ORIGINAL RESEARCH PAPER

General Medicine

STUDY OF THYROID DYSFUNCTION IN HIV SEROPOSITIVE PATIENTS ON HIGHLY ACTIVE ANTI RETRO VIRAL THERAPY (HAART)

KEY WORDS: Haart, Hiv, Thyroid, Overt Hypothyroidism, Sub Clinical Hypothyroidism

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ABSTRACT

BACKGROUND: Subtle alterations in thyroid function tests are more common in HIV infection and at times detectable in the early phase of disease and as well as in late phases. However, there is paucity of Indian studies.
Objectives : To study the thyroid dysfunction in newly diagnosed seropositive HIV patients initiating HAART and pattern of change in thyroid profile with measurement at baseline, after 6 and 12 months of HAART and correlation between thyroid function changes in these patients with their CD4 cell count at 0, 6 and 12 months.
METHODS: Study was included 60 newly diagnosed HIV seropositive patients presenting to JLN Medical College and Hospital, Ajmer (Raj.) and registered at ART Centre JLN Hospital, Ajmer during the period of Jan, 2018 to Oct, 2019 after taking written consent of the patients and the relevant history, these patients were subjected to complete clinical examination. Subjects with HIV serology positive by ELISA test and on HAART regimen were included and Patients with comorbidities eg. T.B., diabetes, CKD, Malignancy, known case of thyroid disorders and patients on drugs that cause thyroid abnormality were excluded.
RESULTS: Out of 60 patients included in the study 65% were males and 35% were females. 10% cases were found subclinical hypothyroidism and 3.33% cases were found overt hypothyroidism. In our study correlation between CD4 counts and thyroid dysfunction was found statistically significant (p=0.02).
CONCLUSIONS: Subclinical hypothyroidism was the most common thyroid abnormality observed followed by overt hypothyroidism. There was statistically significant correlation (negative) between CD4 cell count and thyroid abnormality. Thyroid abnormalities vary with the type and duration of HAART regimen.

INTRODUCTION

HIV infection is associated with multiple organ involvement including the endocrine system. In autopsy studies, adrenal gland is the most commonly involved endocrine gland in the body, but clinical adrenal dysfunction is uncommon, likewise clinical thyroid disorder is rare but altered Thyroid function is common. Human immunodeficiency virus (HIV) infection is characterized by decreased CD4 cell count and immunod eficiency, leading to opportunistic infections (OIs) and tumors [1]. In recent years, increasing number of patients with HIV infection are able to survive for long periods because of the extensive application of highly active antiretroviral therapy (HAART) for the repression of viral replication as well as because of the emergence of new medicines and therapeutic regimens. Many nonacquired immune deficiency syndrome-(AIDS-) related diseases now primarily account for the disease burden in patients with HIV infection. Abnormalities of the endocrine function of the pituitary, thyroid, adrenals, gonads, and pancreas and in metabolism are common in patients infected with HIV and are becoming the main conditions influencing the long-term quality of life in HIV infected patients.[2,3] Some studies have reported complications such as hypertriglyceridemia and hypercho lesterolemia, lipodystrophy and lipoatrophy, glucose intolerance and type 2 diabetes mellitus, gonadal dysfu nction, and osteopenia and osteoporosis during HAART.[2,4] Thyroid hormone, an important hormone regulating metab olism, can also be affected by HIV infection. Numerous studies have reported that the incidence of thyroid dysfunction is much higher (about 36%-37%) in patients infected with HIV than in the general population.[5,6] However, other researchers have suggested that the morbidity of overt thyroid dysfunction in patients infected with HIV is similar to that in the general population.[2,6] Therefore, further research into the prevalence of thyroid dysfunction in patients infected with HIV is required.

Thyroid dysfunction reduces the quality of life of patients infected with HIV. Overt hypothyroidism leads to the insidious onset of fatigue, weakness, dry skin, cold intolerance, slowed mentation, constipation, hoarse voice, paresthesia, bradycardia, and delayed relaxation of tendon reflexes. Overt hyperthyroidism is characterized by irritability, heat intole rance, sweating, warm moist skin, palpitations, tachycardia, fatigue, weight loss with increased appetite, diarrhea, tremor, muscle weakness, hyperreflexia, and lid retraction.

The consequences of subclinical hyperthyroidism include reduced bone mineral density and an increased risk of atrial fibrillation, the risk of which is proportional to the degree of thyroid hyperfunction.[6] Furthermore, subclinical hyperth yro idism may precede overt hyperthyroidism.[7,8] It is unclear why HIV-infected patients are susceptible to thyroid dysfunction, but HIV infection is regarded as a crucial factor. Furthermore, the influence of HIV infection on thyroid function changes with the course of the disease.

Asymptomatic, subtle abnormalities of thyroid function tests have been described in a small minority of patients with stable HIV infection[2,16,17]. With the progression of the disease, a pattern of sick euthyroid syndrome may develop. The most frequent abnormalities in thyroid function tests are those associated with subclinical hypothyroidism.[2,6,8]

The medications used to treat HIV infection are also a vital factor leading to abnormalities in thyroid function. Some reports have indicated that HAART increases the probability of thyroid dysfunction. Stavudine has been suggested to directly affect the production and/or metabolism of thyroid hormones.[2,5,8] Prolonged treatment with stavudine contributes to a decrease in free thyroxine (FT4) level.[2]

A high prevalence of abnormalities in thyroid function tests among HIV infected adults has been noted in previous cross sectional studies. In addition, this thyroid dysfunction correlated with advancement of the infection in conjunction

with lowering CD4 cell counts. Subtle alterations in thyroid function tests are more common in HIV infection and at times detectable in the early phase of disease and as well as in late phases. The thyroid function changes are HIV specific and are consistent with an abnormal response to acute illness. However there is paucity of Indian studies that are needed to evaluate the thyroid dysfunction in HIV infected patients and their clinical correlation.

AIDS-RELATED CONDITIONS THAT CAUSE THYROID DYSFUNCTION -

In patients with advanced HIV disease, a variety of systemic opportunistic conditions that infect or infiltrate the thyroid can decrease or increase T4 secretion.[9] Cases of thyroiditis have been reported in association with *Pneumocystis jiroveci* infection, *Cryptococcus neoformans* infection, visceral leishmaniasis, and suppurative bacterial infection of the thyroid.[10] These infiltrating conditions lead to destructive thyroiditis, which is usually accompanied by neck pain, thyroid enlargement, and increased thyroxine release. After treatment of the infection, thyroid function can return to normal, but it should be closely monitored until it does so. In addition, both lymphoma and Kaposi sarcoma can infiltrate the thyroid and impair function. Cytomegalovirus inclusions have frequently been reported from autopsy studies, but thyroid disease was rarely noted before death.[8] Symptomatic thyroid infection or infiltration has always been uncommon, and in countries where HAART is available, it has become extremely rare.

METHODOLOGY

Study was included 60 HIV seropositive patients presenting to JLN Medical College and Hospital, Ajmer (Raj.) and registered at ART Centre JLN Hospital, Ajmer during the period of Jan, 2018 to Oct, 2019 after taking written consent of the patients and the relevant history, these patients are subjected to complete clinical examination.

INCLUSION CRITERIA:

1. Patients was attending medical outdoor, admitted in various medical wards and attending ART centre in JLN Hospital Ajmer.
2. Patients who had given written informed consent for study.

EXCLUSION CRITERIA:

1. Patients who were not willing for study.
2. Patients with comorbidities eg. T.B., diabetes, CKD, Malignancy.
3. Patients with known thyroid disorders.
4. Patients on drugs that cause thyroid abnormality.

Besides routine investigations, patients were subjected to specific microbiological, pathological and radiological investigations. CD4 Count (Flow cytometry), Thyroid function tests-TSH, free T4, free T3 and anti TPO antibodies were done in every patient. The data was collected on predesigned and pretested questionnaire/record sheet was compiled and master table was made on Excel accordingly. To fulfill the objectives of the present research, most appropriate statistical tools (percentages and chi square test for association) were applied to analyse the data and conclusions were drawn accordingly.

RESULTS Table -1 : Age and gender distribution

Age group	Female		Male	
	No.	%	No.	%
25-35 years	14	66.7	17	43.6
36-45 years	7	33.3	15	38.5
46-55 years	0	0.0	4	10.3
56-65 years	0	0.0	3	7.7

Among the 60 patients included in our study, 39 patients were male accounting for 65% of the total cases. The remaining 21 patients were (35%) women.

Majority of the patients were in the age group between 25-35 years - 31 patients (51.66% of study population) were in this group

Women were more in number in younger age group (25 – 35) whereas there were no women in the elderly age group (≥46).

Table – 2 : Correlation of CD4 count with thyroid para meters

		Ft3	Ft4	TSH (mIU/L)
Cd4 count at Baseline	r value	-0.01	0.08	0.03
	p value	0.97	0.51	0.80
Cd4 count at 6 months	r value	0.01	0.07	0.11
	p value	0.89	0.58	0.40
Cd4 count at 12 months	r value	-0.07	0.20	-0.34
	p value	.58	0.11	<0.01

Negative correlation (-0.01) was found between CD4 count at baseline and FT3 baseline while positive correlation was found with FT4 baseline (0.08) and TSH baseline (0.03) but there was no statistically significance found in this correlation. Positive correlation were found between CD4 count at 6 months with FT3 6months (0.01), FT4 6months (0.07) and TSH 6months (0.011) but there was no statistically significance found in this correlation.

Negative correlation (-0.07 and -0.34) were found between CD4 count at 12 months and FT3 12 months and TSH at 12 months while only positive correlation was found with FT4 12 months (0.20) but there was no statistically significant correlation found between CD4 count at 12 months with FT3 12 months and FT4 at 12 months while statistically significant correlation found between CD4 count at 12 months with TSH 12 months ($p<0.01$).

Graph -1 : Scatter plot showing correlation between CD4 count and TSH level at 12 months

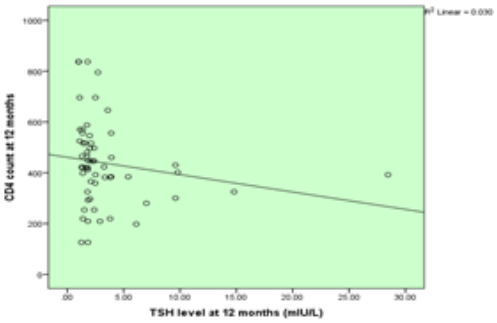

Table – 3 : Association between type of ART drug regimen and thyroid dysfunction

Type of ART regimen	Normal thyroid function		Abnormal thyroid function		P value
	No.	%	No.	%	
TDF+3TC+EFV	21	40.4	5	62.5	0.27
AZT+3TC+NVP	31	59.6	3	37.5	

The predominant drug regimen was with Zidovudine, lamivudine and nevirapine, in both thyroid normal and abnormal group, but there was no statistical correlation between these different drug regimens and the thyroid status.

DISCUSSION

Among the total 60 HIV seropositive patients under study, most of the patients (53/60; 88.3%) were from 25-45 years age group; majority (31/60; 51.67%) being from 25-35 years age group and mean age of the patients under study being 36.73 ± 8.21 years. The study population included 39 male (65%) and 21 female (35%) HIV seropositive patients on HAART.

Maximum number of male and female patients were from 25-35 years age group followed by 36-45 years age group. Mean age in present study is comparable to study group of Madeddu et al.[12] Similar age group is noted in the study done by Beltran et al.[8]

Negative correlation (-0.01) was found between CD4 count at baseline FT3 but there was no statistically significance found in correlation of FT3, FT4 & TSH. Positive correlation were found between CD4 count at 6 months with FT3, FT4 & TSH but there was no statistically significance found in this correlation. Negative correlation (-0.07 and -0.34) were found between CD4 count at 12 months and FT3 12 months and TSH at 12 months while only positive correlation was found with FT4 12 months (0.20) but there was no statistically significant correlation found between CD4 count at 12 months with FT3 12 months and FT4 at 12 months while statistically significant correlation found between CD4 count at 12 months with TSH 12 months ($p<0.01$). According to Dev N et al Significant correlation was observed between CD4 count and, free triiodothyronine, and free thyroxine levels ($r = -0.86$, $r = 0.77$, and $r = 0.84$, respectively, $p < 0.0001$ for all).[11]

In present study, no statistical significant association ($P > 0.05$) could be established between selection of drug regimen and thyroid abnormalities at different points of time. Afhami et al[13] also found no significant association between those drug regimens and thyroid abnormalities. Madge et al[14], in their cohort study, reported that neither HAART regimen nor specifically stavudine use was signifi cantly associated with either overt hypothyroidism or subcli nical hypothyroidism which was in contrast to the findings of correlation detected between stavudine use and thyroid abnormalities by Madeddu et al.[12]

The correlation between duration of drug regimen and thyroid dysfunction was of no statistical significance ($P > 0.05$) and this is in accordance with the findings of Quirino et al[15] who found no statistically significant relationship between the condition and drugs or CD4 cell count and reinforced by Afhami et al[13] with no association between duration of ART and thyroid dysfunction.

CONCLUSION

The present study concluded that thyroid dysfunction occurs significantly in HIV patients on HAART. The prevalence of thyroid dysfunction in the study population was 13.3% (8/60). Subclinical hypothyroidism was the most common thyroid abnormality observed (6/60; 10.0%) followed by overt hypothyroidism (2/60; 3.33%). There was statistically significant correlation (negative) between CD4 cell count and thyroid abnormality. 88.3% patients were from 25-45 years age group; 51.67% being from 25-35 years age group. Correlation of thyroid dysfunction was not found significant with age. Association of thyroid dysfunction with drug regimen (TLE / ZLN) and duration of drug regimen was not found statistically significant. Subsequent studies with larger samples may throw some light on this association. Screening of thyroid parameters is warranted in this population in view of increasing prevalence in the study population.

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