Original Research Article

Study of prevalence of thyroid dysfunction and its correlation with CD4 count in HIV patients

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Abstract

Background: Previous authors have reported thyroid dysfunction in human immunodeficiency virus (HIV)-infected individuals. Thyroid dysfunction may be a marker of severity or progression of HIV as reported by several studies.

Aim and objective: To study prevalence of thyroid dysfunction and its correlation with CD4 count in HIV patients.

Materials and methods: One hundred and fifty HIV positive patients were studied in ART center in the Department of Medicine at Gandhi Medical College and Hamidia Hospital, Bhopal. Thyroid profile (TT3, TT4, TSH, ft3 and ft4) were assessed along with CBP, ESR, LFT and RFT. Clinical examination and X ray chest and sputum examination done for confirmation or to rule out tuberculosis. Chemiluminescence assay was used for detection of thyroid function.

Results: HIV infection was more prevalent in the age groups of 30-40 years (34.6%) and females. Prevalence of thyroid abnormality was 32%. Subclinical hypothyroidism was most common (18.66%) followed by clinical hypothyroidism (11.33%). Out of 80 patients with CD4 count <250, 21 had subclinical hypothyroidism. Out of 70 patients with CD4 count >250, 7 had subclinical hypothyroidism.

Conclusion: Thyroid dysfunction is highly prevalent in HIV patients' mainly subclinical hypothyroidism. Routine thyroid function investigation is recommended in HIV patients.

Keywords: thyroid function test, thyroid dysfunction, HIV infection, CD 4 count.

Introduction

Previous authors have shown an involvement of endocrine system in patients with human immunodeficiency virus (HIV) infection.[1] Abnormal thyroid function tests has become a routine practice in patients with HIV as compared to general population. (Beltran S 2003) Abnormal thyroid function tests includes sick euthyroid state, subclinical hypothyroidism, hypothyroidism, Grave's disease, and thyroiditis.[2] Subclinical hypothyroidism is mainly reported in those on highly active anti-retroviral therapy (HAART).[3] Stavudine has been concerned in some studies. However, another study disprove this. Increased level of thyroxine-binding globulin (TBG) along with alteration in normal serum T4 levels are reported to be significant marker of infection progression. [4-5]

Evidences are lacking on the prevalence of thyroid dysfunction in HIV positive patients. Hence in present study we tried to study prevalence of thyroid dysfunction and its correlation with CD4 count in HIV patients.

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Materials and methods

An observational cross sectional study was conducted on 15p HIV positive patients who were registered in ART center in the Department of Medicine at Gandhi Medical College and Hamidia Hospital, Bhopal.

The study subjects were selected from amongst the patients of age 20-70 years who attended the Medicine OPD, special clinics or Medical Emergency Ward, Art center or are admitted in the medical wards in Hamidia Hospital, Bhopal. Pateints with liver disorders, renal disorders, congestive cardiac failure, pregnant women, patients on oral contraceptive pills, statins and other medications that alter thyroid functions and lipid levels were excluded from the study. Those patients who were under treatment for any thyroid disorder were also excluded from the study.

From the study group baseline demographic data will be collected and a detailed physical examination was performed. Informed consent was obtained from all the study participants. The Institutional Ethics Committee approval was obtained before starting the study.

Thyroid profile (TT3, TT4, TSH, ft3 and ft4) were assessed along with CBP, ESR, LFT and RFT. Clinical examination and X ray chest and sputum examination done for confirmation or to rule out tuberculosis. Chemiluminescence assay was used for detection of thyroid function.

All the data analysis was performed using IBM SPSS ver. 20 software. Baseline characteristics of the study participants were expressed as mean ± standard deviation and percentage. Student t test was used to analyse difference in baseline characteristic of the study group. Chi Square test was used to analyze the association between HIV infection and thyroid dysfunction (both clinical and subclinical and association between HARRT and thyroid dysfunction. P value of <0.05 was considered as statistically significant.

Results

In present study HIV infection was more prevalent in the age groups of 30-40 years (34.6%) and females. Most common mode of transmission in both male and females was heterosexual, 55 (36.66%) males and 83 (55.53%) females acquire infection by heterosexual route. Only 3 (2%) males were IV drug abusers. Rest 2 males (91.33%) and 7 females (4.665%) got infection by other routes.

Out of 60 males, 37 were drives (22%), 13 (62%) males and 32 (35%) females were labor, 10 (16%) males and 18 (20%) females were farmer by occupation.

Out of 150 patients included in present study, 102 (68%) were found to be normal in investigation whereas 48 (32%) patients were found to have thyroid abnormality. Subclinical hypothyroidism was present in 28 (18.66%), 17 (11.33%) had clinical hypothyroidism, 2 (1.33%) had subclinical hyperthyroidism and 1 (0.66%) had clinical hyperthyroidism.

Table 1: Showing the age distribution and its correlation with thyroid dysfunction

Age group	Subclinical hypothyroidism	Clinical hypothyroidism	Subclinical hyperthyroidism	Clinical hyperthyroidism
20-30	2	3	0	0
30-40	12	3	1	1
40-50	6	4	1	0
50-60	2	2	0	0
>60	4	5	0	0

Prevalence of subclinical hypothyroidism was more common in HIV patients in comparison to clinical hypothyroidism, Subclinical hyperthyroidism and Clinical hyperthyroidism. Most common age group in patients with subclinical hypothyroidism was 30-40 years.

Thyroid dysfunction was more prevalent in females in comparison to males. In patients with subclinical hypothyroidism, out of 28 patients, 16 were females and 12 were males. In clinical hypothyroidism patients 9 were females and 8 were males. In subclinical hyperthyroidism, there were 2 patients both were females and in clinical hyperthyroidism there was 1 patients and was female.

Out of 28 patients of subclinical hypothyroidism, 20 patients were found in ART group in comparison to

only 8 patients in non-ART group (p=0.01). Out of 17 patients of clinical hypothyroidism 11 (7.3%) patients were under ART and only 6 (4%) were not on ART. Two patients out of 75 who had subclinical hyperthyroidism and no patients was found in non ART group. One patients with clinical hyperthyroidism was on ART.

Table 2: Comparing CD4 count and thyroid abnormality

Thyroid abnormality	CD 4 count			
	<250 (n=80)		>250 (n=70)	
	Present	Absent	Present	Absent
Subclinical hypothyroidism	21	59	7	63
Clinical hypothyroidism	10	70	7	63
Subclinical hyperthyroidism	2	78	0	70
Clinical hyperthyroidism	1	79	0	70

Out of 80 patients who had CD 4 count of less than 250, 21 had Subclinical hypothyroidism whereas out of 70 patients with CD4 count more than 250, 7 had Subclinical hypothyroidism. Of the 80 patients with CD4 count less than 250, 10 (6.66%) had clinical hypothyroidism whereas out of 70 patients with CD4 count more than 250, 7 had clinical hypothyroidism.

Out of 28 patients of subclinical hypothyroidism 20 patients were presented with HIV TB coinfection compared to only 8 patients non TB HIV coinfection (p<0.001). Similarly out of 17 patients of clinical hypothyroidism 15 were with TB HIV coinfections and only 2 did not have this coinfection. Two patients were with subclinical hyperthyroidism in which 1 was with HIV TB coinfection and 1 was with non TB HIV coinfections. The only patients of clinical hyperthyroidism had HIV TB coinfection.

Discussion

In present study 150 patients (70 males and 80 females) diagnosed with HIV infection were studied. The age ranged from 20-70 years with mean age was 35 years for males and 33 years for females. Majority of the patients were in the age group 30-40 comprising 52 patients (27.33%) patients in present study. Carvalhoet al included 181 patients comprising 138 males and 43 females. Male to female ratio was around 3.2:1 with mean age of around 34 years.[6] Low number of females may be due to the admission pattern in hospital and social pattern in our society where females are decreased to household activities and socialize less compared to males.

In present study predominantly heterosexual transmission was observed. Out of 150 patients, in 138 patients mode of transmission was heterosexual. Sokalskiet al studied a total of 52 patients, in all of them mode of acquisition of infection was heterosexual. Study conducted by Hakim et al showed that all patients were heterosexual and none were admitted to intravenous drug abuse. There were no haemophiliacs[7].

Prevalence of thyroid dysfunction in HIV patients

The prevalence of thyroid dysfunction in HIV infected patients has been reported to range between 30 % to 35 %. In present study out of 150 patients, 102 (68%) patients were found to be normal in investigations and rest 48 (32%) patients were found with thyroid abnormalities. Madge S et al had done a similar study in London teaching hospital including a total 1565 patients. They showed that 75% of the patients had normal function whereas 25% patients were found with thyroid abnormality[4].

Thyroid dysfunction in HIV-positive individuals can result from gland destruction by opportunistic pathogens (Pneumocystis jirovecii or cytomegalovirus) or tumorigenic diseases (Kaposi's sarcoma). These opportunistic infections could be associated with the sick euthyroid syndrome or could cause low reverse T3[8].Pneumocystis thyroiditis has been reported to cause a painful low uptake thyroiditis like picture with hyperthyroidism followed by hypothyroidism[9]. In the present study out of 48 patients with thyroid abnormality, 28 females (18.66%) and 20 males (13.33%) were found to be with abnormal thyroid function. Meena LP et al evaluated the endocrine function in 150 HIV infected male patients at different levels of CD4 counts. They were divided into 3 groups on the basis of CD4 cell counts, out of that 40% of patients were found to be abnormal during

investigation[10]. Beltran et al conducted a cross sectional study to determine the prevalence and risk factors for hypothyroidism in 350 HIV infected patients grouped according to CDC staging. Prevalence of subclinical hypothyroidism was higher among HIV infected men than among HIV-infected women[11].

Screening studies have demonstrated an increased prevalence of hypothyroidism in HIV infected patients. Quinn T et al showed that an infectious trigger for immune activation (by molecular mimicry) is one of the postulated mechanisms for autoimmune disease. However hypothyroidism in HIV infected patients is not associated with autoimmunity. One case of Hashimoto's hypothyroidism has been reported so far after highly active anti-retroviral therapy (HAART) initiation[12].

Subclinical hypothyroidism in HIV infected patients

In the present study prevalence of subclinical hypothyroidism was 18.6%. Out of 70 males 12 (8%) were diagnosed as a subclinical hypothyroidism, similarly out of 80 female patients 16 (10.6%) were diagnosed with subclinical hypothyroidism. Bongiovanniet al studied 190 patients and found 14.4% prevalence of subclinical hypothyroidism in HIV infected patients[13].Beltran S et al conducted a cross sectional study to determine the prevalence and risk factors for hypothyroidism in 350 HIV patients which were grouped according to CDC staging. Study showed that 16% patients of them had subclinical hypothyroidism[11].

Subclinical hypothyroidism has often been hued in the past few years in the HIV infected population, with a higher prevalence compared with HIV-negative individuals[14]. In patients with AIDS, a high prevalence of sick euthyroid syndrome has been reported, probably due to a hypothalamic-pituitary deficit related to the progression of irnunodeficiency and cachexia. Merenich et al conducted study on 46 HIV patients. Finding of subclinical hypothyroidism was revealed in 8% of patients[15].Meena LP et al evaluated the endocrine function in 150 HIV male infected patients, 30% were found to have subclinical hypothyroidism[10].This difference in the prevalence may be due to different age sex distribution. Madge S et al had done a study to investigate the prevalence of overt and subclinical thyroid disease in HIV patients in 2006 in London teaching hospital and determined the occurrence of thyroid dysfunction longitudinally over 3yrs. Out of 1565 patients 4% had subclinical hypothyroidism. This study shows quite different and low prevalence of subclinical thyroid disease[4].This difference can be explain by the possibility of different sample size and prevalence may also be affected by duration of infection in patients included in the study.

Clinical hypothyroidism in HIV infected patients

The prevalence of clinical hypothyroidism in HIV infected patients in present study was found to be 17 (11.33%). Out of that 8 were males and 9 were females, that means prevalence of clinical hypothyroidism in male and female was 6% and 5.6% respectively. Olivieri et al studied 119 HIV infected patients and reported a decreasing trend of thyroid hormones in these patients through different stages of infection. Primary hypothyroidism was found in 10% patients at symptomatic stages[16].Meena LP et al evaluated the endocrine function in 150 HIV infected patients at different levels of CD4 counts. Overall 10% had overt hypothyroidism[10].Madge S et al had done a similar study to investigate the prevalence of overt and subclinical thyroid disease in HIV positive patients and reported that out of 1565 patients 2.5% had overt hypothyroidism[4].Beltran S et al studied over 350 patients and found 2.6% of clinical hypothyroidism. This variation in results may be because of large sample size[11].

Prevalence of subclinical hyperthyroidism in HIV infected patients

The prevalence of subclinical hyperthyroidism in present study was 1.33% (both were females). In line with present study Beltran S et al also found subclinical hyperthyroidism in only 2 (0.57%) patients out of 350 patients[11].

Prevalence of clinical hyperthyroidism in HIV infected patients

In the present study prevalence of clinical hyperthyroidism was 0.6%. Only 1 patient of clinical hyperthyroidism was found, and that was a female. Beltran S et al study reported the incidence of clinical

hyperthyroidism as was 0.28 (22 cases/100 patient-years for males and 0.55 cases/100 patient-years for females). The overall cross-sectional prevalence was 1.1% (0.9% for males and 2.0% for females)[11]. Nelson M et al reported that thyroid dysfunction and relationship to antiretroviral, therapy in HIV-positive individuals in the HAART era[17].

Thyroid dysfunction and its correlation with HAART

In the present study, in ART group, 34 patients were found with abnormal thyroid function and in non-ART group 14 patients were having abnormal thyroid profile. In ART group 20 (13.33%) patients had subclinical hypothyroidism, 11 (7.3%) had clinical hypothyroidism, 3 (1.33%) had subclinical hyper-thyroidism, and 1 (0.66%) had clinical hyperthyroidism. In non-ART group, 8 (5.33%) patients had subclinical hypothyroidism, 6 (4%) had clinical hypothyroidism, and none had clinical or subclinical hyperthyroidism.

Madge S et al studied a total 1565 patients (73% of the clinic population), of that 900 (58%) were on HAART at the start of the study. Thirty-nine (2.5%) were found to have overt hypothyroidism, and eight (<1%) had overt hyperthyroidism. Sixty one (4%) had subclinical hypothyroidism, five (<1%) had subclinical hyperthyroidism and 263 (17%) had a nonthyroidal illness[4].Bongiovanni M et al studied subjects on stable HAART (for at least 1 year) at baseline. At baseline, the prevalence of subclinical hypothyroidism was 14.4%[13]. In Grappin et al study a total of 212 patients were included in the study. Twenty-six patients (12.3%) presented at least one abnormal test of thyroid function. On these no clinical dysthyroidism was noted. No hyperthyroidism was found. Biological thyroid dysfunction was assessed in 22 (10.4%) patients: 18 (8.5%) with subclinical hypothyroidism. In the study on HIV patients on HAART, result of the present study is comparable with other studies[14].As such hyperthyroidism was not found in previous studies, this discrepancy can be explained by difference in the immune status of the patient which depend on the duration, for which patients were on HAART.

Furthermore the correlation between the immune reconstitution evaluated by increase in CD4 cells) and the occurrence of subclinical hypothyroidism might be considered. Although the occurrence of subclinical hypothyroidism in our study was more frequent in subjects starting HAART and was associated with a higher CD4+ cell recovery in the univariate analysis, when adjusting for the other variables this relationship was not confirmed. In Madeddu G et al study the role of HAART was also confirmed by a more recent report, which found that HAART interruption was associated with a normalization of thyroid tests[3].

Thyroid dysfunction in HIV patients and its correlation with CD4 counts

In our study 80 patients were with CD4 count less than 250 and 70 patients had CD4 count more than 250. Out of 80 patients of CD4 count less than 250, 34 patients had thyroid dysfunction. It was also observed that out of 70 patients with CD 4 count more than 250, 14 patients had thyroid dysfunction. Subclinical hypothyroidism was present on 21 patients of CD 4 count less than 250. Patients of clinical hypo-thyroidism, 10 (6.66%) patients have CD4 count less than 250 and 7 (4.66%) patients have CD 4 count more than 250. 2(1.66%) patients were of subclinical hyperthyroidism, both were females. 1 (0.66%) patient was found of clinical hyperthyroidism and that was a female. Gagan Jain et al did a prevalence study of thyroid function changes, HIV infection at various stages of the illness. Fifty (n=50) subjects belonging to both newly diagnosed HIV positives were enrolled for the study. Results showed a direct correlation between CD4 count and free T4 values and an inverse correlation of CD4 counts with serum TSH levels. They concluded that thyroid dysfunction is frequent in HIV infection and with progression of disease there is a primary hypothyroid like stage[18]. Beltran el al found that subclinical hypothyroidism was associated with the use of stavudine and lower CD4+ cell count[11].Meena et al showed that TSH level is inversely proportionate to CD4 count[10].

Correlation of thyroid dysfunction in HIV infected patients and its correlation with tuberculosis

Out of 28 patients of subclinical hypothyroidism, 20 (13.3.%) patients were presented with HIV TB coinfection compare to only 8 (5.3%) patients non TB

HIV co infection, with P value of less than 0.001. Similarly out of 17 patients of clinical hypothyroidism 15 (10%) patients were with TB HIV coinfection and only 2 (1.33%) patients were non TB group. 2 patients were with subclinical hyperthyroidism in which 1 (0.66%) was in HIV TB group and 1(0.66%) was in non TB HIV group. 1 {0.66%} patient was found of clinical hyperthyroidism and that was a female.Hill et al reported that TB patients manifest the expected low T3 of non-thyroid illness, but, unlike most sick patients, usually have normal or increased serum binding of thyroid hormones[19].

Conclusion

Thyroid hormone abnormalities are common in HIV-infected individuals. Sick euthyroid syndrome and subclinical hypothyroidism were the abnormalities observed in this study. The frequency in which these abnormalities occurred was independent of whether the individuals were on HAART or without HAART treatment.

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