THYROID FUNCTION PROFILE OF HIV/AIDS PATIENTS IN KANO, NORTHWEST NIGERIA

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Abstract

Background: Human Immunodeficiency Virus (HIV) infection/Acquired Immunodeficiency Syndrome (AIDS) is known to be associated with several endocrinopathies. Consequently, thyroid gland is a prime target organ that may be affected by the virus, opportunistic infections, or medications that are used in the care of patients afflicted with HIV/AIDS.

Objective: This cross-sectional descriptive study was primarily aimed at determining the thyroid hormone profile and pattern of thyroid function abnormalities among HIV/AIDS patients in Kano, Northwest Nigeria.

Methods: The study recruited a total of two hundred and Ten (210) subjects made up of seventy (70) HIV positive HAART treated patients (group I), seventy (70) HIV positive HAART naïve patients (group II) and 70 apparently healthy controls (group III). An interviewer-administered structured questionnaire was used to collect information on bio data, medical history, duration of diagnosis of HIV infection and HAART regimen. Blood samples were collected for the measurement of serum fT₃, fT₄, and TSH. The results obtained from this study were analysed using STATA statistical package, version 13.

Results: Of all the studied subjects, 139 (66.2%) were euthyroid while 71 (33.8%) had some forms of thyroid dysfunction. The prevalence of thyroid dysfunction among the various groups studied were 55.7% (39), 42.9% (30) and 2.8% (2) for groups I, II and III respectively.

Conclusion: Thyroid dysfunction was commoner among HIV-positive subjects than HIV-negative controls. HIV-positive patients on HAART had higher prevalence of thyroid dysfunction than HIV positive HAART naïve patients.

Key Words: HIV/AIDS, Euthyroid, HAART, Subclinical hypothyroidism, TSH.

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INTRODUCTION

The global prevalence rate of HIV infection in adults was 0.8% in 2016, while that of Sub-Saharan Africa was 4.8%.¹ The prevalence of HIV in Nigeria has remained at about 4% since 2005 till date and Kano has HIV prevalence rate of 1.3%.¹

Infection by HIV may directly or indirectly affect any organ in the human body. Increasing experience in the management of this disease has led to the recognition of a variety of HIV-related endocrine disorders that occur during both the early and late stages of HIV infection.² Among these endocrine disorders, abnormalities of thyroid function have been reported in previous cross-sectional studies.^{2, 3, 4, 6} Various mechanisms have been proposed to explain such abnormalities in thyroid function^{7,8} which include, the possible relationship between the immune and endocrine systems, direct involvement of the glands by HIV itself, opportunistic infections such as *pneumocystis jiroveci*, infiltration of the gland by tumours such as Kaposi sarcoma (KS), effects of humoral factors such as interleukin - 1 β (IL - 1 β) &

tumour necrosis factor (TNF) - α . Other pathophysiologic mechanisms suggested are side effects of the drugs used in the course of HIV management such as Rifampicin, ketoconazole and Highly Active Anti-Retroviral Therapy (HAART).^{7, 8,9}

Consequently, disorders of thyroid function are comparatively commoner in HIV population than the general population.³ Among individuals infected with the disease, 1-2% might experience clinically apparent thyroid disease, and 35% may have subtle abnormalities in thyroid function test findings.³

Due to the fundamental roles thyroid hormones play in regulating general body metabolism and modulation of both humoral and cell mediated immunity,⁸ this research work was conducted to determine the thyroid hormone profile and pattern of thyroid dysfunction among HIV/AIDS patients attending Aminu Kano Teaching Hospital (AKTH) Kano, Northwest, Nigeria. Early and prompt recognition of the various thyroid disorders will be useful in the evaluation and management of HIV/AIDS patients.

SUBJECTS AND METHODS

This was a descriptive cross - sectional study conducted between September, 2016 and January, 2017 at the HIV Management Centre of Aminu Kano Teaching Hospital, Kano.

Two hundred and ten subjects were enrolled, 70 were HIV sero-positive patients on HAART (Group I), 70 were HAART naïve HIV sero-positive patients (Group II) and 70 were apparently healthy HIV negative controls (Group III).

Based on their HAART regimen, Group I study subjects were further subdivided into those on first line HAART regimen (Ia) and those on second line HAART regimen (Ib).

Pregnant women, lactating mothers, patients with acute illnesses, those with history of thyroid dysfunction prior to diagnosis of HIV, individuals who were on medications known to affect thyroid hormone levels (such as Amiodarone, Androgens, Phenytoin), those with history of chronic alcohol abuse among HIV/AIDS patients were excluded from the study.

Similarly, those with history of external irradiation around the neck, pituitary surgery, AIDS- related malignancy, active opportunistic infections, pituitary-, hypothalamic-, neurologic-, chronic kidney- and chronic liver- diseases as well as individuals less than 18 years or above 60 years of age were excluded from the study. Ethical approval for the study was obtained from the Health Ethics Research Committee of Aminu Kano Teaching Hospital, Kano.

Informed and written consent were obtained from each study subject before the commencement of the study.

Well-structured, interviewer- administered pre-tested questionnaires was used to obtain bio-data from each of the study subjects.

All subjects were properly counselled on the protocol of blood collection and a well-lit room was used for all phlebotomy procedures. A vacutainer system comprising a needle holder and a needle,

attached to a serum separator gel container was used to collect five millilitres (5ml) of whole blood specimen from each study subject. Tourniquet was applied only when necessary. The time and date of sample collection and identity of the subjects were recorded. Samples were kept in erect position and allowed to clot and retract before they were placed in a centrifuge and spun at a relative centrifugal force (RCF) of 1200X g for 10 minutes to obtain sera which were stored at -20°C. Samples were analysed in batches within 3 weeks of collection. Serum levels of TSH and free thyroid hormones are stable at this temperature for up to one month.¹⁰

Quantitative measurements of serum fT₃, fT₄ and TSH were performed using highly sensitive and specific electro-chemiluminescence immunoassay technique on e-411 automated immunology analyser (Roche- Hitachi).^{11,12,13}

All laboratory results were interpreted according to the criteria set by the British Thyroid Association (BTA).¹⁴

Data generated from the study were analyzed using the STATA statistical package version 13 (Stata corp, College Station). All quantitative and normally distributed data were summarized as Mean and Standard Deviation (SD). Fairly distributed data were summarized with histograms; skewed quantitative data from TSH were summarized using median and range. All qualitative data were summarized as proportions and percentages. Analysis of variance (ANOVA) test was used to compare the means values of fT₃ and fT₄ between groups I, II and III subjects. A post hoc analysis was then done to identify means that were significantly different. Nonparametric data of TSH were analyzed using nonparametric statistics (Kruskal-Wallis test). In all the analysis, 5% alpha level of significance which corresponds to 0.05 was considered statistically significant.

RESULTS

Baseline characteristics of study subjects

The mean age of all the subjects was 35.4 ± 8.5 years and no statistical difference was observed in the mean age of the three studied groups (p = 0.30).

There was a slight female preponderance in both groups I and II and a slight male preponderance in group III study subjects, with male to female ratio of 1:1.1, 1:1.2 and 1.5:1 for groups I, II and III respectively (Table I).

Majority of the subjects in all the three groups studied were married and this constituted about 58.6%, 61.4% and 68.6% in groups I, II and III respectively (Table I)

Table I also shows the occupational status of the studied subjects. The most prevalent occupation in both groups I and II were business and 'others', while most of the group III subjects were civil servants.

Table I: Baseline characteristics of study subjects

VARIABLE		SUBJECTS		
		Group I	Group II	Group III
Age (Years)		35.3 ± 7.9	34.4 ± 9.0	33.3 ± 8.0
Sex	Male	34 (48.6)	32 (45.7)	42 (60.0)
	Female	36 (51.4)	38 (54.3)	28 (40.0)
	Total	70 (100.0)	70 (100.0)	70 (100.0)
Marital status	Married	41 (58.6)	43 (61.4)	48 (68.6)
	Single	11 (15.7)	8 (11.4)	21 (30.0)
	Divorced	8 (11.4)	6 (8.6)	0 (0.0)
	Widowed	10 (14.3)	13 (18.6)	1 (1.4)
	Total	70 (100.0)	70 (100.0)	70 (100.0)
Occupation	Civil servant	15 (21.4)	6 (8.6)	48 (68.6)
	Business	20 (28.6)	31 (44.3)	2 (2.8)
	Others*	35 (50.0)	33 (47.1)	20 (28.6)
	Total	70 (100.0)	70 (100.0)	70 (100.0)

*others' were made up of petty traders, students and the unemployed

Age is presented as mean ± standard deviation, while the other variables are presented as numbers with the corresponding percentage in brackets.

Serum Levels of fT_3 , fT_4 and TSH of study subjects

The mean serum fT_3 differ in all the studied groups ($P=0.0000$). However, there was no statistical difference between the mean fT_4 of group I and group II subjects ($p=1.000$) but a significant difference was observed when both means were compared to the mean fT_4 of group III (p value = 0.000). (Table II)

A statistically significant difference was observed

in the median serum TSH between the three groups ($p=0.0001$).

Prevalence and patterns of thyroid dysfunction in study subjects

Table III depicts the prevalence and various patterns of thyroid dysfunction among the study subjects. One hundred and thirty-nine (66.2%) of the studied subjects were euthyroid while the remaining 71 (33.8%) had various forms of thyroid dysfunction.

The prevalence of thyroid dysfunction were 55.7% (39/70), 42.9% (30/70) and 2.8% (2/70) in groups I, II and III respectively (Table III). The most frequent type of abnormality was isolated low fT_4 followed by subclinical hypothyroidism and both abnormalities were observed to be more prevalent in HIV patients that were on HAART therapy (group I) than HAART naïve HIV patients (group II).

Table II: Serum fT_3 , fT_4 and TSH levels of study subjects by Group

Parameter	Group I	Group II	Group III	P value
* fT_3 (pmol/L)	4.55 ± 0.90	3.84 ± 0.74	5.14 ± 0.77	0.0000
* fT_4 (pmol/L)	13.24 ± 4.55	13.30 ± 1.85	15.42 ± 1.89	0.0000
*TSH (μ IU/mL)	2.32 (0.06 – 22.69)	2.05 (0.71 – 13.22)	1.29 (0.05 – 9.08)	0.0001

*Results of serum fT_3 and fT_4 are presented as mean ± SD while the results of TSH are presented as median with range in brackets

Table III: Prevalence and Patterns of thyroid dysfunction among study subjects

Category	Group I		Group II		Group III		Total	
	N	%	N	%	N	%	N	%
Euthyroid	31	44.3	40	57.1	68	97.1	139	66.2
Isolated low fT_4	20	28.6	11	15.7	0	0.0	31	14.8
Subclinical hypothyroidism	12	17.1	9	12.9	1	1.4	22	10.5
Overt hypothyroidism	2	2.9	2	2.9	0	0.0	4	1.9
Subclinical hyperthyroidism	2	2.9	0	0.0	1	1.4	3	1.4
Elevated fT_3	1	1.4	0	0.0	0	0.0	1	0.5
Low fT_3 and fT_4	2	2.9	8	11.4	0	0.0	10	4.8
Total dysfunction	39	55.7	30	42.9	2	2.8	71	33.8

Serum levels of fT_3 and fT_4 among Group I subjects by HAART regimen

Table IV shows significant difference in the mean serum fT_4 between patients on 1st line HAART

regimen and those on 2nd line HAART regimen ($p=0.010$). However no statistical difference was observed in the mean serum fT_3 levels between the two groups ($P=1.000$).

Serum TSH of group I study subjects by HAART regimen

The median serum TSH for group Ia and group Ib were analysed and the p - value was 0.001, which shows that the variation among the two groups was statistically significant (Table IV)

Table IV: Serum fT_3 , fT_4 , and TSH of group I study subjects by HAART regimen

Parameter	Group Ia (1 st line HAART regimen)	Group Ib (2 nd line HAART regimen)	P value
* fT_3 (pmol/L)	4.64 $\pm$ 0.72	4.46 $\pm$ 1.06	1.000
* fT_4 (pmol/L)	12.14 $\pm$ 2.21	14.42 $\pm$ 5.95	0.010
*TSH (μ IU/mL)	2.47 (0.58 – 22.69)	1.82 (0.06 – 9.63)	0.001

*Results of serum fT_3 and fT_4 are presented as mean $\pm$ SD while the results of TSH are presented as median with reference intervals in brackets.

DISCUSSION

The HAART treated HIV positive subjects in this study were slightly older than their counterparts who were HAART naïve. This may be due to the effect of HAART on improving the life expectancy of the individuals, thus enabling them to live longer.¹⁵

The slight female preponderance among the HIV infected studied subjects suggested that the disease was commoner among females than males in the area of the study. Studies conducted in Awka (South-East Nigeria)¹⁶ and Nassarawa-Eggon (North-Central Nigeria)¹⁷ reported a female preponderance of 68.9% and 51.5% respectively. Similarly, other studies conducted outside Nigeria also reported female preponderance.^{18,19,20,21}

However, a study conducted previously in Kano by Iliyasu and colleagues²² reported male preponderance of 54.6%. Furthermore, sex distribution among the control group of this study revealed male preponderance. This may be due to the fact that most of the control group subjects were

recruited from blood donor clinic, where most donors were males.

Married couples constituted majority of subjects in the study. This is in agreement with the study conducted in Nassarawa-Eggon.¹⁷ This observation may be due to increased awareness of HIV infection, availability of more voluntary counselling and testing (VCT) services and less stigmatization.

There were more widows in the HAART naïve group compared to the HAART treated group. Most of these widows discovered their HIV status after the demise of their spouses, hence the delay in HIV diagnosis and probably this explains the delay in initiating HAART treatment in them as some of them were HAART eligible but have not commenced ARTs because they were presenting for the first time at the time of their recruitment into this study.

In this series, the prevalence of overt and subtle thyroid dysfunction were observed to be higher among HIV positive subjects on HAART and the prevalence were higher than the previously reported prevalence from other centres (35% for subtle thyroid dysfunction and 1 – 2 % for overt thyroid disease) among HIV infected individuals.³ The higher prevalence observed in this study may be linked to nutritional and geographic differences of the studied populations.^{23,24}

Isolated low fT_4 with concurrent normal TSH and fT_3 values was the most frequent abnormality observed in this study with a prevalence of 28.6% among HIV positive HAART treated subjects and 15.7% among HIV positive HAART naïve subjects. Previous studies also observed similar findings among HIV infected individuals.^{5,25}

Isolated low fT_4 was initially thought to be consistent with a centrally mediated process with failure of either the hypothalamus or the anterior pituitary. However, in one study that involved the administration of exogenous thyrotropin releasing hormone (TRH), neither delayed nor absent TSH response was observed, thus indicating that neither hypothalamic nor pituitary insufficiency was the

likely cause of the isolated low fT_4 in the HIV-infected patients.²⁶ The observed isolated low fT_4 level could also be artifactual.³

Furthermore, the prevalence of subclinical hypothyroidism in this study was higher among the HIV-positive HAART treated patients (17.1%) than HIV-positive HAART naïve patients (9%). Similar findings were observed by previous reports^{27,28,29} In contrast however, Collazo *et al*³⁰ reported a lower prevalence in a Spanish population of 202 HIV patients.

The prevalence of overt hypothyroidism was similar among HIV-positive patients on HAART and HIV positive HAART naïve patients. Similar observations were also reported by some researchers.^{4,5,7,29,31}

Subclinical hyperthyroidism was observed in two HAART treated HIV positive study subjects, accounting for a prevalence of 2.9%. This finding agrees with reports from other centres.^{4,5}

Elevated fT_3 only was found in 1 HAART treated HIV positive patient. Similar finding was reported by Beltran *et al*.⁵

The mean fT_4 was significantly lower among HIV positive patients on 1st line HAART regimen while their median TSH was higher compared to those on 2nd line HAART regimen.

The adult treatment guideline for HIV patients in Nigeria comprises of 2 NRTIs and 1 NNRTIs for first line HAART regimen while the second line HAART regimen is mostly PI based combination. The lower serum fT_4 accompanied by higher levels of TSH among those on 1st line HAART show that they are more prone to develop subclinical hypothyroidism and eventually overt hypothyroidism with continued usage of this regimen. Similarly, the higher fT_4 with lower TSH levels may be a pointer towards the development of subclinical and later overt hyperthyroidism among those on 2nd line HAART.

Several studies within and outside this country have reported similar findings suggesting a higher prevalence of thyroid abnormalities in HIV patients especially those on HAART^{2-7,9,25,27-30,31-40}

CONCLUSIONS

This study has established that thyroid dysfunction is commoner among HIV positive patients than HIV-negative controls (the prevalence, being higher among the HAART treated HIV-positive patients than HAART naïve HIV-positive patients). Isolated low fT_4 and subclinical hypothyroidism were the commonest abnormalities observed. The study also demonstrated a statistically significant difference in mean serum fT_4 and TSH between HIV-positive patients on 1st line HAART and those on 2nd line HAART regimen.

Recommendations

The following recommendations are suggested based on the findings of this study:

1. All stable newly diagnosed HIV positive patients should be encouraged to undergo screening test for the evaluation of their thyroid function.
2. All HIV positive patients that are about to commence treatment should have a thyroid function test done with a view to establishing the baseline.
3. Patients identified to have subclinical or subtle thyroid abnormality should be monitored frequently as subclinical condition may at times be associated with symptoms that may require treatment and the condition may predate overt thyroid disorder.
4. Patients identified to have overt or clinical thyroid dysfunction should be commenced on treatment immediately to prevent adverse effects.

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