Saudi Journal of Biomedical Research
Scholars Middle East Publishers
Dubai, United Arab Emirates
Website: http://scholarsmepub.com/

ISSN 2518-3214 (Print)
ISSN 2518-3222 (Online)

Thyroid Function in HIV Patients at Parirenyatwa Serology Laboratory, Zimbabwe

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Original Research Article

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Article History
Received: 03.11.2017
Accepted: 11.10.2017
Published: 30.10.2017

DOI:
10.21276/sjbr.2017.2.6.1

Abstract: Antiretroviral therapy (ART) causes disturbances in the normal function of the endocrine system and has been associated with thyroid dysfunction in HIV patients on treatment. More data on thyroid dysfunction are needed in Zimbabwe to persuade the country program to institute routine monitoring if needed. We sought to establish if ART exposure is associated with thyroid dysfunction in HIV patients. A cross-sectional study with two comparative groups was conducted between 1 October and 31 December 2016. The participants included HIV-infected persons aged 18^{+} years who attended Opportunistic Infections (OI) clinics in urban areas around Bulawayo, Zimbabwe. Patient samples were tested at the Parirenyatwa Serology Laboratory in Harare, Zimbabwe. The two comparative groups were defined as cases and controls. Cases were HIV positive patients with thyroid dysfunction whilst controls were HIV positive patients without thyroid dysfunction. Participants included 100 females and 93 males who were on ART. The mean age was 34.6 (10.2) years and median age was 33.0 (43.5-68.3) years. The prevalence of thyroid dysfunction was 45.6% and all cases had hypothyroidism. Sex was not associated with thyroid dysfunction, but thyroid dysfunction was more significant in older patients (P=0.031). This study confirms that ART is associated with thyroid dysfunction in older HIV patients on ART. These results are worrying and may suggest a need for the country HIV program to establish strategies to mitigate this. It is cause for concern because the presence of an untreated thyroid dysfunction in HIV patients will worsen their prognosis.
Keywords: ART, Bulawayo, HIV, Hypothyroidism, Parirenyatwa, Thyroid, Zimbabwe

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is a retroviral disease caused by the human immunodeficiency virus (HIV). The virus displays characteristics of infecting and depleting CD4+ T lymphocytes, and profound immuno-suppression which then leads to opportunistic infections, neurologic manifestations and secondary neoplasms [1,2]. According to the National AIDS Council of Zimbabwe the prevalence of HIV infected adults in Zimbabwe is 15% and of those infected 62% are on antiretroviral therapy (ART). Fortunately, history of AIDS has been changed by ART, which prevents loss of CD4+ cells and has contributed to the decline of transmission and stabilization of the epidemic in many countries [3]. ART is a combination of antiretroviral (ARV) drugs which maximally suppresses the HIV virus, stops the progression of HIV disease and prevents onward transmission of HIV. By suppressing replication of the HIV virus, ART improves the immune system and increases $CD4^{+}$ cell numbers [4].

Infection by HIV can lead to multiple organ involvement and the endocrine system (thyroid gland in particular) is not spared. Endocrine function may be altered in HIV patients because of the possible relationship between the immune and endocrine systems, direct involvement of the glands by the HIV itself, opportunistic infections or malignancies. Abnormalities in thyroid function tests (TFTs) can also be caused by any chronic illness that is associated with malnutrition or inflammation [5]. Thyroid diseases are either associated with excessive release of thyroid hormones (hyperthyroidism) or thyroid hormone deficiency (hypothyroidism) [6]. Hyperthyroidism is defined as thyroid stimulating hormone (TSH) level below normal and free thyroxine (FT_4) or free triiodothyronine (FT_3) above that of the normal range. Hypothyroidism is TSH level below normal range and

FT_4 or FT_3 below normal range [7].

Complications have been noted in HIV patients during use of ART, such as lipodystrophy, lipoatrophy, hypertriglyceridaemia, hypercholest-erolaemia, type 2 diabetes mellitus, glucose intolerance, gonadal dysfunction, osteoporosis and osteopaenia. [2, 6. 7] In addition to the common adverse reactions arising from ART, there are reports of thyroid dysfunction. Thyroid dysfunction secondary to ART therapy is classified into overt or subclinical. Overt hyperthyroidism is defined as elevated free triiodoxine (FT_3) and free thyroxine (FT_4) levels in the presence of a very low to undetectable serum TSH value. Subclinical hyperthyroidism is defined as a normal FT3 and FT4 in the presence of a low TSH value. Overt hypothyroidism is defined as elevated TSH level whilst subclinical hypothyroidism is defined as normal FT3 and FT4 in the presence of elevated TSH [8, 9].

Contradictory reports have been noted around thyroid dysfunction in HIV/AIDS patients, but 1-2% of those infected present overt thyroid disease and subtle abnormalities in thyroid functions [10]. Currently the effects of ART on thyroid function are unclear. Although it is noted that the majority of HIV patients display normal thyroid function, there is an increasing awareness of a growing number of patients on ART presenting with symptoms of thyroid disease [11]. There are conflicting results concerning the necessity of routine thyroid screening in HIV patients on treatment with ART. A United Kingdom study suggested that screening is not warranted due to observed low frequency of thyroid abnormalities in their cohort, whereas a longitudinal in Italy reports that screening is recommended [12].

This study therefore aims to investigate whether ART is associated with thyroid dysfunction in HIV patients as published data on HIV patients on ART in Zimbabwe is scant. This is a cause of concern because the presence of an untreated thyroid dysfunction in HIV patients will worsen their prognosis [13]. Therefore this study will seek to establish prevalence of thyroid dysfunction in HIV patients on antiretroviral therapy, who attended Opportunistic Infections Clinics in Bulawayo urban areas and had their samples analysed at Parirenyatwa Serology Laboratory from 1 October to 31 December 2016.

MATERIALS AND METHODS

This comparative study compared cases and controls: cases were defined as HIV positive patients with thyroid dysfunction and controls were HIV positive patients without thyroid dysfunction.

Study setting

This study was carried out at Parirenyatwa Group of Hospitals Serology Laboratory. This hospital was selected because it is a central government hospital and also acts as a referral health centre. The patient samples in this study were collected at various Bulawayo City clinics and sent to Parirenyatwa Serology Laboratory for assaying.

Ethical consideration

Ethical clearance for the study was sought from Africa University Research Ethics Committee (AUREC). All the collected patient data was used for research purposes only and results were saved and recorded on a personal computer which was password protected and only accessible to the researchers.

RESULTS AND DISCUSSION

There were 193 participants recruited in the study whose ages ranged from 18-60 years. Age was not normally distributed as shown by one-sample Kolmogorov-Smirnov test hence median (IQR) was used to describe age (Table 1). Approximately 48% (n=93) of patients were males.

Highest proportion of patients (24.8%, n=36) was from Entumbane Clinic as shown in Figure 1 and Table 2.

The findings of this current study showed 45.6% of patients had thyroid dysfunction (Table 3), which is similar to earlier studies that have reported high prevalence of thyroid dysfunction in patients infected with HIV [14]. For example, 178 participants studied in China showed that 9.4% of patients had thyroid dysfunction and prevalence was more frequent in participants who were on ART. Thyroid dysfunction in the Chinese retrospective study mainly manifested as hypothyroidism [14], similar to results of the current study. However the prevalence in this study (45.6%) was five times higher than the Chinese study (9.4%)

Our findings show that sex was not associated with thyroid dysfunction (Odds Ratio 1.47 (0.83-2.60) at 95% CI but results (Table 4 and 5) revealed that thyroid dysfunction was more significant in older patients (P = 0.031) and this is similar to studies [15, 16].

Table 1: shows demographic and biochemical characteristics of the patients

	Maximum	**Minimum**	**Median**	**IQR**	**N**
Age/years	60.0	18.0	33.0	43.5-68.3	193
	Maximum	**Minimum**	**Mean**	**SD**	**N**
TSH	24.4	0.4	5.5	4.8	193
FT_4	22.2	4.5	11.0	2.7	187

TSH, thyroid stimulating hormone; FT4, thyroxine; SD, standard deviation; N, number; IQR, interquartile range

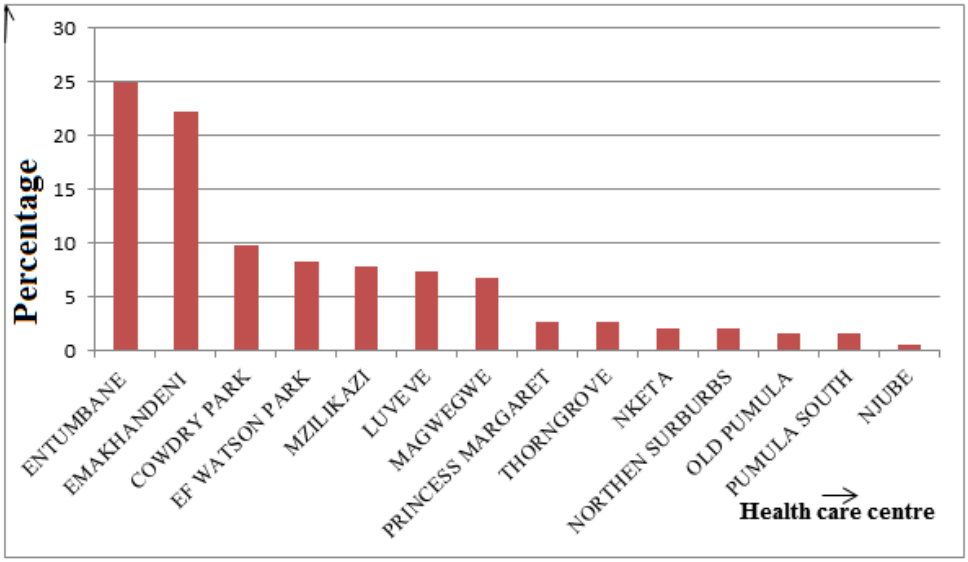

Fig-1: shows proportions of patients by health care centre

Table 2: shows details of patients by health care centre

Health Care Centre	Thyroid dysfunction Number (%)		Total
	Yes	No	
Cowdry Park	5 (26.3)	14 (73.7)	19
EF Watson Park	8 (50.0)	8 (50.0)	16
Emakhandeni	8 (18.6)	35 (81.4)	43
Entumbane	36 (75.0)	12 (25.0)	48
Luveve	5 (35.7)	9 (64.3)	14
Old Pumula	1 (33.3)	2 (66.7)	3
Magwegwe	5 (38.5)	8 (61.5)	13
Mzilikazi	5 (33.3)	10 (66.7)	15
Njube	1 (100)	0 (0)	1
Nketa	3 (75.0)	1 (25.0)	4
Northen Surburbs	4 (100)	0 (0)	4
Princess Margaret	5 (100)	0 (0)	5
Pumula South	0 (0)	3 (100)	3
Thorngrove	2 (40)	3 (60)	5

Table 3: shows the distribution of patients by thyroid function

	Number	Percent
Overt hypothyroidism	31	16.1
Subclinical hypothyroidism	57	29.5
Thyroid dysfunction	88	45.6
Normal thyroid function	105	54.4
Total	193	100.0

Table 4: shows the Mann-Whitney test for association between age and thyroid dysfunction

Ranks				
	Thyroid dysfunction	N	Mean Rank	Sum of Ranks
Age (years)	Yes	88	106.46	9368.50
	No	105	89.07	9352.50
	Total	193		

Table 5: shows the test statistics for the Mann-Whitney Test.

Test statistics	Age (yrs)
Mann-Whitney U	3787.500
Wilcoxon W	9352.500
Z	-2.155
Asymp. Sig. (2-tailed)	0.031

CONCLUSIONS

Although the present study has reported relationships between age and thyroid dysfunction in HIV patients, the cross-sectional nature of the present study prevents an establishment of a causal relationship between ART and thyroid dysfunction. There is however evidence that being older in patients on ART is associated with hypothyroidism in patients from Bulawayo, Zimbabwe. This observation may need change in policy around monitoring of patients on ART as untreated thyroid dysfunction in HIV patients could be life threatening.

RECOMMENDATIONS

The study size needs to be larger to increase the power of the study and to be more representative of the Zimbabwean population so as to confirm the findings in this study. The evidence from this study could be strengthened by assaying for thyroid function in HIV-uninfected as well as ART-naïve patients along with the ART-experienced.

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