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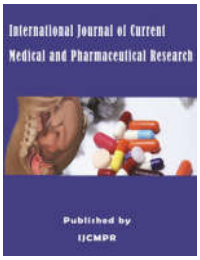

Research Article

STUDY OF THYROID DYSFUNCTION IN HIV SERO-POSITIVE PATIENTS

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ABSTRACT

Introduction: HIV infection is associated with dysfunction of many endocrine organs and their axis. The interaction between HIV infection and endocrine system is complex ranging from subtle biochemical abnormalities in hormone secretion, transport and metabolism to rare instances of hormonal resistance and overt glandular failure.
Aims: To see the prevalence of thyroid dysfunction in HIV seropositive patients and correlate T3, T4, TSH with CD4 cell count.
Material and Methods: This was a cross sectional study done on 50 HIV seropositive patients. The subjects were incorporated into the study after fulfilling the inclusion and exclusion criteria. Newly diagnosed or previously known HIV seropositive patients who were not on ART were included in the study.
Results: Patients with low CD4 cell count were having significantly higher TSH, whereas lower T3 and T4 values. Subclinical hypothyroidism was the commonest biochemical abnormality observed.
Conclusion: Prevalence of thyroid dysfunction was significantly higher in HIV seropositive patients and low CD4 cell counts had strong correlation with development of thyroid dysfunction.

INTRODUCTION

HIV infection is associated with dysfunction of many endocrine organs and their axis. The interaction between HIV infection and endocrine system is complex ranging from subtle biochemical abnormalities in hormone secretion, transport and metabolism to rare instances of hormonal resistance and overt glandular failure.[1] Subclinical diseases like non-thyroidal illness, subclinical hypothyroidism and isolated low thyroxine (T_4) levels are frequently seen in HIV infected individuals while overt thyroid dysfunction occur at similar rates as the general population. Also, highly active anti-retroviral therapy (HAART) can complicate thyroid function further through drug interactions and immune reconstitution inflammatory syndrome (IRIS).[2]

HIV endocrinopathy encompasses a broad spectrum of disorders. Endocrine involvement is related to severity of HIV infection, nutritional status and HAART therapy. There may be primary endocrine dysfunction as a result of direct effect of HIV as well as secondary endocrine dysfunction due to indirect effects of cytokines, opportunistic infections and rarely infiltration by a neoplasm. This may be manifested as subtle biochemical and hormonal changes to overt glandular failure.[3] Endocrine changes in the form of thyroid, adrenal, gonadal, bone, and metabolic dysfunction have been reported in both early and late stages of HIV infection.[4] Systemic inflammation in untreated HIV infection can lead to thyroid dysfunction, adrenal insufficiency, hypogonadism, dyslipidemia, diabetes mellitus and increased bone turnover.[5] It is postulated that HIV infection triggers macrophages to secrete interleukins (IL-1β) and tumor necrosis factor (TNF-α) which exert immunomodulatory effects at every tier of endocrinal axis (hypothalamic–pituitary–effector organ like adrenal, thyroid, gonads).Also, HIV also has the potential to cause polyclonal B cell activation and production of antibodies against glandular cells, thereby inhibiting glandular endocrine function.[6] Nef, a regulatory protein coded by HIV is required for the optimal infectivity of HIV viral particles, plays a critical role in the AIDS pathogenesis and progression. It is noteworthy that there is nucleotide sequence homology between the human TSH-receptor and nef 3.[7] Histologically, the most common finding seen in thyroid gland sections is interstitial fibrosis followed by thyroid dysplasia. HIV infection itself is associated with increased level of transforming growth factor beta (TGF-β).[8]In patients with advanced HIV disease, a variety of systemic

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opportunistic infections can infect or infiltrate the thyroid gland like Cytomegalovirus (CMV), Mycobacterium tuberculosis, Cryptococcus neoformans, Pneumocystis jiroveci.[9]The most common systemic opportunistic infection with thyroid abnormalities is Mycobacterium avium complex (MAC) followed by Candida. HIV/AIDS-related cancers, either AIDS-defining malignancies (ADMs) like kaposi sarcoma or non-ADMs (NADMs) may be seen in HIV infection in advanced stage.[10] Pituitary and hypothalamic destruction can rarely happen by Toxoplasmosis, Cryptococcosis and CMV infection. Autoimmune thyroid disorder (AITD) can occur in association with initiation of potent ART and improved immune function as a component of IRIS. Grave's disease is recognized as a consequence of IRIS and is likely triggered by increase in CD4 count, showing higher prevalence in women (3% for women and 0.2% for men).[11]Although most of the asymptomatic cases with early HIV infection and stable body weight maintain normal thyroid functions, thyroid dysfunction can appear after the initiation of ART.[12] HAART, particularly stavudine, is associated with a high prevalence of subclinical hypothyroidism.[13]With regard to thyroid function, a higher prevalence of subclinical hypothyroidism compared with the general population has been described but the pathogenic role of HAART and of HIV infection itself are still undetermined and till date conflicting results have been published.

MATERIAL AND METHODS

This was a cross sectional study done on 50 HIV seropositive patients, done at Government Medical College and associated Guru Nanak Dev Hospital, Amritsar. The subjects were incorporated into the study after fulfilling the inclusion and exclusion criteria. Newly diagnosed or previously known HIV seropositive patients who were not on ART were included in the study. Patients who were known cases of thyroid disorder and on drugs altering thyroid hormone metabolism along with stavudine based anti-retroviral drugs were excluded.

RESULTS

The study was conducted on 50 HIV seropositive patients. For the purpose of making comparison, the study population was divided into three groups on the basis of CD4 counts.

Table 1 Sex-wise distribution in the groups

	CD4 Count (cells per mm^3)
Group A	<200
Group B	200-350
Group C	>350

Of the total study population, there were 27 (54%) males and 23 (46%) females. The sex distribution amongst the three groups did not reveal any statistical difference, and hence all the three groups were comparable (p value = 0.614).

Table 2 Sex-wise distribution in the groups

Sex	Group A	Group B	Group C	Total
Male	10 (58.8%)	11 (57.9%)	6 (42.9%)	27
Female	7 (41.2%)	8 (42.1%)	8 (57.1%)	23
Total	17	19	14	50

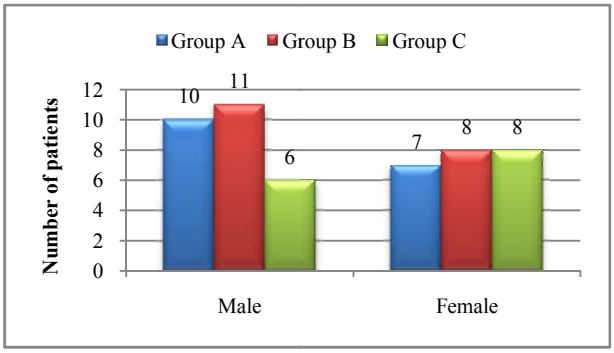
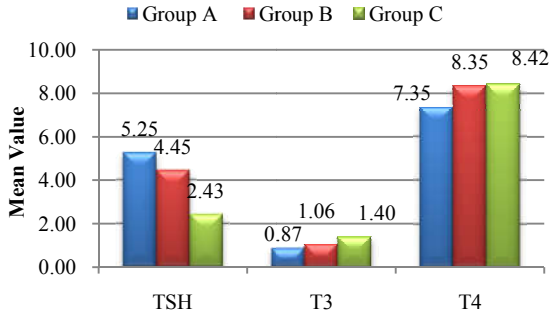


Figure 1 Sex-Wise Distribution In The Groups

	Group A	Group B	Group C	p value
n (F/M)	17 (7/10)	19 (8/11)	14 (8/6)	-
Mean Age (years)	42.76±9.74	39.68±6.58	37.57±6.93	0.191
CD4 Count (cells/mm^3)	<200	200-350	>350	-
Mean T_3 (ng/mL)	0.87±0.32	1.06±0.46	1.406±0.68	0.014
Mean T_4 (µg/dL)	7.35±1.72	8.38±2.04	8.42±1.95	0.197
Mean TSH (µIU/mL)	5.25±2.42	4.45±2.45	2.43±1.106	0.003

Figure 2

Mean T3, T4, TSH in three groups



The mean T_3 was significantly lower in group A which was 0.865 ± 0.32 ng/dL compared to group B and group C which was 1.06 ± 0.46 ng/dL and 1.40 ± 0.68 ng/dL respectively (p value = 0.014). The mean T_4 did not reveal statistically significant difference among three groups, it was 7.35 ± 1.72 µgm/dL in group A compared to 8.38 ± 2.04 µgm/dL and 8.42 ± 1.95 µgm/dL in group B and group C respectively,(p value= 0.197). The mean TSH was significantly higher in group A ,which was 5.25 ± 2.42 µIU/mL compared to group B and group C which was 4.45 ± 2.45 µIU/mL and 2.43 ± 1.106 µIU/mL respectively, a statistically significant negative correlation (r = 0.2795) was found between serum TSH value and CD4 count (p value = 0.003).

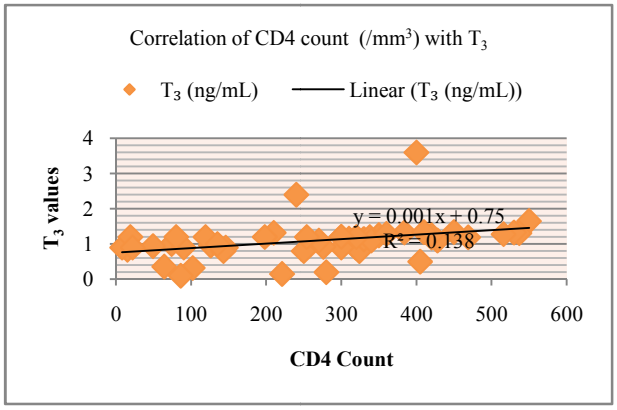
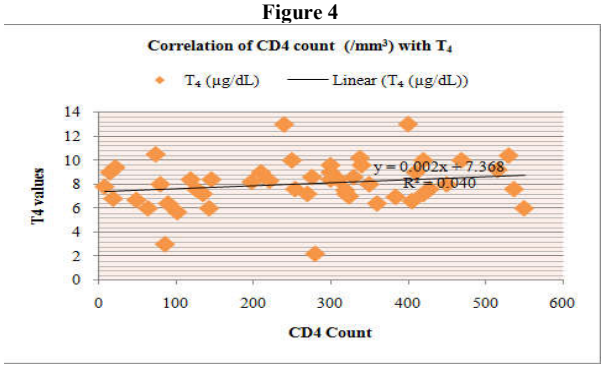


Figure 3 The mean T_3 value in study population was 1.09±0.52 ng/mL. The correlation coefficient was r = 0.1385 and a statistically significant positive correlation was found between serum T_3 value and CD4 count, (p value = 0.008).

Figure 4



The mean T_4 value in study population was 8.04±1.9 µg/dL. The correlation coefficient was r = 0.0408 and a statistically non significant correlation was found between serum T_4 value and CD4 count, (p value = 0.161).

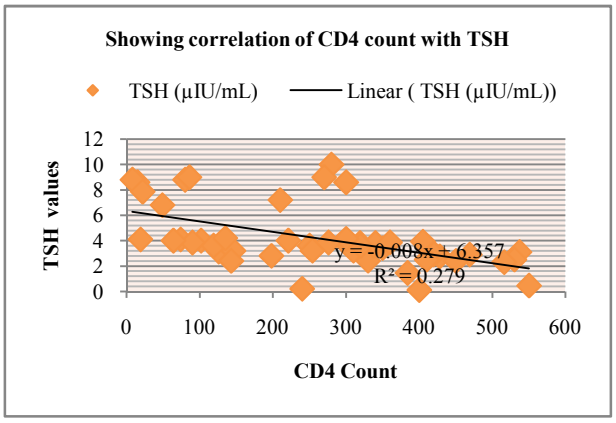


Figure 5 Correlation of cd4 count with tsh

The mean TSH value in study population was 4.16±2 µIU/mL. The correlation coefficient was r = 0.2795 and a statistically significant negative correlation was found between serum TSH value and CD4 count, (p value = 0.003).

DISCUSSION

The mean age of all the subjects was 40.14±8 years while in group A, group B and group C it was 42.76±9.74 years, 39.68±6.58 years and 37.57±6.936 years respectively and it was found that development of thyroid dysfunction was independent of age. In our study, 54% were males and 46% were female. In a study by Joshi B *et al*, there were 55% males and 45% females.[14] Study done by Arya A *et al* showed increased risk for development of thyroid dysfunction in female sex.[15] However, Tripathy SK *et al*[16] demonstrated no significant gender difference among HIV seropositive patients for the development of thyroid dysfunction whereas in our study, thyroid dysfunction was more prevalent in females (39.1%) as compared to males (25.9%) but the difference was statistically not significant (p value = 0.318).

In a study conducted by Sachdeva S *et al* prevalence of thyroid dysfunction was 31.33% in HIV seropositive patients.[17]In the study by Noureldeen AF *et al* prevalence of thyroid dysfunction was 30 %.[18] Our study revealed that prevalence of subclinical hypothyroidism was 16 % which was higher than normal population. However, in the studies done by LP Meena *et al*[19] and Sharma N *et al*[20], prevalence of subclinical hypothyroidism was30% and 14.76% respectively. Our study concluded that 32% of HIV seropositive patients coming to the tertiary care hospital in Punjab were having thyroid dysfunction in the form of subclinical hypothyroidism (16%), hypothyroidism (4%), isolated low T_3 (8%) and hyperthyroidism (4%).

The mean T_3 value of all subjects enrolled in the present study was 1.09±0.52 ng/mL. It was significantly lower in group A (0.865±0.32 ng/mL) compared to group B (1.06±0.46 ng/mL) and group C (1.40±0.68 ng/mL), which was statistically significant (p value = 0.014). The correlation coefficient was r = 0.1385 and a statistically significant positive correlation was found between serum T_3 value and CD4 count, (p value = 0.008). In a study done by Sachdeva *et al*, the mean T_3 value in group A (CD4 <350/mm^3), group B (CD4 350-550/mm^3) and in group C (CD4 >550/mm^3) were 0.93±0.54 µg/dL, 1.16±0.39 µg/dL and 1.31±0.34 µg/dL respectively. There was a direct correlation between progressive decline in T_3 levels as CD4 cell count decreased which was comparable to our study.[17]

Mean T_4 value of all subjects in our study was 8.04±1.94 µg/dL. The mean T_4 value did not revealed statistically significant difference among three groups, it was 7.35±1.72 µg/dL in group A compared to 8.38±2.04 µg/dL and 8.42±1.95 µg/dL in group B and group C respectively, (p value = 0.197). The mean T_4 values in the study done by Sachdeva S *et al* in group A (CD4 <350/mm^3), group B (CD4 350-550/mm^3) and group C (CD4 >550/mm^3) were 6.68±2.69 µg/dL, 7.54±1.86 µg/dL and 8.17±1.59 µg/dL respectively, which was comparable to our study.[17]

The mean TSH value of all HIV seropositive enrolled in our study was 4.16±2.4 µIU/mL. The mean TSH was significantly higher in group A which was 5.25±2.42 µIU/mL compared to group B and group C which was 4.45±2.45 µIU/mL and 2.43±1.106 µIU/mL respectively (p value = 0.003), a statistically significant negative correlation (r = 0.2795) was found between serum TSH value and CD4 count (p value = 0.003). Jain G *et al* demonstrated an inverse correlation of CD4 counts with serum TSH levels (r = -0.470 with p <0.05).[21] In a study done by LP Meena *et al*, CD4 count had strong inverse correlation with TSH (r = -0.257, p value = 0.002), these results were comparable to our results.[19]

CONCLUSION

It can be concluded that the prevalence of thyroid dysfunction was significantly higher in HIV seropositive patients and low CD4 cell counts had strong correlation with development of thyroid dysfunction. Subclinical hypothyroidism was the commonest biochemical abnormality observed. Patients with low CD4 cell count were having significantly higher TSH, whereas lower T_3 and T_4 values

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