributed significantly to maternal deaths in Nigeria and other developing countries [4]. The Traditional Birth Attendant is described as a person who assist the mother at childbirth and who initially acquired her skills in delivering babies by herself or working with other TBAs [5]. Although TBAs are not regarded as skilled birth attendants, they have become an important provider of maternity care in developing countries and are highly patronised [6-8].

In Nigeria, only 38% of births are delivered by a skilled health provider [8]. The persistent and large patronage of TBAs has necessitated significant health organisations and the government to recognise and incorporate traditional birth attendants into the health care system. Trained TBAs are expected to focus on promotion of maternal health services with emphasis on prompt referral of pregnant women especially those with complications in their communities [9-11]. The training usually involves recognition of previous bad obstetric histories and obstetric danger signs during pregnancy, labour and puerperium, and the need for prompt referral of such cases.

However, some TBAs carry out several maternal and child health services meant for skilled birth attendants such as deliveries [9]. In addition, some inappropriate practices like poor management of labour, management of mal-presentations, conducting deliveries for women with previous caesarean delivery as well as unhygienic practices have been observed in their activities [12, 13].

Furthermore, the involvement of Traditional birth attendants (TBAs) during delivery has also been observed to delay hospital referral during any maternal complications [14, 15]. Okafor and colleagues [9] opined that prolonged delays of more than 24 hours in TBA homes occurred in 36.6% of the patients in their study with 48.8% of the patients presenting in a poor clinical state. The most commonly reported situations in which trained TBAs referred women to orthodox facilities included when labour is delayed or contractions are too far apart or too close together and contractions occurred without rupture of membranes [16]. Culture and religious beliefs, availability of health facilities, rejection of referral by mothers and attitude of workers in referral centres are some of the factors associated with the referral decisions and practices of trained TBAs [17, 18].

Crucial factors in maternal care are the recognition of complications, timely referral to a higher level of care which ultimately results in timely management of complications. In many developing countries including Nigeria, this referral relies largely on TBAs as they are highly patronised and are very close to the women in the community. With the high level of utilisation of the services of TBAs and the renewed integration of TBA in formal health services through training, there is need to assess the referral practices of these trained TBAs, how it varies based on urbanisation, their criteria for referral and factors perceived to influence their referral decisions. This will help to identify possible reasons and influencers of their referral decisions which may be contributing to persisting poor referral practices and hence increasing mortality and morbidity.

Materials and methods

This study adopted a cross sectional descriptive design utilising mixed methods (qualitative and quantitative method). The study was conducted from March, 2018 to April, 2018.

Study setting

This study was carried out in Ibadan North Local Government and Lagelu Local Government areas of Oyo state, Nigeria. Ibadan North Local Government area covers a landmass of 132.500 square kilometres with a population density of 2,626 persons per square kilometre.

Lagelu Local Government area was created in 1976 with its administrative headquarters located at Iyana Offa. The Local Government area has a land mass of 310.850 square kilometres. The 2010 estimated population was projected to be 167,828 with a population density of 540 persons per square kilometres.

Study population

Trained TBAs were selected for this study because they have received formal training on the importance of referral and are recognised by the Government. Eligible respondents were Traditional birth attendants who were registered and trained by the government, those who were currently practicing

during the study period and TBAs who had been working for at least 2 years after training. Retired or sick Traditional Birth Attendants and TBAs not resident in the selected communities were excluded from the study.

Sample size determination/Sample Selection
Ibadan has 11 LGAs classified into five urban LGAs and six semi urban LGAs. Random sampling technique (balloting) was employed in selecting one local government each from the two divisions. From the five local governments in the city, Ibadan North Local Government was randomly selected while Lagelu Local Government was randomly selected from the six Local Government areas in the semi urban areas.

A sample frame was collected from the Ministry of Health, Oyo State Community Birth Attendant focal person and combined with the list of the head TBA for each Local government. Ibadan North Local Government had 67 TBAs and Lagelu Local Government had 71 TBAs making a total number of 138 TBAs.

Sample size was calculated using Araoye [19] sample size statistical formula. A hundred and fourteen (114) TBAs participated in the questionnaire survey (Table 1). These TBAs were randomly selected from both local Government Areas. Eight TBA leaders were purposefully selected from the total TBAs to participate in the Key Informant Interviews. Four TBA leaders were selected from each Local Government Area.

Instrument and procedure for data collection
A structured researcher administered questionnaire (TBAQ) was developed for the trained TBAs. The key informant interview guide was also developed for the key informant interviews with the TBA leaders. A reliability coefficient of 0.82 was obtained for the TBAQ after a test retest was done to ensure reliability of the questionnaire.

Data was collected over a period of 6 weeks with the assistance of 4 trained field assistants. On the chosen day for data collection, informed consent was obtained and the questionnaires were administered.

Eight face to face key informant interviews lasting between 45minutes to an hour took place on the selected date and convenient time and place for the key informants. These were audio recorded and notes also taken.

Ethical consideration
Institutional Permission to conduct the study was obtained from the Oyo State Ministry of Health ethical review committee Ibadan before commencement of the study. Informed consent was obtained from the participants. Participants had the right to withdraw at any time during the study. Anonymity was ensured by using codes for identification of the participants. The soft copy of the collected data was pass-worded to ensure that unauthorised individuals did not have access to it. Additionally, the hard copy of data and other files were kept locked in a safe.

Data management and analysis
Quantitative data was sorted, coded, and entered into the computer and checked for errors using Statistical Package for the Social Sciences (SPSS) version 22. The data was subjected to analysis using both inferential and descriptive statistics. Independent t test was used to ascertain the difference in the referral practice between TBAs in both Local Government Areas. The level of significance was set at $P < 0.05$.Qualitative data was analysed with NVivo version 12.

Results
The sample comprises 114 TBAs **(**Table 2). About 9 in 10 of the TBAs were aged above 34 years with mean ±SD age 45.6±7.6 years. About 75.0% were married and 20.2% had no formal education. Majorly, 40.4% of them ran religious TBA center and

Table 1: Proportionate allocation of sample of Trained Traditional Birth Attendants

S/N	Local Government Area	Number of TBA	Proportional Allocation of Sample	Sample size
1	Ibadan North Lga	67	$\frac{67 \times 114}{138}$	**55**
2	Lagelu	71	$\frac{71 \times 114}{138}$	59
	Total	138		114

Table 2: Socio-demographic Variables of the TBAs

Variable	Categories	Frequency	Percentage (%)
Age group (years)	20 – 34	7	6.1
Mean ±SD = 45.6±7.6	35 – 49	71	62.3
	50 and above	36	31.6
Location of TBA	Ibadan North	55	49.1
	Lagelu	59	50.9
Marital status	Married	85	74.6
	Single	7	6.1
	Divorced	9	7.9
	Widowed	13	11.4
Educational status	No formal	23	20.2
	Primary	31	27.2
	Secondary	60	52.6
Type of TBA	Religious	46	40.4
	Traditional/Herbal	36	31.6
	Others (Community)	32	28.1
Mode of Practice	Part time	1	0.9
	Full time	113	99.1
Closest health facility for referral	Private\	24	21.1
	Gen. Hospital	43	37.7
	Teaching hospital	47	41.2
Year of Practice	1 – 10	13	11.4
	11 – 20	66	57.9
	21 – 30	29	25.4
	Above 30	6	5.3

Table 3: Reported Referral Practice of TBAs

Statement	Response	Frequency	Percentage (%)
When do you refer a pregnant woman to the hospital?	Correct	110	96.5
	Incorrect	4	3.5
What do you do when a woman's pregnancy exceed the normal gestational age?	Correct	113	99.1
	Incorrect	1	0.9
What do you do when a woman exceeds the normal duration of labour?	Correct	103	90.4
	Incorrect	11	9.6
What do you do when you observe any danger or signs of complication in a woman's pregnancy?	Correct	102	89.5
	Incorrect	12	10.5
Who do you inform when you need to refer a pregnant woman to the hospital?	Correct	105	92.1
	Incorrect	9	7.9
Who makes the final decision to refer a pregnant woman experiencing difficulty to the hospital?	Correct	111	97.4
	Incorrect	3	2.6

approximately all practiced on full time, 41.2% had the teaching hospital as the closest health facility for referral and about 11.4% had less than 11 years of experience.

Table 3 shows the reported referral practice of participants. Majority 110 (96.5%) of the TBAs correctly responded that a pregnant woman should be referred to a hospital immediately danger signs in pregnancy and labour is recognised. A total of 103 (90.4%) of the respondents correctly understand that when a woman exceeds the normal duration of labour the pregnant woman should be sent to a health facility. Among the TBAs, 105 (92.1%) informed supervising skilled birth attendant when there was need to refer pregnant woman. Majority, 111 (97.4%) of the TBAs said they were in charge of decision making on referrals.

The interviews revealed that the TBA often refer danger signs and complications to the hospital immediately although some of the TBAs stated that they refer pregnant women to orthodox hospital based on spiritual leading.

Table 4: Cumulative Level of Reported Practice

Value	Score	Frequency	Percent (%)	Remark
Mean Score = 14.6±2.2	≤15	44	38.6	Below average
	>15	70	61.4	Above average
Total		114	100.0	

"The best person to take care of pregnant woman during complication in pregnancy and delivery is a doctor. Whenever I recognise any sign of complication, I organize how to take them to big house (Teaching hospital)" (KII TBA leader 2, Ibadan north).

Although most of the TBAs recognise that the hospital is the best place to handle a pregnant woman with danger signs and complications, they reported experiencing difficulty in convincing the women that the decision is the best for them.

"Most of them do not want to go to the hospital, they only rely on us. But during hard labour, they will be regretting not going to the hospital. Some pregnancy and delivery look normal in the beginning but as time goes by you will see that there is a problem. A young girl in labour once came to my house in the midnight…the baby was hooked and could not come out. I had to take her to the hospital myself and on getting there, she said I kept her since morning. She almost died. I have learnt that whether it's a known case or not, I refer if there is danger" (KII TBA leader 1, Ibadan north).

The TBA often accompanied the women to the hospital to ensure compliance. More commonly though, referral is only after the TBA attempts to treat the complication and realises she cannot manage it.

"Yes, I refer them to hospital as soon as we can even though sometimes we try to see what we can do first. Sometimes we ask other TBA for help but if we notice that it is very serious we will now tell them to go to hospital". (KII TBA leader 3, Ibadan north).

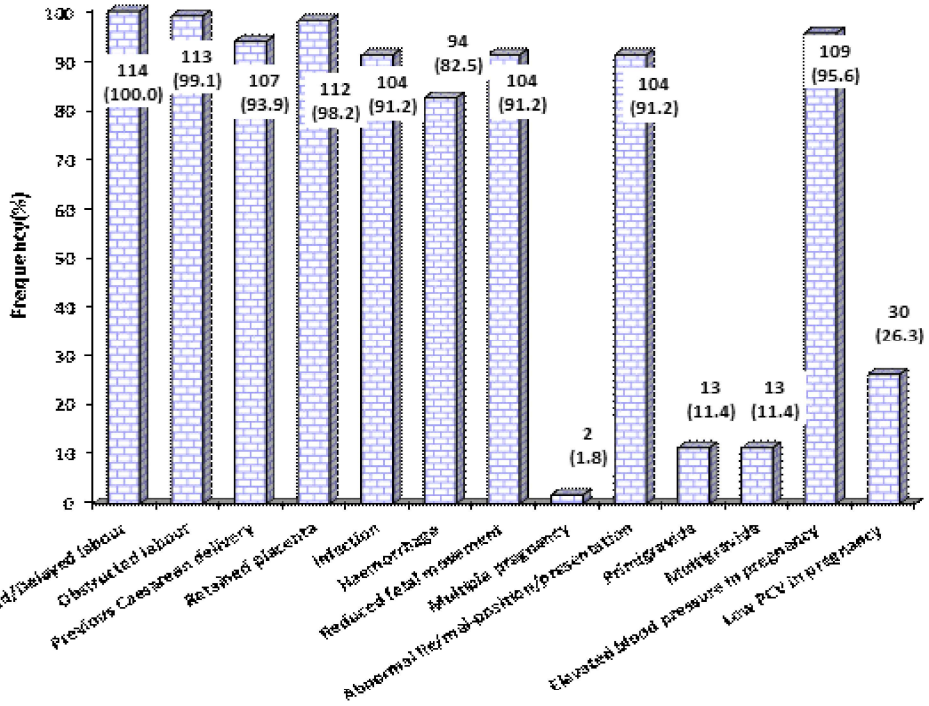

Fig.1: Criteria/indicators for referral

Furthermore, most of the TBAs felt that the conditions listed were criteria for referral (Fig 1). Some of the conditions were seen to be more serious than the other by individual TBAs as evidenced by this quote.

"The common causes of referral is bleeding in pregnancy, prolong bleeding after delivery, baby in wrong position or not moving, convulsion, high blood pressure and retained placenta. I feel bleeding is more dangerous for both mother and child". (KII TBA leader 2, Lagelu).

About 61.4% of the TBAs had above average level of reported referral practice as they scored 15 marks and above out of 19 maximum obtainable marks (Table 4). Most of the TBAs (94.7%), rarely refer pregnant woman for antenatal care in a hospital while majority always refer for investigations and tetanus injection (Table 5). The mean rate of referral score was approximately 11.3±1.5 standard deviation. Majority 69.3% of the TBAs scored above 11 marks

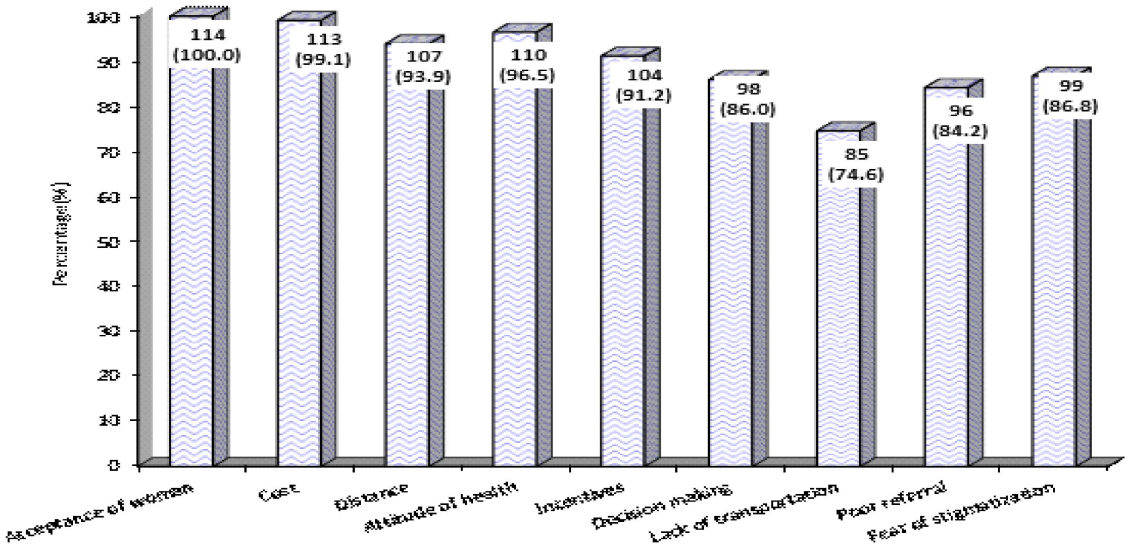

Fig. 2: Perceived factors influencing Referrals of pregnant women by trained TBAs

Table 5: Rate of Reported Referral for Services or Conditions

Service	Frequency (%) Always	Often	Rarely	Never
Antenatal care	1(0.9)	4(3.5)	108(94.7)	1(0.9)
Investigation	90(78.9)	24(21.1)	0(0.0)	0(0.0)
To get tetanus injection	103(90.4)	10(8.8)	1(0.9)	0(0.0)
For delivery	6(5.3)	5(4.4)	103(90.4)	0(0.0)
Routine pregnancy drug	6(5.3)	7(6.1)	98(86.0)	3(2.6)
X-ray/ultrasound to check the size and position of the baby	95(83.3)	14(12.3)	5(4.4)	0(0.0)
Complication	92(80.7)	20(17.5)	2(1.8)	0(0.0)
Postnatal care	11(9.6)	94(82.5)	9(7.9)	0(0.0)
Treatment of malaria including IPT	14(12.3)	97(85.1)	3(2.6)	0(0.0)
Immunization	78(68.4)	33(28.9)	3(2.6)	0(0.0)
Bleeding in pregnancy	103(90.4)	11(9.6)	0(0.0)	0(0.0)
Prolonged bleeding after delivery	101(88.6)	11(9.6)	2(1.8)	0(0.0)
Retained placenta	102(89.5)	8(7.0)	4(3.5)	0(0.0)
Convulsions in pregnancy or delivery	110(96.5)	3(2.6)	1(0.9)	0(0.0)
Infection after delivery	6(5.3)	108(94.7)	0(0.0)	0(0.0)
Septic abortions	104(91.2)	10(8.8)	0(0.0)	0(0.0)
Obstructed labour	56(49.1)	58(50.9)	0(0.0)	0(0.0)

out of 17 maximum obtainable marks which shows that they frequently practiced adequate referral of pregnant woman (Table 6).

Table 6: Classification of Rate of Reported Referral

Value	Score	Frequency	Percent (%)	Remark
Mean Score = 11.3±1.5	≤11	35	30.7	Infrequent
	>11	79	69.3	Frequent
Total		114	100.0	

Table 7: Illustration of the statistical difference in Reported Referral Practice based on Location of TBA Independent Sample Test

	Location	N	Mean	Std. Deviation	Std. Error Mean	T	df	p-value	Remark
Practice score	IbN	55	14.64	.910	.123	0.429	112	0.669	Not Significant
	Lagelu	59	14.54	1.369	.178				

Table 8: Matrix of Qualitative Analysis Showing Themes and Sub Themes Emanating from the Key Informant Interviews

Main Theme	Subthemes
Referral practices and decisions	Decision making on referrals is made by TBAs, the pregnant women and significant others.
	Pregnant women often reject referral to orthodox facilities due to attitude of health care workers
	Skilled health workers are better at managing deliveries and complications
	Personal judgement and experience of TBA guides referral decisions
	Private hospitals collaborate with trained TBAs on referral.
Economic constraints during referrals	Provision of incentives to trained TBAs provides support and strengthen referrals
	Lack of funds for orthodox care encourages referral rejection
	Referrals often entails additional expenses
	Cost of initial care most times falls on the TBA
Faith and beliefs have a role in referrals	Pregnancy and delivery management are perceived to be combination of cultural, medical and spiritual factors.
	Complications in pregnancy can be solved by prayers or herbal treatment.

All the TBAs identified acceptance of referral by the pregnant woman as a factor that influenced their referral practices and decisions. Lack of transportation to convey the pregnant woman to the hospital was the least criteria (74.6%) perceived to influence referral (Fig 2).Similarly, one of the themes from the interviews as shown by Table 8 was that a major difficulty that the TBAs experienced was rejection of referrals by the pregnant women or their family members.

"They reject very well. Sometimes they even go to another TBA after you ask them to go to the hospital. They don't just want the hospital. They complain a lot about the staff attitude". (KII TBA leader 2, Lagelu)

Other reasons given for referral rejection by the TBAs were the previous care many women have received from the hospital, attitude of health care workers, cost and distance (Fig 2). A TBA leader summarised this in the quote below.

"I have heard such complaints but the common one is that the hospital demands for too much money and is sometimes too far for them. Some

people also say the nurses have little experience. One very interesting story was a woman who went to have her second baby in the General hospital, as she was vomiting in labour, the nurses kept saying she will pack it. She said she regretted it. Another woman said she was asked not to give birth on the floor when she wanted to pass faeces while someone else said she was in labour for a whole day and nobody examined her".(KII TBA leader 3, Lagelu)

On getting incentives for every pregnant women referred, one TBA responded thus

"Yes, I receive incentives from some of the private hospitals, because that is my sweat. But government too should give us incentives for the work we do". (KII TBA leader 4, Lagelu)

Lack of transportation was not really seen as a strong influence on referral because some of the TBAs have their own cars and the private hospitals they work with provide ambulances during complications.

"I have one doctor that helps with his car for transportation, any time I call on him he do answer". (KII TBA leader 2, Lagelu)

Discussion

In our study, majority of the TBAs were aged 35years and above. They were mostly married older women with experience in child bearing. This bears similarity with previous studies which shows that TBAs meet the commonly established community criteria of being middle aged with experience in child bearing [20, 21 22]. The level of education of TBAs in this study was low as majority of the TBAs had no formal education and none had tertiary education although they had all received trainings. Other studies [22] showed similar results.This suggests that the level of education as well as the training received by these TBAs contribute to the nature of care provided. Most of the trained TBAs in this study had been in practice for over 10 years. In the same vein, a recent study in Kenya showed the average years of experience of the TBAs to be about 24years [23]. The years of experience of the TBAs possibly influenced their knowledge of recognition of obstetric emergencies.

A large number of TBAs in this study were religious based. According to Adegoke & Jegede [24], spirituality and religion is said to form the basis of purpose and meaning for many people especially during pregnancy which is termed a period of heightened spiritual awareness. Similarly, an earlier study [25] in Enugu Nigeria reported that the choice of health facility or non-health facility deliveries among pregnant women was found to be statistically significant with religion. Religious leaders and organizations should therefore be involved in developing policies for pregnant women and skilled birth attendance.

Although the teaching hospital was the closest facility for referral for majority of the TBA, the number of referrals directly to the teaching hospital volunteered in this study was low compared to that of private hospitals. Our study findings reveal that the TBAs who accompany their clients to the tertiary hospitals experienced discrimination and stigmatisation and that private hospitals were preferred due to previous arrangement with them. In the same vein, findings from the work of Moudi, Tabatabaie, Saeedi, & Vedadhir, [14] also revealed that some TBAs did not refer mothers to EmOC as soon as the TBAs perceived a serious delivery complication due to the process of stigmatisation. Considering the difficulty the TBAs have to go through when there is need for a referral, it is most likely that they will prefer to send their clients to a place that treats them with respect. Professional reorientation and training of health care workers midwives on the need to treat women at childbirth with empathy, respect and dignity should be emphasized.

Level of reported referral practices of Traditional Birth Attendants.

Objectively, the study finding revealed that the reported referral practice of most TBAs to orthodox facilities especially during complications in pregnancy and delivery was far above average. Recent study findings reported that TBAs always referred women to formal health care and did not mind losing their jobs because they believe formal health care have more expertise than they do and has better equipment to diagnose and treat problems [26, 27].

The qualitative analysis findings also complimented the report that most TBAs refer pregnant women at the slightest danger sign or complication or even send them to orthodox facilities when they are pregnant. These findings also agree with that of Keri, Kaye and Sibylle [16] who reported that some TBAs encouraged their pregnant clients to attend prenatal sessions at a local health clinic or hospital. Vyagusa, Mubyazi, & Masatu [28] also documented that TBAs considered it appropriate to send a woman to a hospital under certain problematic circumstances. In contrast, Okafor *et al*. [9] reported

that delays at TBA centers are common before referral and most patients are referred in poor clinical state. Likewise, Moudi, Tabatabaie, Saeedi, and Vedadhir [14], revealed that TBAs prefer to keep their patients under observation' at home as long as possible, often beyond what is reasonable. The adequate practice of referral among TBAs in our study could be as a result of better understanding of skilled birth attendance gained during trainings or as a result of previous negative experiences that have occurred due to poor referral practices. This was supported by Abodunrin, Akande, Musa, and Aderibigbe [29] that TBAs with some previous training were more likely to suggest referral of pregnant women with many risk factors or complications to skilled care. The current and previous studies [16, 28, 29] show a positive view of how trained TBAs perceive skilled birth attendance thus leading to the improvement of maternal health. Consequently, training and retraining of TBAs should be sustained and encouraged.

With regards to obstetric emergencies, TBAs in this study commonly reported referring women to hospitals as soon as danger signs such as obstructed or prolonged labour are noticed. Similarly other studies [16, 28], documented that TBAs in their study refer when labour is prolonged or obstructed. Almost all TBAs in this study inform supervising skilled birth attendant when there is need for referral and they decide when to refer the pregnant women which is consistent with the findings of Reeve *et al*. [23]. This could be attributed to the knowledge gained during training programs and the positive relationship between the TBAs and some skilled birth attendants.

Despite the good reported referral practice in this study, there was notably low referral due to primiparity, multiparity, multiple pregnancy and low PCV in pregnancy. Similarly, other study findings [30] revealed that TBAs were found to be managing high risk pregnancies at extremes of reproductive age. This indicates poor risk assessment and can result in high maternal and perinatal mortality and morbidity. In the opinion of Bisika [31]; Lucey, Andriatsihosena, and Matthew [32], these poor practices were attributed to overconfidence gained during trainings. On this note, the services of TBAs should also be checked to ensure it conforms to stipulated recommendations regardless of training.

Rate of reported referral

The WHO recommendation outlined certain activities and interventions that are permitted to be carried out by trained TBA (lay workers) such as promotion of maternal and newborn care services [11]. The results of our study show that most TBAs did not adhere to this recommendation as they rarely send women to orthodox facilities for antenatal care, routine pregnancy drugs and delivery while the women are frequently sent to facilities for services such as obtaining tetanus injection, ultrasound scan, and treatment of malaria, immunization and any sign of complication like bleeding and retained placenta. Several studies carried out in Africa show similar practice as the TBAs in these studies generally provided antenatal care, delivery services and extensive postnatal care [23, 33, 34]. This shows that most TBAs still carry out delivery and antenatal services and refer only when complications are imminent.

In contrast, studies carried out in several communities in Kenya found out that the TBAs rarely go beyond providing massage, food and herbs to women. Their role was to hold and comfort the woman, rather than actively manage the birth. [20,35]. Although conducting antenatal care and deliveries may be necessary in areas where skilled birth attendants are absent, problems could arise from lack of equipment, absence of evidence-based interventions for complications, and delayed referral. Government, stakeholders and appropriate organizations should develop a strict guideline and recommendation showing the scope and limitations of the activities of trained TBAs. This should be made available to skilled and unskilled birth attendants.

Perceived factors influencing referral of pregnant women by the Traditional Birth Attendants

Rejection of referral by pregnant women stood out in both the qualitative and quantitative findings of this study as a major perceived factor influencing referrals of the pregnant women by the TBAs. This aligns with the findings of Sarmento [36] that compliance and rejection of referrals is a major problem experienced by TBAs making referral difficult. The TBAs stated that the women have to be deceived or forced to go to orthodox health facilities. This illuminates the need to involve the pregnant women, their spouses and leaders as stakeholders in policies to improve referral and promote its acceptability.

Not all the TBAs in our study saw transportation as a major barrier to referral because some of them had cars while others had prearranged transport in the community or with the skilled Birth

attendant. This finding was contrary to the results of Hussein, Kanguru, Astin and Munjanja [18] who reiterated that transportation has been noted as one of the most documented barriers to timely referral of pregnant women.

The TBAs expressed their displeasure during the interviews that they were not respected by skilled health workers. They strongly felt that if the Government has recognised and trained them, skilled health workers should also respect them. If TBAs are to remain integrated in the health system, they need to be accepted by skilled health workers. The health workers should be trained on good and professional attitude to encourage and motivate TBAs in order to achieve the ultimate goal of maternal mortality reduction.

An interesting contrasting finding in the key informant interview is that two TBA leaders believed that their level of experience and training determines how they are treated in the hospital as well as the time the pregnant woman is brought in. This finding agreed with that of Armstrong [37] that trained TBAs with certificates are treated better by medical staff when they refer a patient. Another possible reason for this could be that the TBAs referred pregnant women to facilities that were familiar with their practices.

Results from our quantitative data showed that a large number of the TBAs felt that provision of incentives can influence their referral decisions. The doctors in private hospitals usually provide them with tokens for their efforts. Themes revealed during the interviews showed that the TBAs believed that provision of incentives by government will help encourage referrals because the money they make from their practices is their only source of income. This could be largely due to the mode of practice as all the TBAs except one practiced full time.

There is no significant difference observed in the level of reported referral practices of TBAs in the urban areas and those in the semi urban areas. The statistical analysis showed no significant difference in the means of referral practice of the two locations. The location of the TBAs that did not reflect on their referral practices could be because all the TBAs used in this studies were trained and majority reported good referral practice. It could also be due to the proximity of orthodox facilities to the respective local Governments. This was corroborated by the findings of Vyagusa, Mubyazi, and Masatu [28] that there was no difference in the referral practices of TBAs who lived and practiced in semi urban areas and those who live in urban areas.

Conclusion

Skilled birth attendance has been proven to be the key in the reduction of maternal mortality and morbidity among pregnant women especially those experiencing complications. Although TBAs are not skilled birth attendants, they carry out a range of maternal health services and they are highly patronized even during complications. This study has provided a view into understanding that despite the current positive referral practice of trained TBAs in these communities based on trainings, the contribution of the pregnant women to these practices is important and significantly influences the outcome of the condition and decisions. We recommend reduction in cost of health care for low income pregnant women, initiation and sustained payment of incentives to trained TBAs by government facilities and continuous training and retraining. Professional reorientation and training of health care workers/ midwives on the need to treat women at childbirth with empathy, respect and dignity. Proper definition of TBA roles should also be emphasized. Pregnant women and their significant others should be involved when developing policies on referral and skilled birth attendance.

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Self-reported justification for prolonged indulgence in oral habits in a group of Nigerian school children aged 6 to 12 years old

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Abstract

Background: Oral habits are repetitive behaviors in the oral cavity, which may have deleterious effects on the occlusion when continued beyond four years of age.

Objective: To determine the reasons for the prolonged indulgence in non-nutritive oral habits by school children aged 6 to 12 years old.

*Materials and methods***:** This was a cross-sectional study conducted among two hundred and twenty-one (221) 6 to 12 year old Primary and Junior High schoolchildren. Data Analysis was carried out using Statistical Package for Social Sciences (SPSS) software Version 20.0. Significance was determined at 95% confidence interval and statistical significance set at $p < 0.05$.

Results: Majority of the male participants (57, 63.3%) could not adduce any reason while the females (50, 60.2%) cited "I enjoy doing it" as their reason for indulging in oral habits (p=0.02). Majority of the younger children (6-9 years old) claimed that it helped them to sleep (30, 85.7%, p=0.006) and they enjoyed the habit (57, 68.7%), whilst older children said it helped them to concentrate (19, 38.8%). Statistically significant associations were recorded between 'helping me to fall asleep' and finger sucking, cheek biting, tooth grinding and anterior tongue resting position.

Conclusion: The younger children adduced the habit to their ability to concentrate and shyness, whilst the older participants particularly females adduced pleasure as the major reason. Majority of participants did not have any reason for these habits.

Keywords: *Oral Habits, schoolchildren, self-reported, prolonged indulgence, justification.*

Résumé

Contexte : Les habitudes buccales sont des comportements répétitifs dans la cavité buccale pouvant avoir des effets délétères sur l'occlusion lorsqu'elles sont maintenues au-delà de quatre ans.

Objectif : Pour déterminer les raisons de l'indulgence prolongé d'habitudes orales non nutritives par les enfants écoliers âgés de 6 à 12 ans.

Matériels et méthodes **:** Il s'agissait d'une étude transversale menée parmi deux cent vingt et un (221) écoliers du primaire et du secondaire de premier cycle. L'analyse des données a été réalisée à l'aide du logiciel SPSS (Statistical Package for Social Sciences) version 20.0. La signification a été déterminée à un intervalle de confiance de 95% et la signification statistique établie à $p < 0,05$.

Résultats : La majorité des participants masculins (57, 63,3%) n'ont pu indiquer aucune raison, tandis que les femmes (50, 60,2%) ont cité "J'y prends plaisir à le faire" comme raison de se livrer à des habitudes orales ($p = 0,02$). La majorité des enfants les plus jeunes (âgés de 6 à 9 ans) ont affirmé que cela les aidait à dormir (30, 85,7%, $p = 0,006$) et qu'ils prenaient plaisir de cette habitude (57, 68,7%), tandis que les enfants plus âgés affirmaient que cela les aidait à se concentrer (19, 38,8%). Des associations statistiquement significatives ont été enregistrées entre "aider à m'endormir" et sucement du doigt, morsure de la joue, grincement des dents et la langue antérieure en position de repos.

Conclusion : Les enfants plus jeunes ont cité l'habitude à leur capacité de concentration et à leur timidité, tandis que les participants plus âgés, en particulier les filles, ont cité le plaisir comme raison principale. La majorité des participants n'avaient aucune raison de ces habitudes.

Mots-clés : *habitudes orales, écoliers, auto déclaration, indulgence prolongée, justification.*

Introduction

Oral habits are repetitive behaviors in the oral cavity, which may have deleterious effects on the occlusion and structures of the dentofacial complex. These effects include malocclusion amongst others and are dependent on the frequency, intensity and duration of the habits [1, 3]. In the literature, oral habits have been classified into groups which include; acquired and compulsive, [4] and nutritive and non-nutritive [5]. Whilst nutritive habits are necessary for feeding, non- nutritive oral habits are unnecessary as well as

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detrimental not only to the primary but also to the permanent occlusion of children if continued after the age of four years [6-9]. Although some nutritive habits when prolonged can also have untoward effects on the occlusion. Non- nutritive habits include digit sucking, pacifier sucking, lip sucking and biting, nail-biting, bruxism, self-injurious habits, mouth breathing and tongue thrusting [10]. Malocclusions resulting from these habits vary and are expressed in particular as increased overjet, anterior open bite, posterior crossbite, constricted arches and deep palatal vault [10-12].

The prevalence values for oral habits recorded in different studies carried out among Nigerian children range from 9.9% to 34.1%. [13-15] In a previous study assessing the prevalence of different types of oral habits in 6 – 12 years old, nail biting was found to be the most prevalent habit, accounting for almost half of the study population [16]. A significant gender difference was also observed with more males involved in oral habits such as finger sucking, lip sucking, cheek biting, tongue thrusting, while more females were involved in thumb sucking and chewing gum [16].

Indeed, probably due to lack of knowledge and awareness of the deleterious effects of oral habits on the occlusion, some children may continue to indulge in these habits even up to adolescence [17]. Such behaviour when exhibited publicly may result in ridicule or bullying by peers in school as well as parental displeasure which may cause psychological distress to such individuals [18]. Some of the factors which predispose to the development and persistence of non-nutritive sucking habits have been reported to include social determinants, such as paternal education, maternal age, parental income, the mother's occupation, maternal civil status, the number of siblings, the maternal breastfeeding period and the use of a baby bottle [19]. Although oral habits have been described by psychologists and psychiatrists as a psychodynamic phenomenon [8], little research has been carried out to ascertain from the children and adults who engage in prolonged indulgence of these habits the reasons for their behaviour. This study is seeking to identify such factors in order to render help to these individuals.

Therefore, this study was carried out to determine the reasons for the prolonged indulgence in oral habits by school children aged between 6 to 12 years old. This study will enable us to have a better understanding of the causative agents of prolonged oral habit indulgence, with the view of formulating informed strategies for the cessation of these habits.

Materials and methods

This was a cross-sectional, questionnaire-based study carried out among two hundred and thirty –five (235) Primary and Junior High School children aged, six to twelve years in three private schools in Port Harcourt, Rivers State who indicated that they indulged in one oral habit or the other. Ethical clearance was obtained from the University of Port Harcourt Teaching Hospital Ethics and Research Committee. Children undergoing orthodontic treatment to break oral habits were excluded from participating in the study. Permission was sought and obtained from the Proprietor of each school prior to the commencement of the study. Thereafter, informed consent was sought and obtained from the parents or guardians of the children, whilst verbal assent was obtained from the children.

One of the investigators (EAA) explained in detail the purpose for the study and went over each item with the children and their teachers to ensure proper understanding before the questionnaire was filled individually. Copies of the questionnaires were subsequently filled either by the child alone or assisted by his/ her class teacher in the classroom and returned the same day.

Section A of the questionnaire captured socio-demographic data, Section B supplied information on the reasons for the participants' indulgence in non-nutritive oral habits. A total of 235 copies of the questionnaires were distributed but only 221 were completed properly and consequently analysed.

Data analysis was carried out using Statistical Package for Social Sciences (SPSS) software Version 20.0. The results were presented using frequencies, percentages and proportions for categorical variables and means together with standard deviations for continuous variables. Chi Square and Fisher's exact tests were used to test association between variables. Significance was determined at 95% confidence interval and statistical significance set at $p < 0.05$.

Results

A total of 235 school children admitted to indulging in oral habits, however only 221 (94.0%) were included in this study due to inappropriate filling of the questionnaire. The sample consisted of 118 (53.4%) female and 103 (46.6%) male 6-12 year-old schoolchildren with a mean age of 9.11 ± 2.1 years. Table 1 shows the age and gender distribution of the participants.

Table 2 shows the reasons for the prolonged indulgence in non-nutritive oral habits by

respondents classified based on their gender and age. Majority of the male participants (57, 63.3%) could not adduce any reason for the habit, while a significantly greater number (p=0.02) of females (50, 60.2%) than males, cited "I enjoy doing it" as their reason for indulging in oral habits. The influence of siblings and friends who also engaged in oral habits was the least given reason for both genders. Majority of the younger children (6-9 years old) claimed that it helped them to sleep (30, 85.7%) and they enjoyed the habit (54, 65.1%), whilst older children said it helped them to concentrate (19, 38.8%), they enjoyed it (29, 34.9%) and they did not know why (46, 51.1%) they continued to indulge in the habit. Out of the schoolchildren that cited shyness as the reason for their indulgence in an oral habit, majority (19, 86.4%) were also aged 6-9 years, this finding was also statistically significant (p=0.004).

Table 1. Age and gender distribution of participants

Age (years)	Female N (%)	Male N (%)	Total N (%)	P
6	19 (16.1)	16 (15.5)	35 (15.8)	
7	11 (9.3)	12 (11.7)	23 (10.4)	
8	20 (16.9)	8 (7.8)	28 (12.7)	
9	22 (18.6)	20 (19.4)	42 (19.0)	0.548
10	13 (11.0)	12 (11.3)	25 (11.7)	
11	11 (9.3)	14 (13.6)	25 (11.3)	
12	22 (18.6)	21 (20.4)	43 (19.5)	
Total	118 (53.4)	103 (46.6)	221 (100.0)	

Table 3 shows the association between individual non-nutritive sucking habits and the reasons for indulging in the habit. A statistically significant association was recorded between 'helping me to fall asleep' and the following oral habits: finger sucking, cheek biting, tooth grinding and anterior tongue resting position. 'Helps me to concentrate' was significantly associated with finger sucking and object biting. Furthermore, a significant association was also recorded between 'I enjoy doing it' and chewing gum, while shyness was associated with cheek biting. Chewing gum and tooth biting was associated with 'because my friends do it".

Discussion

The occlusal effects of these deleterious habits have been proven and widely discussed in the literature [8,10-12,15,17] However, the reasons for these habits are still not clear with some researchers having claimed it could be as a result of tiredness, insufficient satisfaction of sucking needs through breastfeeding during infancy, [10,13,19] emotional disturbances and pleasure,[14] while others attribute such to the emotional and learned behavioural theories.[13]

The reasons expressed by children of school age in this study for the prolonged engagement in these oral habits were found to vary with both age and gender. The younger children particularly the nine year -olds were able to adduce reasons for their indulgence in non-nutritive oral habits much more than the older children did. This implies that the younger ones indulged more purposefully in these habits than the older ones. The younger children claimed that they indulged in these habits in order to fall asleep and as a source of pleasure whilst the main reason adduced to this behaviour by the older children was the ability to concentrate. Most of the older children simply stated that they did not know why they indulged in these habits which implies that as people grow older these habits may not have any particular meaning and are simply repetitive actions mainly associated with pleasure. This is an important clinical finding as it may aid clinicians in understanding and proffering solutions to patients and their parents or caregivers that present in their clinics with such problems.

Among the schoolchildren, females claimed to enjoy indulging in non-nutritive oral habits more than the males, this was statistically significant. This may be due to the emotional nature of females, as they are known to feel and are seen to express their emotions more than males do. This suggests that these habits provide an increased level of emotional and psychological comfort and wellbeing to the female child. This is corroborated in other studies among younger children where females were found to indulge more in the oral habit than males. [15, 16, 20] This emotional response of the female child is also similar to findings by other researchers that have

Table 2. Cross tabulation of reasons for indulgence in oral habits by gender and age

Reason	Gender			Age (years) n (%)							
	Male	Female	Fisher's Exact								
	N (%)	N (%)		6	7	8	9	10	11	12	P
Concentration	20 (40.8)	29 (59.2)	0.053	9 (18.4)	6 (12.2)	3 (6.1)	12 (24.5)	5 (10.2)	4 (8.2)	10 (20.4)	0.61
Helps to sleep	20 (57.1)	15 (42.9)	0.589	7 (20.0)	3 (8.6)	9 (25.7)	11 (31.4)	3 (8.6)	1 (2.9)	1(2.9)	0.006*
Enjoy it	33 (39.8)	50 (60.2)	0.002*	16 (19.3)	6 (7.2)	9 (10.8)	23 (27.7)	11 (13.3)	7 (8.4)	11 (13.3)	0.078
Shy	12 (54.5)	10 (45.5)	0.876	5 (22.7)	1 (4.5)	4 (18.2)	9 (40.9)	1 (4.5)	0 (0.0)	2 (9.1)	0.041*
Friends influence	2 (28.6)	5 (71.4)	0.189	1 (14.3)	1 (14.3)	0 (0.0)	3 (42.9)	1 (14.3)	1 (14.3)	0 (0.0)	0.577
Sibling influence	3 (27.3)	8 (72.7)	0.08	4 (36.4)	1 (9.1)	0 (0.0)	4 (36.4)	2 (18.2)	0 (0.0)	0(0.0)	0.111
Do not know	57 (63.3)	33 (36.7)	0.024*	13 (14.4)	8 (8.9)	13 (14.4)	10 (11.1)	12 (13.3)	14 (15.6)	20 (22.2)	0.383

*significant

Table 3: Association between individual non-nutritive sucking habits and the reasons for indulging in the habit.

Reasons for the. Habit	Non nutritive sucket habits Fisher's exact p value										
	Thumb sucking	Finger sucking	Tongue sucking	Lip sucking	Nail biting	Object biting	Chewing Gum	Cheek biting	Tooth Grinding	Tongue Thrusting	Anterior Tongue resting position
'Helps me to fall asleep"	0.127	0.001*	0.591	0.174	0.582	0.697	0.273	0.033*	0.013*	0.001*	0.176
'Helps me to concentrate"	0.077	0.055*	0.489	0.687	0.144	0.037*	0.813	0.155	0.818	0.796	0.134
"I enjoy doing it"	0.184	0.179	0.841	0.297	1.000	0.400	0.022*	0.315	0.548	0.264	0.130
"I am shy "	0.362	0.062	0.196	1.000	0.502	0.028	0.505	0.017*	0.198	0. 074	0.023*
"Because my friends do it"	0.083	0.085	0.597	1.000	0.255	1.000	0.051*	0.597	0.008*	0.562	0.456
"Because my brother/sister does it"	0.079	0.000*	1.000	0.237	1.000	0.747	1.000	1.000	0.000*	0.003*	0.225

*Significant

attributed these habits to the feelings of those that indulge in them. Individuals that indulge in these non-nutritive habits are said to experience happy, warm, contented feelings as well as an increased level of security. [13,15]

Finger sucking and object biting were the habits found most to enable the children to concentrate better in school. This finding may explain the common habit of 'pen biting' which is commonly seen among children and even adults while studying. This reason was found to become increasingly important as the children increased in age, indicating the increasing need for concentration as their studies increased in difficulty over time. This is an important finding because it is essential for schoolchildren to concentrate in order to excel in their studies. In our study, finger sucking, cheek biting, tooth grinding and tongue sucking were all given as reasons enabling sleep, especially by the younger children. The ability to fall asleep while indulging in these habits however was found to reduce with age. The older schoolchildren did not consider this as much of a factor as those aged 6-9 years. This can be related to the increased maturity of children as they grow.

Shyness was a factor for the younger children, though not as much for the older children. Cheek biting and anterior tongue resting position were the habits most significantly associated with being shy. Children tend to either become bolder or use other less obvious means to indicate their shyness as they grow older.

Peer pressure and modelling were also significant factors associated with oral habits among our participants. Sibling influence was associated with such habits as finger sucking, tooth grinding and tongue sucking; while modelling and influence from friends was associated with chewing gum and tooth grinding habits. Thus, it may be said that some oral habits, like other habits in general, may be learnt or copied from others.

One of the limitations of our study is the cross-sectional design of the study which may be prone to memory bias, bearing in mind also that the respondents were children. However, this does not invalidate the findings of this study, but provides a basis for future prospective studies in this area, in our environment.

It is of note that many of the children did not know why they indulged in these habits, thus did not attribute their behaviour to any particular reason. This makes a case for collaboration of orthodontists with psychologists in the management of prolonged indulgence in non-nutritive oral habits which are deleterious to the occlusion. Furthermore, this may also be a pointer to a possible genetic basis for some of these oral habits. In particular, some recent studies have reported that the digit sucking habit, may have a genetic basis. [21,22] Indeed, there is a need for further studies to explore the possibilities of behavioural genetics as possible aetiological factor for oral habits.

Conclusion

The younger children adduced various reasons particularly their ability to concentrate and shyness, to their indulgence in non- nutritive oral habits whilst the older participants particularly females adduced pleasure as the major reason. Majority of participants did not have any reason for these habits.

Recommendations

Based on the findings of this study, we recommend that orthodontists co-manage these patients with psychologists in order to achieve better patient cooperation and outcomes. In addition to this, there is a need for further studies to explore the possible role of genetics, as an aetiological basis for some of these oral habits.

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Design and evaluation of extemporaneous formulations for treating pulmonary hypertension in children.

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Abstract

Introduction: Children, being the most vulnerable group, whose health status require urgent attention, are constantly in need of extemporaneous formulations for the treatment of several clinical conditions, such as pulmonary hypertension (PH)

Method: Amiloride hydrochloride/ Hydrochlorothiazide (AH) combination, (1mg/ 10mg)/mL, and furosemide, 1mg/mL, were separately formulated into liquid dosage forms using simple syrup BPC, commercially available ascorbic acid syrup, deionized water and deionized water: propylene glycol (ratios 75:25, 65:35 and 50:50) as solvents. The formulations were analyzed for stability over a 7-day period at different storage conditions (27±2ºC protected from and exposed to sunlight, and refrigeration at 4±1ºC) using physical parameters, pH analysis, UV spectrophotometric assay and microbial count as assessment parameters.

Results: Significant changes were observed for formulations exposed to sunlight (27º±2ºC), while refrigerated formulations were the most stable to physical changes, but had increased viscosity. All formulations had reduction in pH values, however, formulations containing deionized water and propylene glycol were the most significant, with formulations protected from light at 27º±2ºC providing the least pH changes. Refrigerated formulations retained higher medicament percentages within official limits, while formulations exposed to light (27º±2ºC) had the highest loss of potency. Virtually all the formulations prepared with simple syrup BPC aided growth of lactose fermenters. Refrigerated formulations resisted microbial growth most. In terms of stability, the storage conditions can be ranked as $4^0 \pm 1^0$C > $27^0 \pm 2^0$C protected from light > $27^0 \pm 2^0$C exposed to light.

Conclusion: The refrigerated extemporaneous formulations were the most physically stable. Deionized water: propylene glycol (75:25) is the most appropriate solvent for formulating the formulations and should be used only for a maximum of 6 days. It is recommended that extemporaneous formulations containing Amiloride hydrochloride-Hydrochlorothiazide (AH) combination or furosemide are preferably stored at 4º±1ºC protected from light, as this offers good resistance to microbial growth.

Keywords: *Extemporaneous preparations, Children, Amiloride hydrochloride-Hydrochlorothiazide combination, frusemide, storage conditions.*

Résumé

Introduction : Les enfants, qui constituent le groupe le plus vulnérable et dont l'état de santé appelle une attention urgente, ont constamment besoin de formulations extemporanées pour le traitement de plusieurs affections cliniques telles que l'hypertension artérielle pulmonaire.

Méthode : Une combinaison d'hydro-chlorure d'amiloride et d'hydrochlorothiazide (AH) (1 mg / 10 mg) / mL et de furosémide, 1 mg / mL, a été formulée séparément dans des formes posologiques liquides en utilisant du sirop simple BPC, du sirop d'acide ascorbique disponible commercialement, et de l'eau désionisée : propylène glycol (rapports 75 : 25 ; 65 : 35 et 50 : 50) en tant que solvants. La stabilité des formulations a été analysée sur une période de 7 jours dans différentes conditions de stockage (27 ± 2 ° C protégés et exposés au soleil, et réfrigération à 4 ± 1 ° C) en utilisant des paramètres physiques, une analyse du pH, un dosage spectrophotométrique UV et une numération microbienne comme paramètres d'évaluation.

Résultats : Des changements significatifs ont été observés pour les formulations exposées à la lumière solaire (27 ° ± 2 ° C), alors que les formulations réfrigérées étaient les plus stables aux changements physiques, mais avaient une viscosité accrue. Toutes les formulations présentaient des valeurs de pH réduites. Cependant, les formulations contenant de l'eau désionisée et du propylène glycol étaient les plus significatives, les formulations protégées de la

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lumière à 27 ºC ± 2 ºC fournissant le moins de changements de pH. Les formulations réfrigérées conservaient des pourcentages de médicament plus élevés dans les limites officielles, tandis que les formulations exposées à la lumière (27 ° ± 2 ° C) présentaient la perte de puissance la plus élevée. Pratiquement toutes les formulations préparées avec du sirop simple BPC ont contribué à la croissance des fermenteurs de lactose. Les formulations réfrigérées ont le plus résisté à la croissance microbienne. En termes de stabilité, les conditions de stockage peuvent être classées de 4 ^{0}± 1^{0}C> 27 ^{0}± 2 ^{0}C à l'abri de la lumière> 27 ^{0}± 2 ^{0}C exposées à la lumière.

Conclusion : Les formulations réfrigérées extemporanées étaient les plus stables physiquement. Eau désionisée : propylène glycol (75 : 25) est le solvant le plus approprié pour la formulation des formulations et ne doit être utilisé que pendant 6 jours au maximum. Il est recommandé de conserver les formulations extemporanées contenant une association de chlorhydrate d'amiloride et d'hydrochlorothiazide (AH) ou du furosémide à une température de 4 ± 1 ºC, à l'abri de la lumière, comme ceci offre une bonne résistance à la croissance microbienne.

Mots-clés : *Préparations extemporanées, enfants, combinaison d'hydro-chlorure d'amiloride et d'hydrochlorothiazide, furosémide, conditions de stockage.*

Introduction

A significant quality of any extemporaneously prepared formulation is the assurance of the safety and efficacy of the pharmaceutical product in relation to a specified use, which has been reviewed and accepted by an official expert body [1]. In most cases, extemporaneous formulations are intended to satisfy a medicine or dosage form requirement that is not commercially available. A working definition of extemporaneous compounding is the mixing together of the ingredients in a prescription or drug formula, usually performed by a pharmacist to fill an individual order of a drug product that will be used for a relatively short period of time [2].

Children, being the most vulnerable group, whose health status requires urgent attention [3] are constantly in need of extemporaneous formulations for the treatment of several clinical conditions that do not have registered dosage forms for their treatment. This lack of drug formulations suitable for children is a worldwide concern, taken into consideration by some developed countries, as well as by organizations such as the World Health Organization [4]. This is further buttressed by the fact that pharmaceutical companies are sometimes reluctant to study drugs in children because of the complexity, difûculty, and cost of such trials [5]. However, the formulation of licensed drugs as extemporaneous preparations for children use has become common practice in our hospitals and community pharmacies [6, 7]. This development is based on therapeutic advances and adventure that has necessitated the compounding of drugs to suit the clinical needs of such patients. The common dosage form for children is liquid preparations; hence, almost all extemporaneous preparations for children are usually in this dosage form, thus, necessitating the need to ensure the delivery of requisite quality and safe dose consistently to the patient [2].

Pulmonary hypertension is a normal and necessary state for the fetus, however, when cardiopulmonary transition (characterized by a rapid fall in pulmonary vascular resistance and pulmonary artery pressure, and a rise in pulmonary blood flow) fails to occur at birth, then pulmonary hypertension becomes an issue of utmost emergency [8]. Pulmonary hypertension (PH), in children is a rare disease that may lead to morbidity and mortality in this vulnerable group. Unfortunately, the lack of sufficient controlled studies in children makes PH management challenging in paediatrics, with most therapeutic strategies based on extrapolation from adult studies and expert consensus [9]. In Nigeria, the commonest therapeutic approach to the treatment of paediatric PH is the use of first line PH drugs which are formulated extemporaneously on a child-by-child basis.

Diuretics (Amiloride hydrochloride-Hydrochlorothiazide (AH) combination, and furosemide) are the most prescribed of all the first line PH drugs [10, 11] and are readily available as tablets for adult use [12]. Therapeutic advances and adventure has necessitated the extemporaneous compounding of AH and furosemide in the treatment of PH in children. This study is aimed at examining the stability (physical, chemical and microbial) and content uniformity of extemporaneous formulations of Amiloride-hydrochlorothiazide combinations and Frusemide for use in children less than five years of age.

Materials and methods

Materials

Commercially available brands of combined 5mg amiloride hydrochloride and 50 mg hydrochlorothiazide tablets, 40 mg frusemide tablets,

ascorbic acid syrup (100mg/ml) and granulated sugar were procured from a registered pharmacy in Ibadan, Nigeria. De-ionized water, freshly prepared simple syrup (BPC), distilled water and analytical grade propylene glycol were obtained from the research laboratories of the Centre for drug discovery, development and production, University of Ibadan, Ibadan, Nigeria. Nutrient agar, petri dishes and agar plates were procured and made available by the Molecular Laboratory, University of Ibadan, Ibadan, Nigeria. All other reagents used were of analytical grade.

Methods

Preparation of extemporaneous formulations:

Powdered tablets equivalent to 1.0 mg amiloride hydrochloride and 10 mg hydrochlorothiazide per ml of the different solvents [Simple syrup BPC, commercially available ascorbic acid syrup, deionized water (boiled for 15 minutes and cooled prior to usage) and deionized water: propylene glycol (ratios 75:25, 65:35 and 50:50)] were prepared by trituration. The entire procedure was repeated for formulations containing 1mg/ml of frusemide for each solvent. Sufficient quantity of all the formulations were kept in transparent air tight bottles and stored at three different conditions: 27º±2 ºC protected from light, 27º±2 ºC exposed to light and 4º±1ºC over a 7-day period.

Physical examination:

The formulations from the three storage conditions were examined daily on days 0 to 6 for changes in colour, smell, redispersibility and turbidity.

Evaluation of the hydrogen potency of the formulations:

The change in the hydrogen potency (pH) of the extemporaneous formulations over the 7-day period was monitored using a Mettler Toledo pH meter (Mettler Toledo instruments and services, Greinfensee, Switzerland). The pH meter was set to the pH Mode and the temperature was adjusted to the working temperature of the electrode. The electrode was removed from the storage buffer solution, rinsed with de-ionized water and wiped dry. The electrode was then placed in the extemporaneous formulation to be tested, and the pH reading was taken after the display unit stabilized. The operation was conducted in triplicates daily over a 7-day period for all the formulations at the different storage conditions. The electrode was carefully rinsed with de-ionized water, wiped and returned to the storage buffer solution.

Ultra-violent spectroscopic assay of drug content

Assay of drug content of amiloride hydrochloride-hydrochlorothiazide (AM-HCT) formulations: The method developed by Abdelaleem *et al* [13] was adopted to determine the percentage of API in the AM-HCT tablets used for the formulations. Standard working solutions of hydrochlorothiazide and amiloride hydrochloride were prepared in the respective solvents and also in methanol at a concentration of 1 mg/ml. Accurate aliquots equivalent to (40 -200 µg) and (20 - 160 µg) of hydrochlorothiazide and amiloride hydrochloride respectively were transferred from their working solutions into a series of 10 ml volumetric flasks and volumes were completed to the mark with methanol (or the respective solvents) mixed well. Absorbance of the spectra of laboratory-prepared mixtures containing different ratios of amiloride hydrochloride and hydrochlorothiazide hydrochloride were measured at 361 nm corresponding to the contents of amiloride hydrochloride only, and at 277.2 nm corresponding to the total content of amiloride hydrochloride and hydrochlorothiazide in the mixture, using a UV Spectrophotometer (Shimadzu UV spectrophotometer UV-VIS model UV-1280). The concentration of amiloride hydrochloride alone and the total concentration of the two drugs were calculated from their corresponding regression equations. By subtracting amiloride hydrochloride concentration from the total mixture concentration, the actual concentration of hydrochlorothiazide in the mixture was obtained. The assay was carried out for all the extemporaneous formulations containing amiloride hydrochloride-hydrochlorothiazide at different storage conditions on days 0 to 6 (7 days).

Assay of drug content of frusemide formulations:

The method described by Naveed *et al* [14] was adopted to determine the percentage of API in the frusemide tablets used for the formulations. The absorption maximum for frusemide was obtained at 276nm. Standard stock solution containing accurately weighed 5mg of furosemide was transferred to a volumetric flask and sufficient solvent (used in preparing the extemporaneous sample undergoing assay) was added to produce 50ml. This was further diluted to obtain 1mg/ml of frusemide. Several serial dilutions of the standard solution were made and scanned at the wavelength of 276nm to obtain the calibration curve. Volume exactly equal to 1ml of the extemporaneously prepared formulations were also serially diluted and scanned at the wavelength of 276nm and the strength of the frusemide was extrapolated from the

calibration curve obtained. The assay was carried out for all the extemporaneous formulations containing frusemide at different storage conditions on days 0 to 6 (7 days)

Each colony forming unit (CFU) per mL of extemporaneous formulations (and the control formulations) was computed using equation (i): CFU/mL =

Table 1: List of abbreviations

Abbreviation	Description of Abbreviation
F/AA	Frusemide tablet dissolved in commercially available ascorbic acid syrup (1mg/mL)
F/DW	Frusemide tablet dissolved in deionized water (1mg/mL)
$F/DW_{75}PG_{25}$	Frusemide tablet dissolved in deionized water: propylene glycol, ratio 75:25 (1mg/mL)
$F/DW_{65}PG_{35}$	Frusemide tablet dissolved in deionized water: propylene glycol, ratio 65:35 (1mg/mL)
$F/DW_{50}PG_{50}$	Frusemide tablet dissolved in deionized water: propylene glycol, ratio 50:50 (1mg/mL)
F/SS	Frusemide tablet dissolved in simple syrup BPC (1mg/mL)
M/AA	Amiloride-hydrochlorthiazide tablets in commercially available ascorbic acid syrup (1.0mg/10mg)/mL
M/DW	Amiloride -hydrochlorthiazide tablets dissolved in deionized water (1.0mg/10mg)/mL
$M/DW_{75}PG_{25}$	Amiloride -hydrochlorthiazide tablets dissolved in deionized water: propylene glycol, ratio 75:25 (1.0mg/10mg)/mL
$M/DW_{65}PG_{35}$	Amiloride -hydrochlorthiazide tablets dissolved in deionized water: propylene glycol, ratio 65:35 (1.0mg/10mg)/mL
$M/DW_{50}PG_{50}$	Amiloride -hydrochlorthiazide tablets dissolved in deionized water: propylene glycol, ratio 50:50 (1.0mg/10mg)/mL
M/SS	Amiloride -hydrochlorthiazide tablets dissolved in simple syrup BPC (1.0mg/10mg)/mL
NIL	No colony forming units observed
TNC	Colony forming units are too numerous to count

Any code with an extension of" _C "(in the microbial analysis table) is serving as the control of that code

Microbial analysis of the extemporaneous formulations

The extemporaneous formulations were observed for growth of microbial colonies. Total bacterial counts, coliform counts as well as presumptive *Salmonella* counts for the formulations were ascertained using the viable count technique over a 7 day period. Sampling was carried out on days 0, 1, 5 and 7. Exactly 0.1 mL of each formulation was serially diluted in 9.9 mL of 0.85 % normal saline. Exactly 0.1 mL of appropriate dilutions was aseptically inoculated into different plates containing nutrient agar, MacConkey lactose fermenting (LF) agar and MacConkey non-lactose fermenting (NLF) agar, and spread evenly on the agar surface with the aid of a pre-sterilised glass spreader. The dilution was increased as the days progressed. Formulations containing only the solvent without the active pharmaceutical ingredients were also prepared to serve as controal and subjected to the same conditions described for the extemporaneous formulations. Plates were then incubated at 37^0C for 24 hours after which plates were observed and the colony forming units (per mL) were counted and computed.

$$\frac{\text{Number of colonies counted per plate x dilution factor}}{\text{Volume of inoculum (=0.1)}}$$

Eqn (i)

Results and Discussion

Physical examination

Formulation failures in extemporaneously prepared oral suspensions usually result from physical incompatibilities, drug-excipient interaction issues and drug degradation. An insoluble drug suspended in a suitable vehicle may be less susceptible to drug degradation, but may settle out of the suspension over time, leading to sedimentation and caking. In this state, there will be a higher concentration of drug at the bottom of the bottle than at the top. If taken as it is, this will result in the patient being under dosed at the beginning and overdosed towards the end of a treatment course [15] (Tucker *et al*, 2010). In order to ensure uniformity of dose, these formulations need to be shaken properly before use and patients need to be adequately counseled.

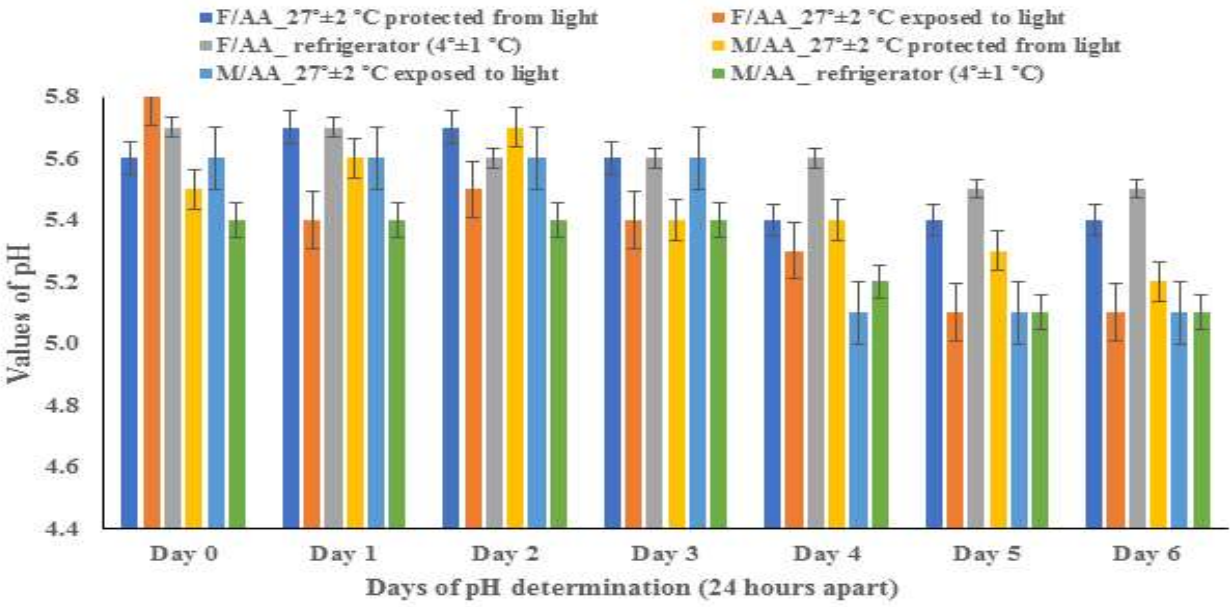

Fig. 1: Plot showing the effect of storage condition on pH of extemporaneous formulations prepared with ascorbic acid syrup.

Significant changes were generally observed for formulations stored at 27º±2 ºC exposed to sunlight, while formulations that were refrigerated were the most stable to changes in physical appearance, but had an observed increase in viscosity. Takeomo *et al* [16] documented that the rate of chemical degradation usually increases with temperature, a factor which is the basis for accelerated stability trials of pharmaceutical formulations. Thus, exposure to sunlight could have been responsible for the pronounced changes noticed in the formulations stored at 27º±2 ºC exposed to sunlight. The relatively insignificant changes observed for the formulations refrigerated (4º±1 ºC) is justifiable because, at low temperatures the rate of chemical reaction slows and physical appearance tends to remain unchanged [17]. However, formulations prepared using different ratios of deionized water: propylene glycols were observed to be relatively stable at all storage conditions, with the following physical stability ranking: $DW_{75}PG_{25}$ < $DW_{65}PG_{35}$ < $DW_{50}PG_{50}$. In 2015, Nalawade *et al* [18] observed that the presence of propylene glycol in a medium enhances the stability, thus providing an explanation for the relative stability as the content of the propylene glycol was increased. Generally, the formulations containing ascorbic acid as the solvent were noticed to become the most difficult to re-disperse with time. This is due to the highly viscous nature of the solvent. Patel *et al* [5] reported that loss of re-dispersibility of liquid formulations may create an impression of loss of efficacy.

Evaluation of potency of hydrogen (pH)

Hydrolysis, oxidation and reduction are the most common reactions usually associated with liquid preparations [19]. Usually the reaction rate or type is influenced by pH. The presence of excipients may reduce chemical stability of extemporaneous formulations prepared from tablets by changing the pH to a value at which more rapid degradation occurs. Thus, optimal pH is therefore required to maintain stability [19]. All the formulations had a reduction in pH values; an indication that the formulations had increased acidity with time. However, formulations prepared using different ratios of deionized water and propylene glycol had the most significant reduction in pH values. The storage condition that provided the least changes in pH was 27º±2 ºC protected from light, with the ranking for frusemide formulations as F/$DW_{50}PG_{50}$ > F/$DW_{75}PG_{25}$ > F/DW = F/SS > F/$DW_{65}PG_{35}$ > F/AA, while those containing amiloride-hydrochlorthiazide ranked M/$DW_{65}PG_{35}$ > M/$DW_{50}PG_{50}$ > M/DW > M/SS > M/AA, thus showing that the most acidic solvent was ascorbic acid as shown in Fig. 1. It was observed that the formulation containing frusemide stored at 4^0±1^0C (refrigerated) had the highest pH value, while frusemide formulations stored at 27^0±2^0C (exposed to and protected from sunlight) and amiloride-hydrochlorthiazide formulations stored in the refrigerator had the least pH values.

The significance of pH changes in extemporaneous formulations cannot be overemphasized. An extemporaneous preparation may have its safety profile compromised as a result of significant changes in pH, which could lead to therapeutic failures and subsequently hospital admission [5]. An alkaline product could become acidic and vice-versa, and since most extemporaneous formulations rarely contain buffers, pH changes must remain insignificant at the storage conditions of the formulations.

Ultra-violent spectroscopic assay of drug content

Extemporaneous preparations are often given arbitrary shelf-lives or shelf-lives based on published information [20]. It is important to ensure that an extemporaneous formulation packaged in a specific container will remain within its physical, chemical and microbiological specifications during storage for a specified time [21]. A major goal of extemporaneous formulations is to ensure that the active pharmaceutical ingredient (API) remains within the stipulated quantity throughout the duration

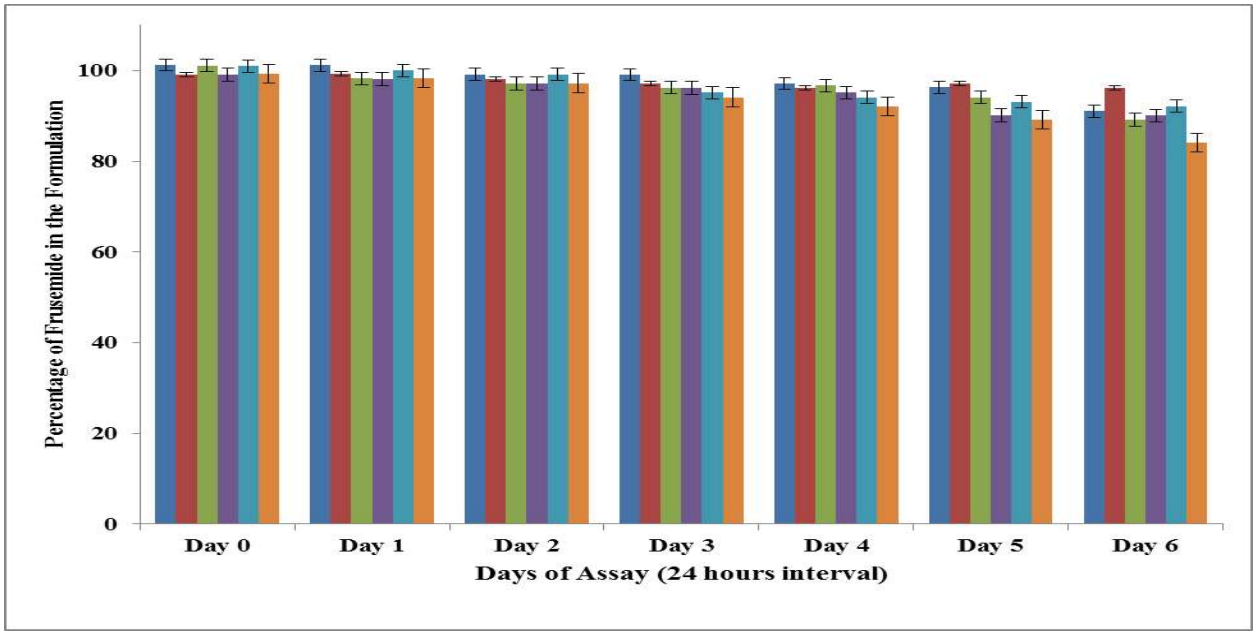

Fig. 2: Representative Plot showing percentage of frusemide in extemporaneous formulations stored at 4º±1 ºC (refrigerated).

API of use [22]. Practically, the shelf life can be assumed to be the time taken for the concentration of the drug to be reduced to 95% of its value when originally prepared [21]. On the other hand, a reduction of content down to 90% of theoretical value (with possible 95% confidence bounds) is generally regarded as the maximum reduction acceptable [23]. Thus, the limit of ≥90% of the initial concentration is also acceptable for extemporaneous formulations [24].

Assay of the formulation were carried out spectrophotometrically and some results are represented in Fig. 2. Formulations stored in the refrigerator (4º±1ºC) retained the highest percentage of the APIs (F/AA > F/SS > $M/DW_{75}PG_{25}$ > M/SS > F/DW > $M/DW_{65}PG_{35}$ > $M/DW_{50}PG_{50}$ > $F/DW_{65}PG_{35}$ > M/DW > M/AA > $F/DW_{50}PG_{50}$ > $F/DW_{75}PG_{25}$) as shown in Fig. 2, while formulations stored at 27º±2 ºC exposed to light had the highest loss of potency (F/AA > F/DW > M/DW > $F/DW_{75}PG_{25}$ > $M/DW_{75}PG_{25}$ > F/SS > $M/DW_{50}PG_{50}$ > $F/DW_{50}PG_{50}$ > M/SS > $F/DW_{65}PG_{35}$ > M/AA > $M/DW_{65}PG_{35}$). For the frusemide formulations stored in the refrigerator (4º±1ºC), the formulation containing deionized water: propylene glycol (75:25) as solvent had the highest loss of potency (From 99.45±0.23% to 81.13 ±1.16%). This further establishes the report that propylene glycol has the ability of restraining changes in the medium where it is prevalent [18]. Relatively, formulations containing deionized water as solvent were able to retain the percentage of the APIs above the limit of ≥ 90% (Fig.2) as proposed by Glass and Haywood (2006). This reflects that the absence of specific ions (in de-ionized water), helped to maintain the shelf life of the formulations at all the storage conditions evaluated. The use of commercially available ascorbic acid syrup (containing antioxidants) and simple syrup BPC (containing a high glucose content) did not offer any

Table 2: Microbial evaluation of formulations stored at 4º±1 ºC (refrigerated): Day 6 count

Sample	CFU/mL(Nutrient Agar)				CFU/mL(MacConkey Agar_LF)				CFU/mL(MacConkey Agar_NLF)			
Dilution Factor	10^{-1}	10^{-2}	10^{-4}	10^{-6}	10^{-1}	10^{-2}	10^{-4}	10^{-6}	10^{-1}	10^{-2}	10^{-4}	10^{-6}
F/AA	1600	5000	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
F/AA_C	500	2000	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
F/DW	4400	11000	8	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
F/DW_C	1400	3000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$F/DW_{75}PG_{25}$	1900	4000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$F/DW_{75}PG_{25}$_C	4400	9000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$F/DW_{65}PG_{35}$	5300	11000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$F/DW_{65}PG_{35}$_C	900	7000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$F/DW_{50}PG_{50}$	2600	7000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$F/DW_{50}PG_{50}$_C	800	9000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
F/SS	1600	11000	500000	30000000	TNC	TNC	TNC	120000000	700	5000	400000	40000000
F/SS_C	100	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
M/AA	600	1000	NIL	NIL	NIL	NIL	NIL	NIL	3	NIL	NIL	NIL
M/AA_C	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
M/DW	2300	11000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
M/DW_C	1200	10000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$M/DW_{75}PG_{25}$	1900	8000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$M/DW_{75}PG_{25}$_C	1400	13000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$M/DW_{65}PG_{35}$	1600	8000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$M/DW_{65}PG_{35}$_C	1100	9000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$M/DW_{50}PG_{50}$	1200	10000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
$M/DW_{50}PG_{50}$_C	1100	9000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
M/SS	2400	14000	100000	10000000	TNC	TNC	TNC	10000000	NIL	NIL	NIL	NIL
M/SS_C	1100	9000	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL

advantage as the APIs still degraded in these solvents.

Microbial analysis of extemporaneous formulations

The assessment of the microbiological content of non-sterile formulations is important in view of the fact that microbes can reduce the therapeutic efficiency of the formulation or introduce infections to the consumer of such products. It becomes even more pertinent for extemporaneous formulations that contain oral tablets that are not originally expected to be in liquid medium prior to administration. Thus, at every stage of formulation, products should be prevented from microbial contamination. The extemporaneous formulations were observed for microbial growth over a 7-day period using nutrient agar, MacConkey (Lactose fermenting,LF) agar and MacConkey (Non-Lactose fermenting, NLF) agar as the bacteria growth substrates. MacConkey agar is a selective and differential medium designed to isolate and differentiate enterics based on their ability to ferment lactose. The crystal violet and bile salts present inhibits the growth of gram-positive organisms which allows for the selection and isolation of gram-negative bacteria. Enteric bacteria that have the ability to ferment lactose can thus be detected. Lactose Fermenters (LF) such as *Escherichia coli, Citrobacter* and *Klebsiella* may be isolated using MacConkey (LF) agar, while lactose non-fermenters (LNF) such as Salmonella may be isolated using the MacConkey (NLF) agar.

The formulations that were refrigerated resisted the growth of microbes more than the other formulations. In terms of formulation stability, the storage conditions can be ranked as $4^0\pm 1^0C >$ $27^0\pm 2^0C$ (protected from light) > $27^0\pm 2^0C$ (exposed to light). The control formulations had no growth on the first day of microbial analysis, however, growth was observed towards the last two days for the control formulations, with special reference to formulations stored at $27^0\pm 2^0C$ exposed to ligh as shown in Table 3t. Growth of lactose fermenting microbes was observed for relatively all the formulations prepared with simple syrup BPC, while formulations prepared with commercially available ascorbic acid had the highest observed resistance to microbial growth.

Conclusion and Recommendation

Physical stability of the formulations is best at storage condition of 4º±1 ºC (refrigerated), while deionized water/propylene glycol (75:25) is the most appropriate solvent for the formulations and should be used only for a maximum of 6 days. Quantitative estimation of the active pharmaceutical ingredients in the extemporaneous

formulations indicate that the presence of propylene glycol has the ability of restraining changes in the medium, and subsequently retarding loss of potency within 7 days. Refrigeration of extemporaneous formulations containing frusemide or amiloride-hydrochlorothiazide combinations at 4º±1 ºC protected from light offer good resistance to microbial growth.

It is recommended that more research into different solvents for use in extemporaneous formulations containing different medicaments be carried out, to enable community and hospital pharmacists have a data base of compatible solvents and medicaments. This is especially useful for targeted patient groups, such as children, whose dosage forms are often in this category.

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Knowledge, attitude and practice of breast self-examination among female medical students of the University of Ibadan, Oyo State, Nigeria.

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Abstract
Introduction: Breast cancer is one of the leading causes of cancer deaths among women. Early detection using clinical breast examination (CBE), mammography, and breast self-examination (BSE) is important in improving treatment outcome and prognosis of persons with breast cancer.
Objectives: This study investigates the knowledge, attitude and practice of BSE among female medical students at University of Ibadan, Oyo state, Nigeria.
Materials and methods: A hundred and twenty (120) medical students were selected by stratified random sampling methods and their knowledge, attitude and practice of BSE were assessed by self-administered questionnaires.
Results: The mean age of the participants was 20.53 ± 2.18 years. Few students (5.8%) reported a positive family history of Breast cancer. About two thirds, (69.2%) of students had good knowledge of BSE and this was higher among clinical students (p>.005). Almost three quarters, (74.2%) of students practice BSE and good practice was highest in the 300 level class (95%). There were significant associations between age, academic level and knowledge of BSE with the practice of breast self- examination.
Conclusion: The study showed that good knowledge and attitude towards BSE corresponded with a good practice of BSE. This might be explained by the health care information they have received in the course of their studies. One can therefore safely propose that giving relevant health care information to other students may improve the practice of BSE and help increase early detection of breast cancer.

Keywords: *Breast cancer, mammography, stratified random; CBE, BSE*

Résumé
Introduction : Le cancer du sein est l'une des principales causes de décès par cancer chez les femmes. La détection précoce au moyen de l'examen clinique du sein (CBE), de la mammographie et de l'autoexamen du sein (BSE) est importante pour améliorer les résultats du traitement et le pronostic des personnes atteintes du cancer du sein.
Objectifs : Cette étude examine les connaissances, l'attitude et la pratique de BSE chez les étudiantes en médecine de l'Université d'Ibadan, État d'Oyo, Nigéria.
Matériels et méthodes : Cent vingt (120) étudiantes en médecine ont été sélectionnées selon des méthodes d'échantillonnage stratifié aléatoirement et leurs connaissances, leur attitude et la pratique de BSE ont été évaluées à l'aide de questionnaires autoadministrés.
Résultats : L'âge moyen des participantes était de 20,53 ± 2,18 ans. Peu d'étudiantes (5,8%) ont signalé des antécédents familiaux de cancer du sein. Environ deux tiers (69,2%) des étudiants avaient une bonne connaissance de BSE, ce qui était plus élevé chez les étudiantes en clinique (p> 0,005). Près de trois quarts (74,2%) des étudiantes pratiquent BSE et les bonnes pratiques étaient plus élevées dans la classe de 3ème année (95%). Il existait des associations significatives entre l'âge, le niveau universitaire et la connaissance de BSE avec la pratique de l'autoexamen des seins.
Conclusion : L'étude a montré qu'une bonne connaissance et une bonne attitude à l'égard de BSE correspondaient à une bonne pratique de BSE. Cela pourrait s'expliquer par les informations sur les soins de santé qu'ils auraient pu recevoir au cours de leurs études. On peut donc suggérer en toute sécurité que le fait de donner des informations pertinentes sur les soins de santé à d'autres étudiantes pourrait améliorer la pratique de l'BSE et contribuer à accroître la détection précoce du cancer du sein.

Mots-clés : *cancer du sein, mammographie, stratifiée aléatoire, CBE, BSE*

Introduction

Breast cancer is the most frequently diagnosed malignancy in women both in the developed and less developed world [1]. It is the leading cause of cancer related death in women with a global estimation of

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over 508,000 women death in 2011 resulting from breast cancer (Global Health Estimates, WHO 2013) [1]. In Nigeria, the burden of breast cancer is enormous with more than two third of cancer patients presenting with stage 3 or 4 diseases as at the time of first visit to the hospital [2]. This is further worsened by limited resources in terms of skilled personnel and available equipment for diagnosis and treatment of cancer patients as well as poverty, as most cancer patients in Nigeria pay from their pocket to access these facilities.

Favourable survival outcome is associated with increased cancer awareness, early detection and improvement in therapy [3]. Breast self-examination (BSE) is one of the screening methods currently recommended by the American cancer society for the early detection of breast cancer [4]. Segni *et al* found that over 90% of cases of breast cancer can be detected by women themselves, stressing the importance of Breast self-examination [5]. BSE is a simple, quick and cost-free method of screening for breast cancer. In view of this, BSE will likely be the most feasible approach to wide population coverage in many developing countries like Nigeria [6].

Previous study done among undergraduate had shown low level of knowledge and attitude towards the practice of BSE among undergraduate in Nigeria [7]. However, Adeyemo *et al* demonstrated that majority of nursing students at a tertiary institution in Ogbomoso, Oyo State were knowledgeable about BSE and most of them practiced BSE [8]. To the best of our knowledge, no similar study was carried out among female medical students. Therefore, there is need to evaluate knowledge, attitude and practice of BSE among female medical students who are going to be our future health personnel. The aim of this study is to assess knowledge, attitude and practice of BSE among female medical students at University of Ibadan, Oyo State, Nigeria.

Methods

A descriptive cross-sectional study was carried out between January and February, 2017 on female undergraduate medical students of University of Ibadan. A total number of 120 students were recruited for the study. Participants were selected using a stratified random sampling which ensured that each stratum (class level) was represented in the study. A structured and validated questionnaire consisting of mainly closed ended questions about socio-demographic characteristics, knowledge, attitude and practice of BSE was used to collect data. The data was analysed using frequencies, percentages, tables, bar and pie charts and hypotheses were tested using chi square with the statistical package for social sciences (SPSS) version 21.

Results

Socio-demographics characteristics

The mean age of the respondents was 20.53 ± 2.185 years, with age range of 16 to 26 years (figure 1). Majority, (66.7%) of the students were in the clinical blass (300-600 levels) 75 out of 120 (62.5%) were receiving below N20, 000 monthly and 5.8% of students reported a positive family history of Breast cancer (Fig. 2)

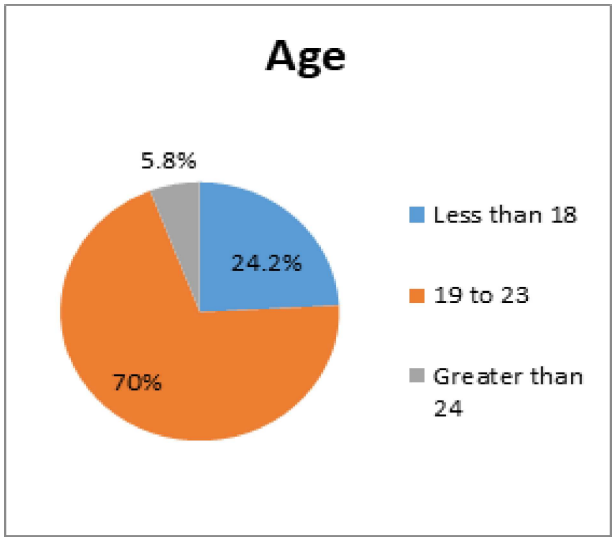

Fig. 1: Age distribution of students

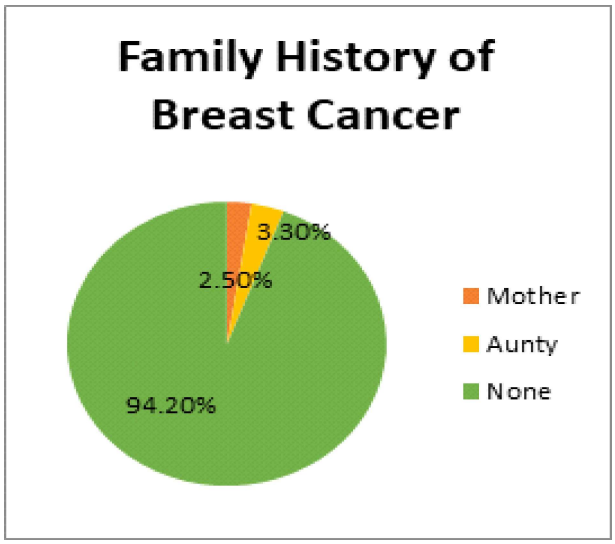

Fig. 2: Students with family history of breast cancer

Knowledge of breast self - examination

Most respondents, 83 (69.2%) learnt about BSE first from health professionals after crossing to the clinical year, 30 (25%) from the internet, 26 (21.7%) learnt from television, 14(11.7%) from friends, 12

(10%) from radio and 5 (4.2%) learnt about BSE only from this study (figure 3).This means that many students learnt about BSE from health professional in their clinical year as compared to their pre-clinical year. As regards knowledge of how BSE is done, 78 (65%) students knew BSE should be done monthly, 103 (85.8%) students knew BSE is done by palpating with the palm and 3 fingers and 50 (41.7%) knew BSE should be performed in 2 positions: when lying down and standing in front of a mirror. More than half of the students (61.6%) did not know the correct age to begin BSE and 68.3% knew that both male and female are required to perform breast self-examination.

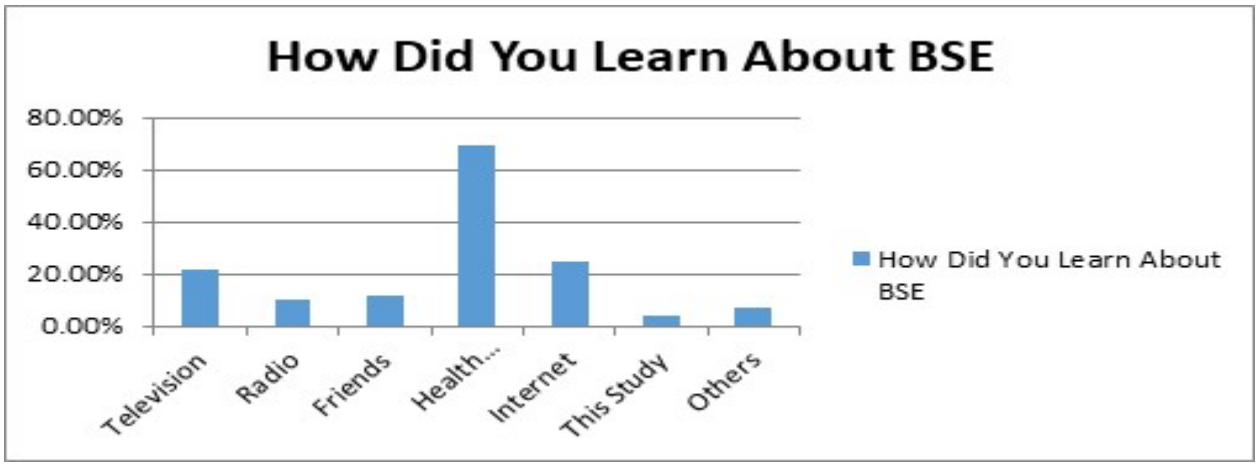

Fig. 3: How students learnt about BSE

good knowledge of how to properly perform BSE. This showed that good knowledge of BSE was higher among clinical students while poor knowledge of BSE was higher among the preclinical students (figure 4).

Attitude towards breast self - examination

Majority, 119 (99.2%) students think BSE is necessary (Figure 5) though 14 (11.7%) students think it is necessary only when one has a family history of breast cancer and 2 (1.7%) students think it is necessary simply because other people perform it.

Most of the participants (94.2%) in this study indicated that they would like to learn more about BSE (Fig. 6)

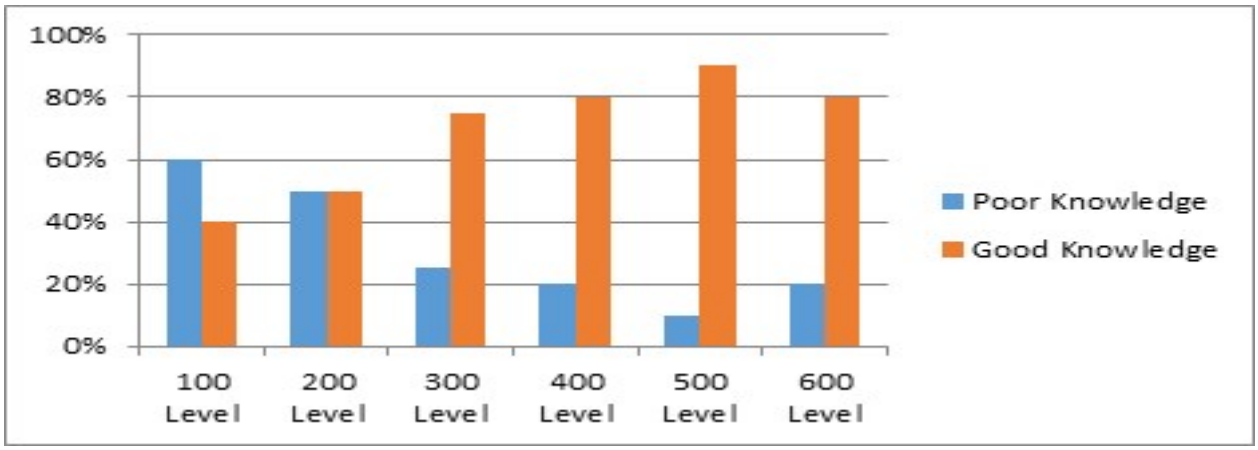

Fig. 4: Knowledge of BSE across the different academic levels.

Knowledge of how to properly perform BSE was further categorized into good and poor knowledge. Those who correctly answered 3 or more questions in this section, were said to have good knowledge, while those who answered 2 or less questions correctly were said to have poor knowledge of BSE. In all, 69.2% of students had

Practice of breast self-examination

The study revealed that 89 (74.2%) students practiced BSE. Among those who practiced BSE, about half, 46 (52.3%) performed it monthly, 46 (51.2%) started practicing BSE after 19 years of age, 70 (78.7%) felt their armpit when performing BSE, 78(87.6%) raised one hand above their head when performing

BSE, 64 (71.9%) performed BSE in the morning and less than half, 37 (41.6%) performed BSE in 2 positions; while standing in front of a mirror and lying down. The percentage of students who practiced BSE was higher among clinical than pre-clinical students (figure 7). The level of good practice of BSE was highest in the 300 level students while poor practice was highest in the 200 level pre-clinical students (figure 8). The study found a statistically significant association between academic levels and practice of BSE (p = 0.004).

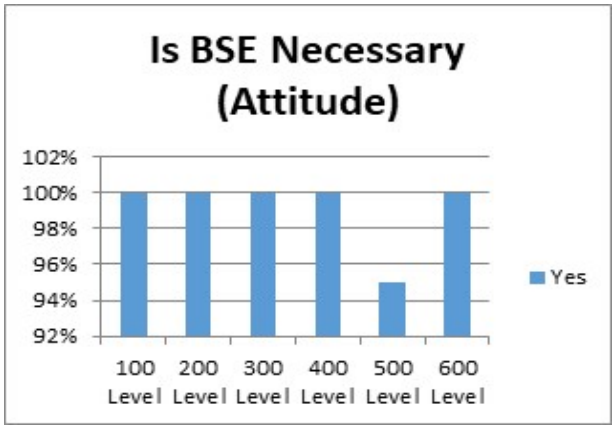

Fig. 5: Attitude towards BSE

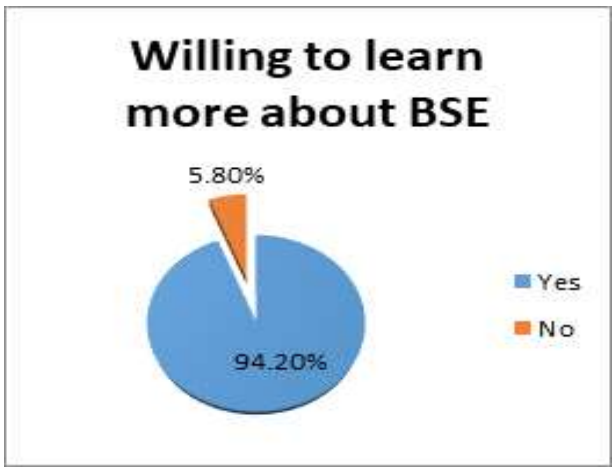

Fig. 6: Students willing to know more about BSE

Almost three-quarters 74.2% of students who practiced BSE also discussed BSE with someone. Among these, 43.2% discuss with colleagues, 45.9% discuss with non-medical friends 29.7% with mother, 25.7% with sisters, 23% with female relatives 14.2% and others 8.1%. 14 out of 89 (15.7%) students who practiced BSE have found something unusual in the course of BSE. Ten (11.2%) students found a breast lump, a student (1.2%) found milky nipple discharge and three students (3.4%) found armpit lump/lymph node. Among 14 students, who found something unusual, 10 consulted a doctor, out of which 2 students had a lumpectomy and 4 did nothing about it. The factors that affects the practice of BSE is shown in (figure 9) below.

Students who received more income were observed to practice BSE more than those who received less income, this finding was not statistically significant (p-value 0.834).

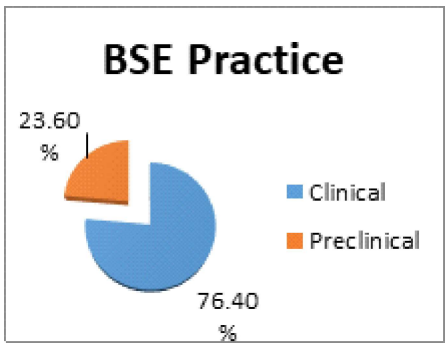

Fig. 7: comparing BSE practice between clinical and preclinical students

There was a statistically significant association between age and practice of BSE (p=0.000002). This could however be due to the fact that those in clinical class were older, had more knowledge of and practiced BSE more than those in the preclinical class.

This study found a statistically association between knowledge and practice of BSE (p =0.014). Although the practice of BSE was higher among those family history of breast cancer, there was however, no statistically significant association between family history of breast cancer and practice of BSE (p =0.584).

Discussion

Knowledge about Breast self - examination

The age of the students ranged from 16 years to 26 years with the mean age group as 20.53 ± 2.185 years. The study was appropriate in this age group as most of them were young adults in the medical field and should have in-depth information about breast self-examination to enable them educate and advice their patients effectively. Similar age group of 15 to 26 years was used in a study carried out at the University of Lagos by Bassey *et al* [9]. This is the usual age range for medical students who spend minimum of six years in the university.

The study revealed that medical students at the University of Ibadan, Nigeria, were well informed about BSE as 83 (69.2%) of the 120 respondents had good knowledge. This contrasts the results found in similar studies among medical students by Ayed A *et al* [4] in Jenin, Palestine and Nemenqani *et al*.[12] in Taif, Saudi Arabia that found only 15.5% and

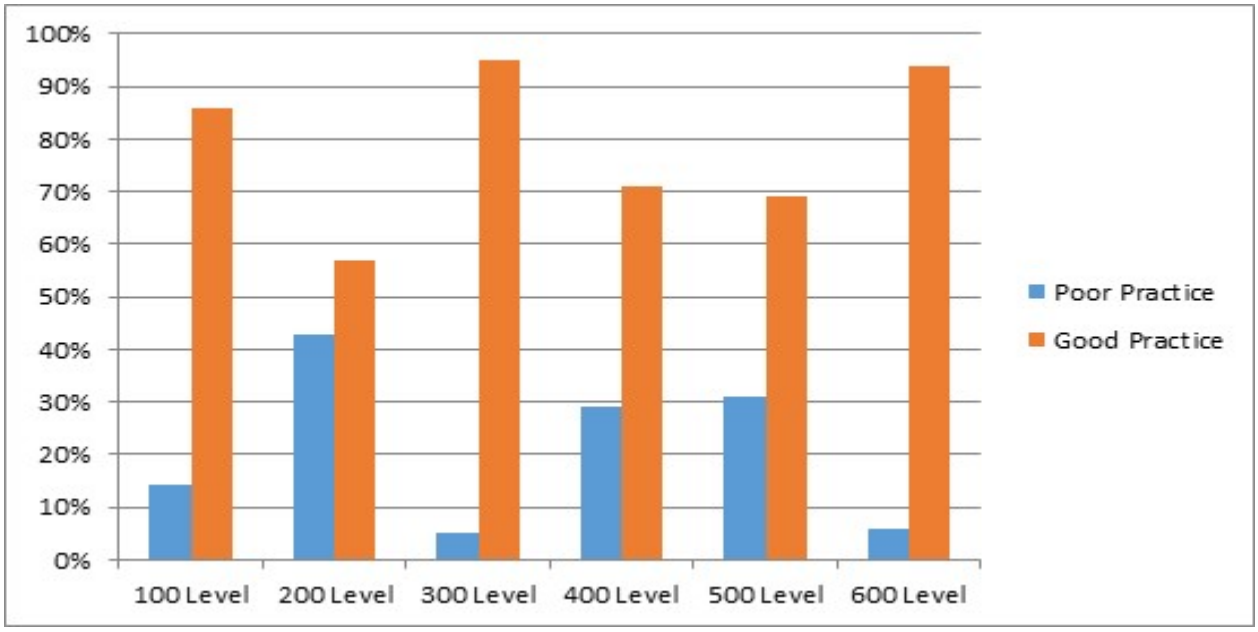

Fig. 8: Practice of BSE across academic levels

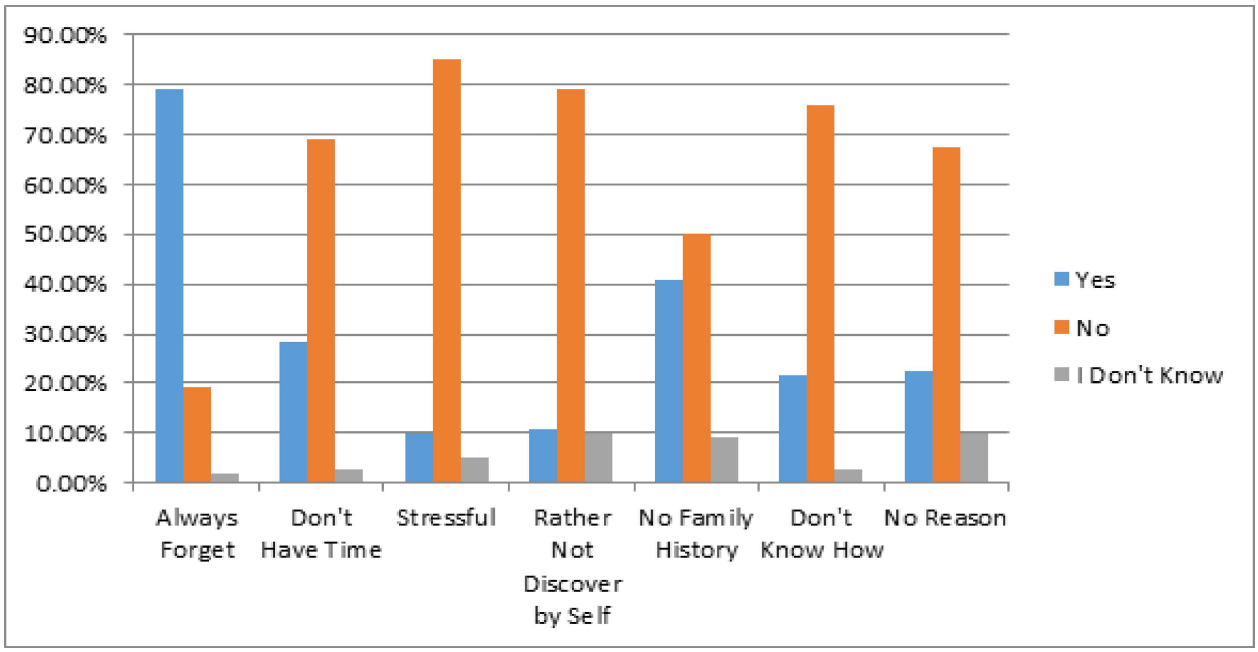

Fig. 9: Factors affecting BSE practice

28.1% with good knowledge of BSE . The reasons for this high disparity cannot be immediately identified.

The commonest source of information about BSE in this study was health professionals (i.e. Medical Teachers). This is in contrast to findings by Gwarzo *et al* [14] and Nemenqani *et al* [12], whose respondents learnt mainly from television and radio. Another similar study done among secondary school teachers in Oyo state, Nigeria by Faronbi and Abolade [11] found majority, 55% of respondents learnt about BSE from television and radio. This result found in this study is not surprising considering that this cohort are medical students, with frequent contacts with health professionals who are involved in their training.

In this study, good knowledge of BSE was higher among clinical students compared to the pre-clinical students. This was expected because medical students at the University of Ibadan are taught breast examination as part of their curriculum and are exposed to the management of breast cancer patients during their clinical clerkship years in Department of Surgery, the posting which starts only in the third year in medical school.

Attitude to breast self - examination

Almost all, 119 out of 120 (99.2%) students had good attitude towards BSE. One student however thought it wasn't necessary because BSE didn't detect breast cancer early enough. Ayed A *et al* [4], Rosemary *et al*. [9] Nemenqani *et al.* [12] and Yakubu *et al* [13] all found good attitude towards BSE among their respondents with no negative attitude. This is explained by the category of respondents being medical students. Faronbi *et al* [11] found a contrasting result in a similar study among secondary school teachers in Oyo state where 48% had negative attitude compared with 24% with positive attitude towards BSE. It can be inferred that prior lecture and discussion about breast cancer can improve attitude of people to BSE. Majority of the students (94.2%) were willing to get more information about BSE. This was similar to 93.2% found in Lagos Nigeria [9].

Practice of breast self - examination

The study revealed that 89 out of 120 (74.2%) students practiced BSE. In a similar study among nursing students it was also found that 87.5% of the respondents performed breast self-examination regularly [9]. On the contrary, Nemenqani *et al.* [12] studied BSE among medical students in Saudi Arabia and revealed that only 17% of female medical students reported that they performed BSE regularly, once per month. This could be explained by the fact that about 75% of their study population was in the preparatory or preclinical class in contrast to our study. Another contrasting result was found in Zaria, where poor practice of BSE 32.1% was observed among female university students [14].They however found that respondents in the health related disciplines were two times more likely to know and three times more likely to practice BSE than respondents in other disciplines.

Majority, 79.2% of students attributed forgetfulness as the major factor affecting practice of BSE. Among other reasons given were absence of family history of breast cancer 40.8%, busy schedules 28.3%, no reason 22.5%, lack of knowledge on how to perform BSE 21.7%, undisclosed reasons 10.8% and too stressful 10%. A similar study in Borno state, Nigeria revealed that the highest proportion, 36.7% of their respondents said the reasons for not practicing breast self-examination was forgetfulness, 22% showed time constraint as their reason, 16.3% stated lack of skills in performing breast self-examination, 11.0% fear of unknown, 11% stress and 2.8% show other reasons for not performing breast self-examination[15].

Though, in this study, the practice of BSE was higher among those who had family history of breast cancer, there was however, no statistically significant association between family history of breast cancer and practice of BSE. This was similar to results obtained by Adeyemo et al. [8] in Edo state, Nigeria, which also revealed no relationship between family history of breast cancer and practice of BSE.

Conclusion

This study revealed good knowledge, good attitude towards BSE and a good practice of Breast self-examination among female medical students at University of Ibadan, Nigeria. This was attributed to their exposure to training on breast cancer in the course of study. Therefore, adequate and regular lectures and training on prevention of breast cancer will improve the practice of BSE among general female population irrespective of their profession.

Recommendations

Breast self-examination is a simple and inexpensive tool for early detection of breast cancer. We recommend that efforts should be intensified by health professionals and the government to provide relevant breast cancer information through the media; television/ radio as these were common means by which respondents got their information about BSE. The proper method and frequency of BSE should however be emphasized to eliminate poor practice and the overall practice would translate to a good practice of BSE. Students should be advised to seek medical care for any unusual finding in their breast and be encouraged to set a monthly reminder to practice BSE as this will help eliminate forgetfulness which is a major factor affecting the practice of BSE. Since most students have smartphones, the reminder could be set on their phones. On the other hand mobile apps could be created to remind people of BSE, teach how to perform it and provide facility to record and recall results and findings.

The respondents generally discussed BSE more with their peers, thus medical students should therefore create awareness in the university campus on BSE and should be encouraged to also discuss BSE with their siblings and parents irrespective of the presence of a family history of breast cancer.

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Correlation of whole blood viscosity and HbA1c with age in diabetes patients: implications for diabetes research and management in low-mid income countries

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Abstract

Background: There is a concept of association between whole blood viscosity (WBV) and glycated haemoglobin (HbA1c), but the odds that both biomarkers increase with age are yet to be exhaustively investigated. The aim of this Health records-based study was to determine the correlation of age with HbA1c as well as age and WBV in diabetes patients.

Methods: The setting of this work was a medical General Practice in a regional Australia. De-identified pathology data of diabetes patients, which included HbA1c, routine biochemistry and haematology results were mined. WBV was derived from haematocrit and serum total protein levels. Statistical analyses included comparison of biomarkers between stratified aged-groups, the correlations with age, and the odds ratio of the variables to increase with age.

Results: Age showed a weak negative correlation with HbA1c (r = -0.25), there were odds that HbA1c can increase by 1% in 2-years ($p < 0.04$). There was weak positive correlation of WBV with age in oldest aged-group (r = 0.27), but a confounding effect of anaemia causing the odds to decrease 1% in 3-years. HbA1c and WBV were moderately positively correlated in patients with good glycaemic control (r = 0.39).

Conclusion: The notion that HbA1c and WBV increase with age requires rethinking, especially for individuals living with diabetes and undergoing treatment. Implications for interpreting the results of these two tests in diabetes research and clinical management is discussed in the context of limitations in low and middle income countries.

Keywords: *Age; blood viscosity; diabetes treatment; glycated haemoglobin; associations*

Résumé

Contexte : Il existe un concept d'association entre la viscosité du sang total (WBV) et l'hémoglobine glyquée (HbA1c), mais les probabilités que les deux biomarqueurs augmentent avec l'âge ne font pas encore l'objet d'études exhaustives. Le but de cette étude basée sur les dossiers de santé est de déterminer la corrélation de l'âge avec l'HbA1c ainsi que de l'âge et WBV chez les patients diabétiques.

Méthodes : Le cadre de ce travail était une pratique médicale générale dans une région de l'Australie. Des données de pathologie non identifiées de patients diabétiques, comprenant l'HbA1c, les résultats de routine en biochimie et en hématologie, ont été extraites. WBV était dérivé de l'hématocrite et des taux de protéines sériques totales. Les analyses statistiques comprenaient la comparaison de biomarqueurs entre les groupes d'âge stratifiés, les corrélations avec l'âge et le rapport de cotes des variables pour augmenter avec l'âge.

Résultats : L'âge montrait une faible corrélation négative avec HbA1c (r = -0,25). Il y avait des chances pour que HbA1c augmente de 1% en 2 ans ($p<0,04$). Il y avait une faible corrélation positive entre WBV et l'âge dans le groupe le plus âgé (r = 0,27), mais un effet de confusion de l'anémie entraînant une diminution de 1% de la probabilité en 3 ans. HbA1c et WBV étaient modérément corrélées positivement chez les patients ayant un bon contrôle glycémique (r = 0,39).

Conclusion : La notion selon laquelle HbA1c et WBV augmentent avec l'âge nécessite de repenser, en particulier pour les personnes atteintes de diabète et en cours de traitement. Les implications pour l'interprétation des résultats de ces deux tests dans la recherche sur le diabète et la gestion clinique sont discutées dans le contexte des limitations dans les pays à revenu faible et intermédiaire.

Mots - clés : *âge ; viscosité du sang ; traitement du diabète ; hémoglobine glyquée ; associations*

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Introduction

There are indications of positive associations between age and some biomarkers of diabetes management including glycaemia (plasma glucose level, glycated haemoglobin (HbA1c), haemorrheological indices (white blood cells, blood viscosity), serum lipid profile and renal function [1, 2]. There is a suggestion of correlation between glycaemia and haemorrheological indices since some treatment regimens in diabetic patients have favourable effects on HbA1c, blood glucose and blood viscosity [3]. The suggestion also corroborates with the speculation that whole blood viscosity (WBV) increases with age [4, 5] and possibly by a mechanism that does not involve the effects of haematocrit and plasma viscosity [5]. Suffice to say that there is abundance of literature supporting the notion that aging impacts on HbA1c [3-6], as well as WBV [7-9]. However, the extent that this notion impacts on interpretation and utilization of HbA1c and WBV test results in diabetes research and clinical management requires elucidation. It must be pointed out that most of the studies reporting on association of aging with HbA1c are on non-diabetes individuals; but how this association may be confounded in diabetic patients is not sufficiently elucidated.

Studies also report that GFR decreases with advancing age and that old age is associated with chronic kidney disease (CKD) [10], which results in proteinuria [11], that leads to hypoproteinaemia [12, 13]. Albuminuria leads to hypoalbuminemia, increases synthesis of apolipoproteins and reduces plasma oncotic pressure, which increases renal sodium reabsorption [14]. The change in serum protein level is affected by renal excretion [13], and besides GFR as well as by factors such as sex, age, race, weight and smoking status [15]. It is reported that albuminuria may be caused by high WBV in non-CKD essential hypertensive patients in view of the fact that increased blood viscosity is associated with decreased renal function [16].

It is important to consider the physiological feedback effect of albuminuria that leads to hypoproteinaemia, which then reduces the WBV (Fig 1) – i.e. that blood viscosity can be influenced by the effect of proteinuria [17]. There is knowledge that:

- Reduced glomerular filtration may proportionally increase blood viscosity [18, 19]
- High blood viscosity induces proteinuria [20-23].
- Proteinuria leads to hypoproteinaemia [24] which feedforwards to low viscosity of blood.

Indeed, blood viscosity may be a target for management in renal complication of diabetes [22], and a useful biomarker in assessment of cardiovascular risk [23]. The implication is the potential for WBV to increase with age, which is complicated or confounded by the impact of renal function on plasma protein as per the negative feedback cycle (Fig 1). Therefore, the question is *what are the odds that WBV increases with age?* Factors such as age and red blood cell (RBC) indices may be responsible for high WBV [16, 25, 26], and indeed, there is opinion that haematocrit (HCT) is an important factor for WBV [16]. HbA1c values and interpretation are affected by haemoglobin

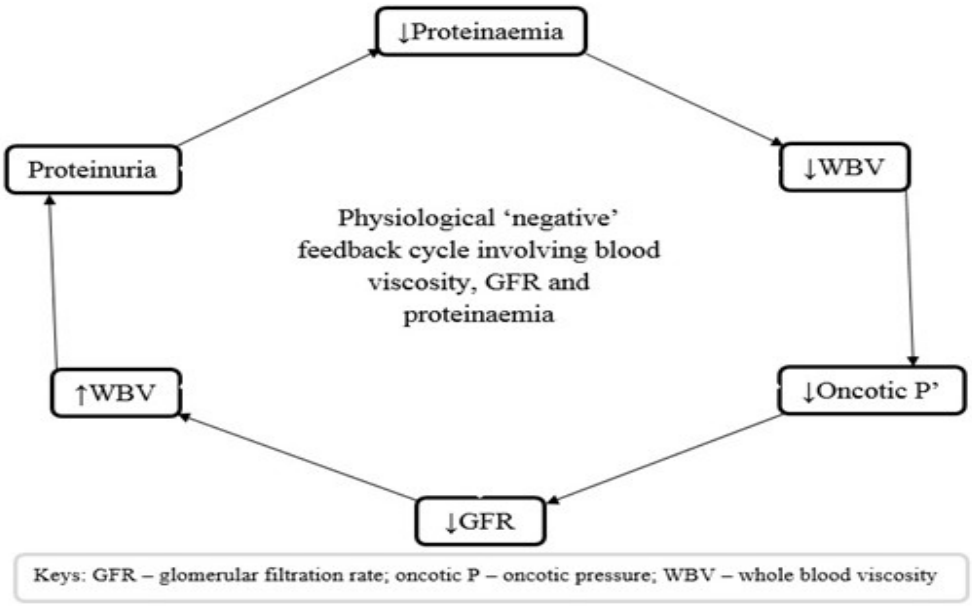

Fig 1. Negative feedback cycle of WBV-GFR-proteinaemia

variants or adducts, as well as conditions that alter the erythrocyte life-span and these include anaemia and renal failure. More so, it is reported that HbA1c goes up by about 0.1% with every 10 years of age [27], and there may be gender differences [28], as well as the impact from platelet functions [29]. Anaemia is a concern in old age with prevalence increasing from 20% to a 63% or more [30]. The idea of aging being associated with both anaemia and HbA1c foretells the question: *Is anaemia (i.e. low haematocrit) inversely or positively related to HbA1c?* This connotes a further conundrum in regards to the association of age and WBV in the sense that:

- It is not clear if anaemia (i.e. low haematocrit) is inversely [31]; or positively related to HbA1c [32]
- WBV is a physiological variable dependent on proteinaemia and haematocrit [25, 33].
- Age is associated with hypoproteinaemia and low haematocrit [12, 13, 30].
- Considering the above points, aging is supposed to be associated with low WBV

In the series on WBV assessment from serum proteins levels and haematocrit [33], WBV and HbA1c were analysed and WBV was reported to be lower in good glycaemic control relative to poor control [34]. However, HbA1c is known or speculated to increase with age, especially in non-diabetic individuals [6-9], and this may be confounded in diabetes patients who are responsive to treatment, given that glycaemic control indicated by lower HbA1c is the target. It has been reported that association of age with higher HbA1c is unexplained by the features of aging and may reduce diagnostic speciûcity of HbA1c [35]. Thus an addition to the first question expounds to: '*what are the odds that HbA1c and WBV increase with age among diabetes patients?*'

Study aims and hypothesis

Aims: The overreaching objective of study was to evaluate archived clinical data in terms of the three questions posited in the introduction. Specific aims of this study were to determine HbA1c and WBV in diabetes patients in terms of: (1) how the biomarkers compare between stratified aged-groups, (2) the separate correlations of HbA1c and WBV with age; and (3) the odds ratio and probabilities of the variables to increase with age.

Hypotheses

These objectives are based on consideration that given that anaemia is a concern in old age [30], haematocrit is positively associated with WBV [16, 25, 33], and may be inversely related to HbA1c [31]; it is not clear how HbA1c and WBV can both positively correlate with age. It is hypothesized that correlations between age and HbA1c as well as age and WBV may not be consistent or significant in all stratified age groups. This hypothesis is based on the notion that diabetes patients' management has favourable effects on HbA1c and blood viscosity [3]. A secondary hypothesis is that HbA1c is reduced with advancing age of diabetes patients.

Materials and methods

Design and setting

De-identified archived clinical pathology data for the period of 2014 – 2016 were obtained from community-based General Practice (The Wellness House) in Orange, NSW for retrospective review.

Ethics and data

This study was approved by the University's Human Research Ethics Committee (protocol number 2014/158). The most recent of each data case (N = 245) collected were laboratory results of diabetes patients including HbA1c and routine haematology; as well as liver and renal function tests. All data were de-identified and re-coded before delivery to the researcher. WBV values were derived by extrapolation from haematocrit and serum total protein levels based on validated formula [25, 33]. Among the 'N = 245', 17 were excluded from analysis – including 16 with missing eGFR results and one that could not be differentiated by the code.

Statistical analyses:

For the first research objective, age stratification was done on all the included data (n = 228), which was ranked by age and grouped into 1st – 4th quartiles. Descriptive statistics (mean, median and standard deviation values) and MANOVA assessed significant differences between age groups.

On the second objective and main hypothesis that *correlations between age and HbA1c as well as age and WBV may not be consistent or significant in all stratified age groups, Pearson's* correlations of age with HbA1c and WBV were performed three times.

- First, with a presumption to avoid confounding impacts of kidney failure and poor glycaemic control; only the patients with eGFR e" 90 mL/min/1.73m^2 and HbA1c d"6.5% were selected (N = 26) – there were 66 cases with HbA1c d"6.5% out of which 26 had eGFR e" 90 mL/min/1.73m^2.
- Second and third correlations analyses were performed in 1st and 4th quartile age groups,

respectively; to determine the hypothesized inconsistency i.e. possible differences. Interpretation of correlations was based on statistical guidelines [36].

On the secondary hypothesis, two groups of HbA1c levels were generated using 6.5% value as initial dichotomizing cut-off point. The 'low-HbA1c' group comprised all 66 cases with HbA1c < 6.5% values (representing good diabetes control). The 'highest HbA1c group comprised the 66 cases at the other end of the sorted data (representing poor diabetes control). Age and WBV levels were compared between the groups.

For the third objective, the odds of HbA1c and WBV increasing with age were assessed using 'R statistical package version 3.3.2. In this analysis, both HbA1c and WBV were categorical while age remained a continuous variable. Further, the model generated was used to convert to a probability ($P = 1/(1+e^{-Logit\,P})$) – that is, whether HbA1c and/or WBV increase, given a particular age.

Results

Descriptive statistics and multivariate comparison between age groups show directional, but statistically non-significant decreases in HbA1c and WBV from youngest age-group to the oldest (Table 1).

The results show low correlation between biomarkers and age but in varying circumstances. Age appears to show negative correlation with HbA1c, only if glycaemic control and renal functions are normal. The eGFR levels show a weak negative association and WBV weakly positively associated with age; but both only in the oldest age-group (Table 2).

When age and WBV are separately compared between groups of good diabetes controls (n = 66) versus those with highest HbA1c levels; statistical significant differences are observed in age, but not in WBV (Table 3). In particular, the mean age of the group with good glycaemic control is significantly higher ($p < 0.04$). Therefore, there is contrasting observations that may underlie confounding pathophysiology worthy of note.

The analyses of odds ratio show that the chance of HbA1c changing with age is 12.99 (RR = 1.02; $p < 0.04$) while that of WBV is 1.01 (RR = 0.99; $p > 0.12$). Going step further in the analysis, the probabilities were derived based on model from the summary using the following formulae:

HbA1c: the model from the summary is 'Logit P = 0.019133 x Age - 0.555026'

- To convert to a probability: $P = 1/(1+e^{-Logit\,P})$, or $P = 1/(1+e^{-(0.01933xAge-0.555026)})$

WBV: The model from the summary is: Logit P = -0.013405 x Age + 0.785269

- To convert to a probability: $P = 1/(1+e^{-Logit\,P})$, or $P = 1/(1+e^{-(-0.013405xAge+0.785269)})$

The derived values were plotted against unit increase in age visualize probability trends over time, using line plot in Microsoft Excel – with age on the X-axis while HbA1c and WBV probabilities are on the Y-axis. The results show that HbA1c probably

Table 1: Descriptive statistics of variables among age groups (N = 228)

		Agee (years)	GFR	HbA1c (%)	HCT (%)	Sr. Protein (g/L)	WBV (208/sec)
1st Quartile	Mean	42.18	88.21	8.28	0.45	71.33	11.83
	Median	45	90	7.6	0.44	71	11.77
	SD	6.86	7.68	2.23	0.03	4.24	0.72
2nd Quartile	Mean	53.26	85.47	8.03	0.44	71.3	11.82
	Median	53	90	7.6	0.44	71	11.77
	SD	3.02	8.85	4.99	0.03	3.97	0.68
3rd Quartile	Mean	63.53	76.11	7.96	0.44	70.88	11.75
	Median	63	80	7.6	0.44	70	11.61
	SD	3.28	16.72	1.91	0.04	4.59	0.78
4th Quartile	Mean	75.82	65.16	7.65	0.42	70.91	11.75
	Median	76	63	7.4	0.43	71	11.77
	SD	6.64	17.89	1.59	0.05	4.07	0.69
P values (MANOVA)		NA	0.00001*	NS	0.001**	NS	NS

*Except between 1st vs. 2nd Quartile groups; **between 1st vs. 4th Quartile groups onlyNA: not applicable, NS: not significant at $p < 0.05$

Table 2: Correlation of age and HbA1c variation with WBV groups

A: Normal eGFR and normal HbA1c (N = 26)						
	WBV	Sr. protein	HCT	Age	eGFR	HbA1c
WBV (208/Sec)	1.00					
Serum protein (g/L)	1.00	1.00				
HCT (%)	0.22	0.21	1.00			
Age (years)	-0.04	-0.04	0.31	1.00		
eGFR (mL/min/1.73m$^{2)}$	0.30	0.30	0.26	0.13	1.00	
HbA1c (%)	0.39	0.39	-0.10	-0.26	-0.11	1.00
B: 1st Quartile age group (N = 57)						
	WBV	Sr. protein	HCT	Age	eGFR	HbA1c
WBV (208/Sec)	1.00					
Serum protein (g/L)	1.00	1.00				
HCT (%)	0.25	0.24	1.00			
Age (years)	-0.13	-0.13	-0.21	1.00		
eGFR (mL/min/1.73m$^{2)}$	0.29	0.29	0.23	0.06	1.00	
HbA1c (%)	-0.17	-0.17	0.16	-0.17	0.02	1.00
C: 4th Quartile age group (N = 57)						
	WBV	Sr. protein	HCT	Age	eGFR	HbA1c
WBV (208/Sec)	1.00					
Serum protein (g/L)	1.00	1.00				
HCT (%)	0.19	0.18	1.00			
Age (years)	0.22	0.22	-0.19	1.00		
eGFR (mL/min/1.73m$^{2)}$	0.14	0.13	0.53	-0.25	1.00	
HbA1c (%)	0.15	0.15	0.02	-0.15	0.16	1.00

Table 3: Comparison of age and WBV between groups of HbA1c

	HbA1c groups	Mean	Std. Dev'	N
Age (years)	Good glycaemic control	61.42	15.65	66
	Poor glycaemic control	55.3	17.09	66
WBV (208 Sec-1)	Good glycaemic control	11.83	0.71	66
	Poor glycaemic control	11.80	0.87	66

increases by 0.01 (or 1%) in every two to three years, whereas WBV may decrease by the same margin in every three years (Fig 2).

Discussion

The first and preliminary aim of this study was to determine the association of age with HbA1c as well

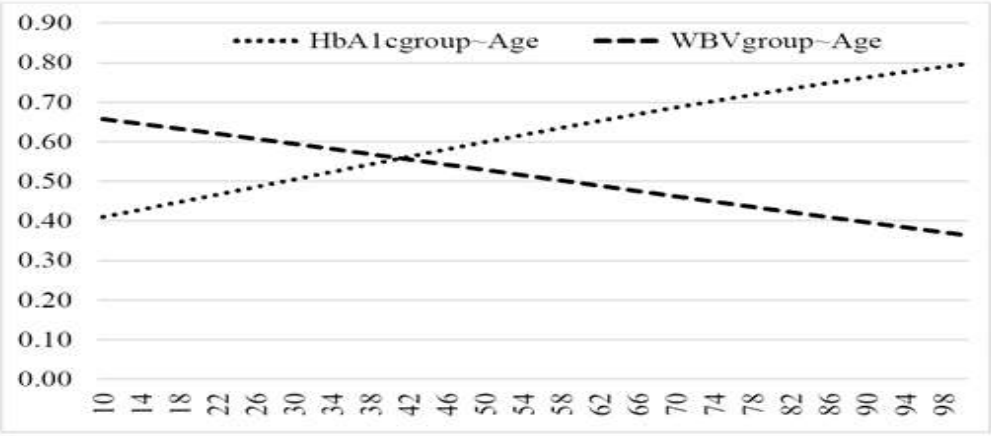

Fig 2. Probability* of HbA1c increasing and WBV decreasing with age*X-axis while HbA1c and WBV probabilities are on the Y-axis

as age and WBV in diabetes patients. Results of the analysis show that neither HbA1c nor blood viscosity achieved statistical significance changes with age, although there was directional decrease in both parameters from youngest aged-group to the oldest (Table 1). Here we report observation of association that implies negative correlation of age with both HbA1c and WBC. This is in contrast to abundance of literature supporting the notion that aging impacts on HbA1c [3-6], as well as WBV [7-9]. However, it is noteworthy that the cohort of this particular study is strictly individuals living with diabetes.

The second, but main research objective was the correlation analysis. The age of patient appears to show negligible to weak negative correlation with HbA1c only among those with good glycaemic control (r 0.15 – 0.26); and a weak positive association with WBV only in the oldest age-group (r = 0.22). This supports our first hypothesis that correlation between age and HbA1c as well as age and WBV may not be consistent or significant in all stratified age groups. HbA1c and WBV are moderately and positively correlated in patients with good glycaemic control and normal renal function (r = 0.39; Table 2). This in part supports the notions in the literature. However, age ($p < 0.04$), but not WBV was statistically significantly different between 'good versus poor' glycaemic control subgroups (Table 3).

Again, similar to the results reported in Table 1, this observation does not appear to support the idea that HbA1c and WBV positively associate with aging [3-9]. Repeat evaluation of age and WBV separately compared between quartile groups of WBV showed no statistical difference, although there was a more linear inverse correlation between age and WBV. Thus, the results further uphold the first hypothesis of this study that HbA1c and blood viscosity may not consistently increase with aging, especially among diabetes patients. However, WBV being correlated with HbA1c in good glycaemic control corroborated our previous report "that WBV is statistically significantly lower ($p < 0.05$) in the group with excellent glycaemic control compared to the group with poor glycaemic control" [34].

The subgroup with good glycaemic control appeared to comprise older people with mean age H" 61 years, compared to the poor control group of mean age H" 55 years (Table 3). This corroborates observations in Table 1 that show directional decrease (8.28 > 8.03 >> 7.96 >>> 7.65) in HbA1c inferring that lower HbA1c can be associated with aging among individuals living with diabetes. A plausible interpretation of the observation is that the patients were obviously younger at the time of diagnosis and when glycaemic control treatment (i.e. HbA1c reduction) commenced. Therefore, age at post-treatment check-up is higher while HbA1c level became lower – where glycaemic control was achieved in the diabetes patients. Further, the contrasting observation reported in regards to Table 3 indicates that good glycaemic control can occur in any age group. In the cohort evaluated, an older people showed lower HbA1c level possibly indicative of adherence to clinical management, relative to a non-adherent younger individual ($P < 0.04$). This indicates that medical treatment may cause negative correlation, which contrasts with expectation of HbA1c increasing with age. This is in agreement with proposition that diabetes patients' management has favourable effects on HbA1c and blood viscosity [3].

The third research objective was about odds ratio; and results show that there is the probability of HbA1c to increase with age ($p < 0.04$), while that of WBV may be insignificant ($p > 0.12$). This observation agrees with the general notion (6-9). It is inferred that the probability of HbA1c to increase with age is significant, and indeed, a critical review of the correlations show that HbA1c is negatively correlated only among the subgroup with good glycaemic control and WBV is only positive in the oldest aged group. In the further analysis where Logit models are converted to probabilities of WBV changing with age, the results show that HbA1c probably increases by 0.01 (or 1%) in every 2 to 3 years, whereas WBV may decrease by the same margin in every 3 years (Fig 2). The observation of the probability that HbA1c increases with age is closely in line, but slightly differs, with the existing reports that indicate about 0.1% increase per 10 years [27, 35].

However, it must be recognized that whereas our observation of 1% in 2 – 3 years is based on diabetic patients undergoing treatment, the reports indicating 0.1% were note. Indeed, one of the reports is exclusively based on non-diabetes population. Thus the contribution and implication of this observation is affirmation and elucidation of another existing report [35], that the HbA1c diagnostic speciûcity is confounded by age and medical treatment. That is, on the basis of incremental increase

- Age will confound diagnosis of diabetes with HbA1c, if the same reference is used e.g. for young and old adults
- The incremental increase in HbA1c may also confound response to treatment regimen. Or vice versa, medical treatment is a confounding factor to

the incremental increase if the diabetes is very well under control

The decreasing of WBV with increase in age is evident from descriptive statistics shown in Table 1 and appears to disagree with the notion that blood viscosity increases with age. However, a critical review of the data shows that there is significant decline in haematocrit with increasing age (Table 1). Given the importance of haematocrit in WBV [16, 25, 26], and the knowledge that the effect of age is independent of serum protein level contribution to viscosity [5], it is inferred that the tendency for haematocrit to decrease with age is a confounder in this observation. The significance is that WBV may increase with age [4, 5], and the presence of anaemia is a confounding factor that age-induced anaemia can cause the opposite effect of anaemia-induced hypoviscosity. The addition of this observation to knowledge regarding the speculated WBV increase with age is:

- Firstly, affirmation that it may not be based on haematocrit [5], which tends to decrease with aging, but
- Secondly, age-related ill-health possibly associated with hyperproteinaemia that needs to be further determined.

Implications for diabetes research and management in low-mid income countries

Two themes that are of significance in this report are research and management. This paper discusses two laboratory tests that are integral in diabetes pathophysiology, research and clinical practice.

- HbA1c is well appreciated and pushed for expounded clinical utility, but currently not accessible at most pathology facilities in low-mid income communities and will incur major costs to adopt.
- WBV is useful for therapeutic decisions, but yet to be accepted or acknowledged by clinicians. Yet, it is easily adoptable (i.e. can be extrapolated) at no extra operational cost from haematocrit and serum protein results.

Diabetes research:

Over the years, diabetes research has brought the idea that HbA1c should be delimited to glycaemic control monitoring of patients who are already diagnosed. At least, guidelines recommended blood glucose for diagnosis of diabetes as at 2010. The push to use HbA1c for diabetes screening and diagnosis of new cases, i.e. in addition to the traditional usage in monitoring of patients' management, has garnered momentum and integrated into recommendations within the last decade [37, 38]. However, the need for variations in reference values is still being discussed [38, 39]. This paper contributes to the discourse by reporting the probability of HbA1c increasing with age by 1% in 2-years, which confounds HbA1c diagnostic speciûcity and sensitivity.

Until date, haemorrheology research, specifically WBV testing, has yet to be fully translated from research to bedside. Previous reports have attempt to advance the specificity of the test parameter [40], and "that WBV is a valid clinical laboratory parameter for evidence-based contraindication, indication and monitoring of antiplatelet medication" [41]. Yet, discussion about antiplatelet is without recourse to WBV test for evaluation of stasis [42]; either for initial determination of bleeding risk, or post-intervention to assess antiplatelet efficacy towards reduction in level of stasis. Given the continued interest to elucidate the relative significance of haemorrheological alterations in the pathophysiology of cardiovascular diseases [43], and the basis of ineffectiveness of aspirin [44], our observation that WBV may decrease by 1% with every 3 years constitutes addition to knowledge. This new knowledge calls for validation to support adoption in clinical practice, especially with regards to antiplatelet monitoring.

Diabetes management

Considering that the basis of overlooking the odds ratio of HbA1c has been because 0.1% increase in 10-years "is unlikely to necessitate a change in treatment goals" [27], our observation of 1% in 2 years calls for a re-evaluation of recommended laboratory result interpretation in diabetes monitoring. More so, due to the fact that diabetes perhaps manages to reduce HbA1c level relative to when diagnosis was made is confounding factor to consider. The same applies for screening and diagnosis in terms of reference values. The need to interpret HbA1c results with references to both stratified age-groups and any ongoing medical treatment is warranted.

Diabetes care has involved prophylactic management of patients with antiplatelet, which is meant to maintain blood stasis *vis-à-vis* WBV [41, 45]. Guidelines for the clinical prescription of antiplatelet recommends albeit with limited evidence that risk of bleeding is a contraindication [46]. Yet, current platelet function tests assess only antiplatelet effectiveness or failures, but not stasis *per se*. Blood viscosity (whether plasma or WBV) test that assesses stasis level is neither fully appreciated for this

purpose, nor accessible outside very few referral laboratories. What this report advances is the knowledge that WBV test can be performed at no extra cost or need of resources in a clinical laboratory facility that already has capacity to perform haematocrit and total serum protein.

Conclusion

This study investigated the correlation between age and HbA1c as well as age and blood viscosity. It is observed that both HbA1c and WBV tend to decrease with increasing age among individuals living with diabetes. For HbA1c, this was inferred to be due to post-intervention glycaemic control test – i.e. that age has increased while HbA1c is lower at the time of post-intervention test. For WBV, the negative correlation with age is attributable to anaemia. In the subgroup who indicated good glycaemic control, the biomarkers show positive correlations with age, but only in the oldest aged-group. Thus proving the main hypothesis that *correlations between age and HbA1c as well as age and WBV may not be consistent or significant in all stratified age groups*. This report provides elucidation of a complex pathophysiology in diabetes that need consideration when interpreting pathology results of patients.

Acknowledgements

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