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Research Article

Evaluation of Thyroid Hormones, CD4+ T Cells, BMI and Blood Pressure in HIV Seropositive Subjects in Nkpor, Anambra State, South East Nigeria

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Abstract

Human immunodeficiency virus (HIV) infection may directly or indirectly affect organ functions. Thyroid dysfunction, immune deficiency and cardiovascular disorders have been associated with HIV infection and the use of antiretroviral therapy. The study aimed to evaluate the levels of thyroid hormones, CD4 + T cells, body mass index (BMI) and blood pressure of HIV seropositive subjects in Nkpor, Anambra State, South East Nigeria. A total of one hundred and fifty subjects were investigated; 50 HIV seropositive subjects who were not on antiretroviral therapy (ART), 50 HIV infected subjects who were on ART and 50 apparently healthy non HIV subjects (control). Thyroid stimulating hormone (TSH), tri-iodothyronine (T_3) and thyroxine (T_4) were assayed using ELISA methods. CD_4+T cells were determined using flow cytometry. Body Mass Index (BMI) was derived from the heights and weights of the subjects. The results showed that the levels of thyroid hormones and systolic blood pressure of HIV seropositive subjects on ART were significantly increased when compared with HIV seropositive subjects not on ART and the control subjects. CD_4+ T cell counts and BMI showed significant decrease while the diastolic blood pressure did not show significant increase. There was a significant decrease observed in the level of TSH in subjects on Lamivudine, Zudovudine and Efavirenz (LZE) antiretroviral combination compared with those on Lamivudine, Efavirenz and Stavudine (LES) combination whereas there were significant increases in the levels of T_3 and T_4 in the subjects respectively. It was concluded that thyroid dysfunction as well as variations in BMI and blood pressure are present in HIV seropositive subjects especially during antiretroviral therapy.

Keywords: *Thyroid hormones, CD4+ cells count, BMI, Blood pressure*

Introduction

In Nigeria, it has been shown that about 3.1% of the population is living with HIV/AIDS (NACA, 2012). Human immunodeficiency virus (HIV) and Acquired immunodeficiency syndrome (AIDS) may directly or indirectly affect any organ system. Multiple endocrine mechanisms may interact in complex syndromes such as wasting, lipodystrophy, and other metabolic abnormalities (Kofler, 2004). Characteristic of these disorders is a high prevalence of abnormalities in thyroid function tests (Jain *et al*, 2009). Cardiovascular events such as diastolic dysfunction have also been associated with HIV infection (Hernandez *et al*, 2001; Oluboyo *et al*,2006) as well as atherosclerosis and this may be more common with the antiretroviral therapy (Hodder *et al*, 2001; Oluboyo *et al*, 2009). The thyroid hormones have been reported to be crucial for optimal immune function (Souba and Smith 1996).Thyroid dysfunction may contribute to morbidity from osteoporosis, hyperlipidemia, cardiovascular disease and neuropsychiatric illness, all of which have been associated with HIV infection or its treatment (Arnten *et al*, 2007; Amadi *et al*, 2008). Although, the use of highly active antiretroviral therapy (HAART) in clinical practice has been associated with benefits in the management of HIV infection with a dramatic reduction in HIV-related morbidity and mortality (Danoff *et al*, 2006), this is not totally free of some consequences. There has been an increase in the number of patients receiving HAART presenting with symptoms of thyroid disease requiring treatment. This is especially true during HAART, when Graves' disease may be triggered by immune reconstitution and the presence of subclinical hypothyroidism (Madeddu *et al*, 2006). This study was designed to evaluate thyroid hormones, CD4+T cells, BMI levels and blood pressure in HIV seropositive subjects in Nkpor, South East Nigeria.

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Materials and Methods

The study subjects comprised one hundred HIV seropositive subjects attending a voluntary counseling and testing unit (VCT) in Nkpor, Anambra State, South East Nigeria and fifty apparently healthy individuals who served as the control subjects. All the subjects comprised both males and females within the ages of 20-50 years. The HIV seropositive subjects were further divided into two groups; 50 HIV infected subjects not on antiretroviral therapy and 50 HIV infected patients who were receiving antiretroviral therapy. The administered therapies were Lamivudine, Efavirenz and Zudovudine (LZE) combination i.e Lamivudine, 150mg twice daily; Efavirenz, 600mg once daily , and Zudovudine, 300mg twice daily while the second group were on Lamivudine, Efavirenz and Stavudine (LES) combination (i.e. Lamivudine , 150mg twice daily; Efavirenz, 600mg once daily and Stavudine 40mg twice daily). The height and weight of the subjects were measured using standard procedures. The weight taken in kilograms (kg) and the height in meters (m) were used to calculate the Body mass index (BMI in Kg/m^2). The CD4+T-cells were measured using flow cytometric method (Partec GMBH. Germany) and the thyroid hormones were analyzed using Enzyme Linked Immunosorbent Assay (ELISA) Method.

Statistical analysis: The mean and the standard deviations of the data were obtained using SPSS version 16. t-test and Analysis of Variance (ANOVA) were used to compare the mean and the standard deviations of the results and $p<0.05$ was taken as the level of significance.

Results

The results were expressed as mean ± standard deviation and are shown in tables 1 and 2. Table 1 shows the thyroid function tests (TSH, T3, T4), CD4+ cell counts, BMI, systolic and diastolic blood pressure (BP) in the HIV seropositive subjects and control subjects. The levels of TSH, T3, T4 and systolic blood pressure of HIV seropositive subjects on ART showed significant increase ($p<0.05$) when compared with HIV seropositive subjects not on ART and the control subjects. CD4+ T cell counts and BMI showed significant decrease ($p<0.05$) while the diastolic blood pressure did not show any significant change.

Table 2 shows the thyroid function tests, CD4+ cell counts, BMI and blood pressure in HIV seropositive subjects based on different ART combinations. There was significant decrease observed in the level of TSH in subjects on Lamivudine, Zudovudine and Efavirenz (LZE) antiretroviral combination compared with those on Lamivudine, Efavirenz and Stavudine (LES) combination whereas there were significant increase in the levels of T3 and T4 in the subjects on LZE compared with those on LES. There was no significant change in the levels of CD4 + T cells, systolic and diastolic blood pressure in the subjects.

Table 1:
Thyroid function tests, CD4+ cell counts, BMI and blood pressure in HIV seropositive subjects and control subjects

Parameter	HIV subjects on ART (N=50)	HIV subjects not on ART (N=50)	Control subjects (N=50)	F-value	*p*-value
TSH (µIU/ml)	2.39±0.81	1.75±1.37	0.81±0.36	5.47	0.005*
T4 (µg/dl)	9.72±5.11	7.95±2.15	7.28±1.96	6.77	0.002*
T3 (ng/ml)	2.41±2.24	1.44±1.21	1.19±0.62	8.93	0.000*
CD4+count (cells/µL)	167.00±54.69	449.62±199.20	977.15±171.38	344.64	0.000*
BMI (Kg/m^2)	20.26±3.94	34.27±3.47	34.00±8.61	24.21	0.000*
Systolic BP(mmHg)	120.80±15.33	115.30±5.71	114.17±5.68	6.16	0.002*
Diastolic BP(mmHg)	78.90±5.22	75.10±5.58	77.50±6.28	0.401	0.670

* Significant at $P<0.05$

Table 2:
Thyroid function tests, CD4+ cell counts, BMI and blood pressure in HIV seropositive subjects based on different ART combinations.

Parameters	HIV Seropositive subjects on LZE (N=41)	HIV Seropositive subjects on LES (N=9)	t-value	*p*-value
TSH (µIU/ml)	0.89± 0.41	9.27± 3.81	11.29	0.000*
T4 (µg/dl)	10.99±4.44	3.94±o.99	4.38	0.000*
T3 (ng/ml)	2.80±2.27	0.69±0.94	2.71	0.009*
CD4+Tcells (cells/µl)	164.00±51.26	184.00±69.61	0.95	0.348
BMI (kg/m^2)	20.41±4.12	19.56±3.07	0.59	0.561
Systolic BP(mmHg)	116.83 ±12.34	126.67± 17.32	-1.62	0.138
Diastolic BP(mmHg)	78.42 ±8.47	81.67 ±7.91	-1.10	0.291

Significant P< 0.05;* ***LZE = Lamivudine, Zudovudine and Efavirenz;* ***LES** = Lamivudine, Efavirenz and Stavudine*

Discussion

HIV infection is a chronic, systemic disease leading to multiple-organ involvement and affecting the endocrine system as well (Maddedu, *et al*, 2006). In this study, significantly increased T_3, T_4 and TSH were detected in HIV subjects compared with control. It has been shown that abnormal thyroid function is not uncommon in HIV and there may be a number of contributory factors (Qureshi *et al*, 2005; Hoffmann and Brown, 2007, Noureldeen *et al*, 2012). Although the three hormones were significantly higher in the HIV subjects on ART compared with the HIV subjects not on ART and control subjects, T4 and TSH were still within the normal reference range used in the locality but T3 was abnormally raised suggesting T3 toxicosis. T3 is the most active form of thyroid hormone but the clinical utility of measuring T3 is limited to a few situations. For instance, measurement of T3 is necessary in patients with a low TSH level and to evaluate for isolated elevation of the T3 level (Qureshi *et al*, 2005). On the other hand, there was a significant decrease observed in the level of TSH in subjects on Lamivudine, Zudovudine and Efavirenz (LZE) antiretroviral combination compared with those on Lamivudine, Efavirenz and Stavudine (LES) combination whereas there were significant increases in the levels of T_3 and T_4 in the subjects. This is in line with the work of Sen *et al* (1996) who reported greater incidence of hypothyroidism in HIV-seropositive subject after taking highly active antiretroviral therapy (HAART). These findings are also in line with the work that showed that the use of HAART, particularly stavudine, is associated with a high prevalence of subclinical hypothyroidism (Maddedu, *et al*, 2006). Furthermore, the low level of thyroid-stimulating hormone and elevated T_3 and T_4 levels observed in subjects on LZE in this study may occur during immune reconstitution as reported by Hoffmann and Brown (2007). Furthermore, decrease in T_3 levels in HIV seropositive subjects have been associated with severe weight loss and reduced BMI as well as decline in immune system which can cause subjects to be prone to infections. Decrease T_3 have been associated with lower CD_4+ T-cell count, active opportunistic illness and severe weight loss. In this study, a significantly decreased CD_4 + T cells was observed in HIV seropositive subjects on ART compared with HIV seropositive subjects not on ART and control subjects. The low levels of CD_4 + T cells observed in these subjects are in line with the works of Maddedu, *et al* (2006). HIV-infection leads to low level of CD_4+ T-cells through direct viral killing of infected cells, increased rate of apoptosis in the infected cells and killing of infected CD_4+ T-cells; by CD_8 cytotoxic lymphocytes that recognize infected cells (Cunningham *et al*, 2010). Thus, low level of CD_4+ (helper T-cells) is common when the immunity is greatly reduced. The BMI was significantly low in HIV subjects on ART compared with those not on ART and control subjects. The reason for this may be due to the reduction in the weights of the subjects which is a characteristic of AIDS. The systolic and diastolic blood pressures were significantly raised in the HIV subjects on ART compared with those not on ART and control subjects. This finding supports the works of Carl *et al* (2006) who reported that other actions of thyroid hormone include stimulation of adrenergic activity with increased heart rate and myocardial contractility and those who reported that other cardiovascular events such as diastolic blood pressure and as well atherosclerosis have been associated with HIV infection and they are more common with the anti-retroviral therapy (Hodder *et al*, 2001; Hernandez *et al*, 2001). It was concluded that thyroid dysfunction as well as variations in BMI and blood pressure are present in HIV seropositive subjects especially during antiretroviral therapy.

References

Amadi, K, Sobo A.M, Ogunkeye, O.O and Oluwole, F.S (2008): Thyroid Hormone: A prime suspect" in human immunodeficiency virus (HIV/AIDS) patients? Nigerian Journal of physiological sciences **23** (1-2): 61-66.

Arnten ,J.H, Freeman R, Howard A.A, Flores-Moore, M, Lo Y, Klein, R.S (2007): Decreased bone mineral density and increased fracture risk in aging men with or at risk for HIV infection. AIDS:21:617-623.

Carl AB, Edward RA, David EB (2006): Tietz Textbook of clinical Chemistry and Molecular Diagnostic 4th Edn. Pp: 1065-1095.

Cunningham, A., Donaghy, H., Harman, A., Kim, M., Turville, S. (2010): "Manipulation of dendritic cell function by viruses". Current opinion in microbiology 13 (4): 524–529.

Danoff A (2006). HIV and the thyroid- what every practicising endocrinologist needs to know. Nat. Clin. Pract Endocrinology Met **2**:602-603.

Hernandez, H.F, Gascuena, R.R, Escribano S.P, Yelazquez M.T, Lombera R.T, Rubic G.R, Putido O.F, Ramon-Costal, Perez H.J, Saenz-De-La-Cazada C.(2001): Diastolic Dysfunction in human immunodeficiency virus infection. Rev.Esp. Cardiol **54** (10) 1183-1189.

Hodder S, Brurteel B, Kawabata H, Dezill C, Lillienfeld D, Stevens M. (2001): Coronary heart disease in patients with human immunodeficiency virus infect. Programme and Abstract of the 39th Annual Meeting of the infectious disease society of America. San Francisco, California. Abstract 18.

Hoffmann, C.J and Brown, T.T.(2007): Thyroid function abnormalities in HIV-infected patients. Clin Infect Dis. 45(4):488-494.

Jain G., Devpura ,G ., Gupta, B.S (2009): Abnormalities in the Thyroid Function Tests as Surrogate Marker of Advancing HIV Infection in Infected Adults. Journal of the Association of Physicians of India 57:508-510

Kofler D (2004): Low-dose maintenance therapy with recombinant human growth low Testosterone Levels Int. J. STD AIDS. 12 (1): 75-83.

Madeddu G, Spanu A, Chessa F, Calia G.M, Lovigu C, Solinas P, Mannazzu M, Falchi A, Mura M.S, Madeddu G. (2006): Thyroid function in human immunodeficiency virus patients treated with highly active antiretroviral therapy (HAART): a longitudinal study. Clin Endocrinol (Oxf). 64(4):375-83.

National Agency for the Control of AIDS (NACA) 2012 : WOMEN, GIRLS AND HIV IN NIGERIA.http://naca.gov.ng/index2.php?option=com_docman&task=doc_view&gid=110&Itemid=268 Assessed on 12/10/2013

Nelson M.R, Gazzard B.G (2005):"Thyroid dysfunction in individuals with HIV infection: the effect of HAART" International AIDS Conference (IAS) Rio de Janeiro, Brazil. Conference Reports for NATAP **8** :1-3.

Noureldeen, A., Qusti, S.Y., Khoja, G.M.S (2012): Thyroid function in newly diagnosed HIV-infected patients. Toxicol Ind. Health, doi: 10.1177/0748233712466133

Oluboyo,A.O.,Okogun,G.R.A.,Duru,L.A.D.Oluboyo,B.O., Emenike E,F., Obasikene, C.N (2006): Pattern Of Blood Pressure,CD4+ T Cells Count And Some Cardiac Enzymes In HIV Seropositive Subjects. Journal of Biomedical Investigation. 4(2):37-41.

Oluboyo,A.O.,Onyenekwe,C.C.Okeke.,A.C.,Oluboyo,B.O.,Odeyemi,S.O.,Chukwuanukwu,T.O.,(2009): Pattern Of Lipid Profiles In HIV Seropositive Subjects On Antiretroviral Therapy. Journal of Biomedical Investigation.7 (1):32-35

Qureshi, A.,Panahloo, A and Seal, L.J. (2005): Thyroid dysfunction in HIV. Endocrine Abstracts. 10:95

Sen P, Scourfield A, Smythe J, Stefanovich M, Jones R, Mandalia S, Sullivan AK, Souba, W.W. and Smith, R.J. (1996) :Characteristics of HIV – Infected Men with hormone sustains effect of previous r-hGH treatment in HIV +patients with excess center fat: treatment results at 60 weeks. 11th conference on retroviruses and opportunistic infections. San Francisco, Abstract 80.

Souba WW and Smith RJ (1996). Characteristics of HIV-infected men with low testosterone levels int. J STD AIDS 12 (1): 75-83.