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PREVALENCE OF THYROID DYSFUNCTIONS AND DYSLIPIDEMIA AMONG PATIENTS WITH HIV INFECTION: A HOSPITAL BASED STUDY FROM EASTERN INDIA

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ABSTRACT

The aim of this study was to estimate the prevalence of thyroid dysfunctions and dyslipidemia among patients living with HIV and to investigate the associated factors. This cross sectional comparative group study was conducted between Feb 2013 to Jan 2014 at a single centre. The enrolled subjects were grouped in three categories, Group A (n= 42) comprising of ART naïve HIV patients at baseline, Group B (n= 48) comprising of HIV patients starting ART at baseline, Group C (n= 19) comprising of HIV patients at baseline and after 6 months follow-up. Study population included 109 (59 males, 50 females) HIV patients with a mean age of 35.59 ± 10.2 years. Taken together, in Group A and B, 20% had hypothyroidism. Further, 1 patient each from both the groups had hyperthyroidism. In the present study, 12 % of HIV patients with CD4<200 Cells/mm^3 had thyroid dysfunctions whereas 2% with CD4 200-350 Cells/mm^3 and 7 % patients with CD4>350 Cells/mm^3 had abnormal thyroid profile. In the follow up Group C, 2 patients developed Thyroid dysfunctions after 6 months on ART. Additionally, hypertriglyceridemia was found prevalent among HIV subjects with hypothyroidism in all the groups. Current National AIDS Control organization (NACO), India guidelines doesn't recommend mandatory monitoring of thyroid function tests (TFT) in asymptomatic HIV patients. Considering the prevalence of Thyroid dysfunctions among HIV patients, TFT along with other blood investigations is suggested. However, larger population based study is required for proper validation.

Key Words: TSH, Lipids profile, HIV

INTRODUCTION

According to UNAIDS, Globally, 34.0 million [31.4–35.9 million] people were living with HIV and 1.7 million died of AIDS related illnesses at the end of 2011 [1]. The estimated number of HIV/AIDS cases in India was 2,088,642 and overall adult prevalence was 0.27 percent at the end of 2011 [2]. It is estimated that India had approximately 1.16 lakh new adult HIV infections in 2011. HIV infection directly or indirectly through opportunistic infections and/or by antiretroviral drugs causes a variety of endocrine problems. Thyroid hormones have profound effects on body metabolism and exert their influence in protein, carbohydrate and lipid metabolism [3]. Abnormal thyroid function is common among human immunodeficiency virus (HIV) infected individuals [4]. During antiretroviral therapy, the prevalence of subclinical hypothyroidism, sick euthyroid syndrome, Graves's disease is increased [5-7]. Hypothyroidism is more among patients on PI–based regimens whereas hyperthyroidism has been reported in increased frequency among those on NNRTI containing regimen [8].

Patients not receiving ART have increased production of inflammatory cytokines due to active disease, and the presence of opportunistic infections can all contribute to development of endocrine disorders. With the initiation of treatment, immune reconstitution can precipitate autoimmune diseases such as hyperthyroidism [9-12]. In India very few

studies have so far been conducted to evaluate the status of Thyroid hormones among HIV subjects [11, 12]. Further, the assessment of Thyroid hormone functions among patients from eastern part of India is also very few [12]. In light of the paucity of literatures and considering the important role played by the Thyroid hormones on body metabolism their status among HIV subjects was investigated along with their serum lipid profiles and CD4 count. This was a small pilot study to understand the extent of thyroid dysfunctions along with their association with dyslipidemia in HIV infection.

STUDY POPULATION

The study was carried out in a government run tertiary care hospital, Calcutta School of Tropical Medicine during the period Feb 2013 to Jan 2014. The study was approved by the Institutional ethics committee and was initiated subsequently. This was an observational prospective hospital based study. All ART naïve adult patients excluding pregnant women who were enrolled consecutively and registered to receive ART during this period were included in the study. Those lost to follow-up or transferred to other ART were excluded. Further patients on any hormone therapy were also excluded from the study. Wasting in HIV patients was considered at BMI <18.5 kg/m^2.Patients were grouped based on their ART status, in three categories, Group A (n= 42) comprising of ART naïve HIV patients at baseline, Group B (n= 48) Comprising of HIV patients starting ART at baseline, Group C (n= 19) comprising of HIV patients at baseline and after 6 months follow-up.

LABORATORY METHODS

Five millilitres of venous blood sample was collected from all patients who came with laboratory requisitions for the testing of HIV antibodies. Venous blood was drawn after 8-12 hrs overnight fasting. The blood was allowed to clot for 45 minutes at room temperature and the serum was separated after centrifugation at a low speed. These samples were analyzed for lipid levels using autoanalyser ERBA XL 600. The lipid profile includes Cholesterol, Triglyceride, VLDL, LDL, HDL cholesterol were done by standard biochemical analysis using Autoanalyser Erba XL 600. The samples were also analyzed for Thyroid hormone profile (T3, T4 and TSH) using ELISA (Monobind, USA) with a sensitivity of 0.078 µIU/ml. Absorbance value was read in each well at 450nm using reference wavelength of 650nm to minimize well imperfection by ELISCAN elisa reader.

DATA ANALYSIS

Data are presented in mean (SD). A *P* value < 0.05 for a two-sided test was considered statistically significant. All analyses were performed with the statistical software Graphpad.

RESULTS

Taken together, Group A, B and C, a total of 109 (59 males, 50 females) HIV patients with a mean age of 35.59 ± 10.2 years were studied. The mean BMI was 19.05 ± 4.5 kg/m^2 and 9 patients had wasting (< 18.5 kg/m^2) in Group A and B, the demographic characteristics of the study groups have been briefly tabulated (Table 1). The mean BMI for Group C was 22.3 ± 7.6 kg/m^2 and 5 patients had wasting (<18.5 kg/m^2) (Table 3). This study consisted of 35 (32.1%) patients with advanced HIV illness (CD4<200). ART was being used by 67 (61.4%) and they were categorized to ART group and the remaining who were not using ART were categorized to ART-naïve. ART regimens being used were of four types based on the different combination of zidovudine or stavudine with either nevirapine or efavirenz; lamivudine was common in each regimen. Patients in ART-naive group were either newly diagnosed or were those who did not fulfill the NACO criteria for initiation of ART based on WHO clinical staging and CD4 counts.

Thyroid function test (TFT) was done in all the patients, of them, 18 (20%) had raised TSH in Group A and B. Only 2 patients had low TSH titers [Table 2]. TFT was also done in the recruited follow up subjects, 2 of the 19 patients developed raised TSH values [Table 3].

Further analysis of the serum lipids of all the 22 hypothyroid patients from group A, B and C revealed high triglyceride levels in 6 patients, high cholesterol in 2, high LDL cholesterol in 5 patients whereas 11 patients had low HDL cholesterol levels.

The coefficients of correlation between the thyroid values and the lipid values revealed a significant positive correlation between all patients with elevated TSH and TG (r = 0.64; P value 2 tailed = 0.002 alpha <0.05). However, no significant correlation was obtained with the other Lipid parameters [Table 4]. Similarly, coefficients of correlation between T4 and VLDL cholesterol revealed a significant positive correlation (r = 0.99; p value 2 tailed <0.001; alpha< 0.05), however, no similar correlation was obtained with other lipid variables. The coefficients of correlation were also not significant between T3 and any other lipid parameter in the study.

Further, among the hypothyroid HIV patients with CD4<200, significant positive coefficient of correlation was obtained with Triglyceride (r = 0.89;

P value 2 tailed = 0.002). However, none of the other lipid parameters had any other statistically significant relation. Additionally, these patients also had no significant correlation of increased TSH titers with their decreased BMI. Thus, muscle wasting in these patients could not be contributed due to thyroid dysfunction.

DISCUSSION

HIV infection is a chronic, systemic disease possibly leading to multi-organ involvement and affecting the endocrine system as well. Hypothyroidism is highly prevalent in HIV infected population. Different studies have reported the cause of hypothyroidism in HIV patients to be either due to ART intake or due to low CD4 count of patients. Grappin *et al*.[13] demonstrated that both stavudine and lamivudine was significantly related to the presence of hypothyroidism, whereas Beltran *et al*.[14] found that the use of stavudine along with lower CD4+ cell count were associated with subclinical hypothyroidism. Further, Nelson *et al*.,[12] reported a high incidence of hypothyroidism in patients receiving ART, and they recommended universal screening of subjects on therapy.

The present study demonstrated that the prevalence of thyroid dysfunctions in HIV-positive individuals was 6% among naïve and 13 % among ART-treated subjects. However, no association between thyroid dysfunctions and ART treatment could be obtained (p value 0.65). This observation is similar to studies reported by Collazos *et al*. and Quirino *et al*. [15, 16]. In this study we found that 11 % of male and 9 % of female patients had thyroid dysfunctions. Earlier studies of Madge S et al [17] and others mainly concentrated on male patients; however, in this study we recruited almost equal number of male and female patients and found that the prevalence of thyroid abnormality was similar in both the sexes. Low CD4 is a known risk factor for presence of thyroid abnormalities. Here we found that HIV patients with low CD4 had statistically significant ($p<0.05$) relationship with thyroid function abnormalities.

In the present study, only 2% patients had low TSH, Earlier, the prevalence of hyperthyroidism (overt and subclinical) in HIV infected patients have been reported to be <1%[18].Thus, commonest thyroid abnormality in the present study is hypothyroidism followed by hyperthyroidism.

The present study found that lipid profile was altered in both early and advanced stages of HIV illness (Group A vs. B). Hypertriglyceridimia was found to be the prevalent manifestation among the studied HIV population. The coefficients of correlation between patients with elevated TSH and Triglyceride was significant ($p<0.05$). This may suggest that patients developing hypertriglyceridimia after ART initiation are those at higher risk of hypothyroidism, so this population should be monitored for thyroid function. As a consequence, subjects who develop an increase in Triglyceride after ART introduction should also be specifically monitored for thyroid dysfunctions.

Previous investigations have demonstrated that hypothyroidism associated with hypertriglyceridemia may increase the risk of accelerated atherosclerosis and premature coronary artery disease in some patients [18].Thus, elevated levels of both TSH and Triglyceride levels may also serve as added risk factors of HIV patients and thus their levels should be monitored.

The limitations of this study are the small number of study subjects and the role of single antiretroviral drugs could not be evaluated due to the highly heterogeneous types of drug regimes in this study. Thus, larger and more prolonged studies are needed to better assess the clinical impact of thyroid dysfunctions in HIV-positive subjects.
Taken together, our results suggest that thyroid function has to be monitored in all HIV-infected subjects, especially in those starting ART.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

Table 1: Demographic characteristics of the study groups

Parameters	Total	Group A	Group B
Sex	90 (47 males, 43 females)	42(16 males, 26 females)	48 (31 males, 17 females)
Mean age (mean ± SD; years)	34.47 ± 10.07	36.75 ± 10.27	35.45± 9.8
Age (range) yrs	16-65	16- 56	20- 65
Body mass index (kg/m2)	20.83 ± 5.65	19.93 ± 5.45	17.48 ± 5.82
CD4+ cell count (Cells/mm^3)	355 ± 200	511 ± 131	219 ± 141

Table 2: Hormone levels in the study population (Group A and B)

Name of the hormone	Levels	Group A and B combined Number of patients (N %)	Group A (N %)	Group B (N %)
TSH (µIU/ml)	<0.39	2 (2.2)	1(2.3)	1(2)
	0.39-6.16	70 (77.7)	35(83)	35(72.9)
	>6.16	18 (20)	6(14.2)	12(25)
T4(µg/dl)	<4.4	2 (2.2)	1(2.3)	1(2.3)
	4.4-11.6	88 (97)	41(97.6)	46(95.8)
	>11.6	1(1)	-	1(2)
T3(ng/ml)	<0.52	2(2.2)	2(4.7)	-
	0.52-1.85	87(96)	40(95.2)	47(97.9)
	>1.85	1(1)	-	1(2)

Table 3: Characteristics of Group C at baseline and 6 months follow up

Parameters	Range	Baseline	Follow up
Sex		Total 19 (12 male, 7 female)	
Mean age (mean ± SD; years)		33.84 ± 10.3years	
Age (range)yrs		22- 65	
Body mass index Mean (kg/m2)		22.3 ± 7.6	
Body mass index < 18.5 (n)		5	
CD4+ cell count (Mean, Cells/mm^3)		211± 130	245± 114
TSH (µIU/ml) (N, %)			
	<0.39	-	
	0.39-6.16	19 (100)	17(89)
	>6.16	-	2(10)
T4(µg/dl) (N, %)			
	<4.4	-	1(5.2)
	4.4-11.6	19(100)	18(94.7)
	>11.6	-	-
T3(ng/ml) (N, %)			
	<0.52	-	1(5.2)
	0.52-1.85	19(100)	18(94.7)
	>1.85	-	-
Total cholesterol (mg/ dl) (N, %)			
	<200	17(89)	17(89)
	>200	2(10)	2(10)
Triglyceride (mg/dl) (N, %)			
	<160	17(89)	17(89)
	>160	2(10)	2(10)
HDL-cholesterol (mg /dl) (N, %))			
	40-70	10(52.6)	10(52.6)
	<40	9(47.3)	9(47.3)

LDL-cholesterol (mg /dl) (N, %)			
	<100	14(73.6)	14(73.6)
	>100	5(26.3)	5(26.3)
VLDL-cholesterol (mg /dl) (N, %)			
	2-30	15(78.9)	15(78.9)
	>30	4(21)	4(21)

Table 4: The level of total cholesterol, triglyceride, HDL, LDL and VLDL in the study population (Group A and B).

Parameters	Range	Group A (N, %)	Group B (N, %)
Total cholesterol (mg/ dl) (N, %)			
	<200	36 (85.7)	43 (89)
	>200	6 (14)	5 (10)
Triglyceride (mg/dl) (N, %)			
	<160	34 (80)	21 (43.7)
	>160	8 (19)	13 (27)
HDL-cholesterol (mg /dl) (N, %)			
	40-70	17 (40)	23 (48)
	<40	25 (59.5)	25 (52)
LDL-cholesterol (mg /dl) (N, %)			
	<100	20 (47.6)	38(79)
	>100	11(26)	10 (20)
VLDL-cholesterol (mg /dl) (N, %)			
	2-30	34(80.9)	39(81.2)
	>30	8 (19)	9(18.7)

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