Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: www.saspublishers.com

OPEN ACCESS

Medicine

Thyroid Dysfunctions in HIV Positive Patients

Bose Sreyasi[1], Padhiyar Rupal[2*], Chavan Swati[3], Karnik Niteen[4]

[1]Senior Registrar, Department of Medicine, LTMMC & GH, Sion, Mumbai 400022 India
[2]Associate Professor, Department of Medicine, LTMMC & GH, Sion, Mumbai 400022 India
[3]Professor, Department of Medicine, LTMMC & GH, Sion, Mumbai 400022 India

***Corresponding author:** Padhiyar Rupal
| **Received:** 25.02.2019 | **Accepted:** 05.03.2019 | **Published:** 11.03.2019
DOI: 10.36347/sjams.2019.v07i03.001

Abstract | **Original Research Article**

Thyroid function abnormalities are associated with a number of systemic conditions, including patients infected with human immunodeficiency virus (HIV). Opportunistic infections involving the thyroid gland, neoplasms such as lymphoma and Kaposi's sarcoma, and medications can alter the thyroid function in individuals with advanced HIV infection. If thyroid dysfunction is diagnosed in an HIV-infected patient, it should be treated in the usual manner. However, high index of suspicion and caution in the interpretation of thyroid function tests in patients with HIV disease are needed for optimal diagnosis and treatment. A cross-sectional study was conducted in OPD of Tertiary care centre. Serum thyroid hormone concentrations (FT4, FT3, and TSH) were measured. A total of 176 HIV-infected outpatients were included. 111 (63.7%) patients were men. Mean duration of HIV infection was 70 months and 35 patients had previous opportunistic infections (OI). Mean baseline CD4 cell count was 339 cells/cmm. Of the total study population, 146 patients received antiretroviral therapy (ART). Abnormal thyroid function test was detected in 31 patients (17.61%), including 17 (54.8%) patients with subclinical hypothyroidism, 2 (6.4%) with overt hypothyroidism,5 (16.1%) patients with low T4, and 7 (22.6%) patients with sick euthyroid syndrome. TSH values and CD4 count of the first visit had significant negative correlation in patients on HAART. 141 patients did not have pre existing opportunistic infections, out of them 122(86.5%) had normal thyroid parameters. Out of 88 patients on TLE, 6 (6.8%) had subclinical hypothyroidism. Out of 31 patients on ZLN, 6 (19.3%) had subclinical hypothyroidism. Baseline CD4 was significantly lower in patients with subclinical hypothyroidism. Duration of infection is significantly higher in patients with overt hypothyroidism. It is therefore suggested that screening and monitoring of thyroid functions in HIV-infected patients should be considered.

Keywords: Thyroid Dysfunction, Subclinical hypothyroidism, HIV patients, CD4 Count.

INTRODUCTION

Since the advent of highly active antiretroviral therapy (HAART), there has been significant increase in the survival of HIV infected patients. This has given rise to increased occurrence of HIV related complications, like endocrinopathies in HIV infected patients [1]. Thyroid dysfunction is among the commonest endocrinopathies in HIV [2]. Subtle thyroid dysfunction is common, believed to occur in as many as 35% of all HIV infected individuals. In contrast overt thyroid dysfunction is less common, seen in 1-2% of all patients [3-5]. Prevalence of overt primary hypothyroidism in HIV infected individuals from different studies across the globe has been reported to be 0–2.6%. The prevalence of subclinical hypothyroidism has also reported to be higher in HIV infected individuals. Most of the hypothyroidism in general population is believed to be of autoimmune etiology, in contrast to HIV, where a majority is believed to be of non autoimmune origin. Stavudine as well as opportunistic infections have been linked with hypothyroidism in some studies [6]. Also factors, which determine the occurrence of thyroid dysfunction, have not been well determined. Patients with HIV infection often have associated comorbidities like infections, malignancies that are associated with significant stress, which may have an impact on hypothalamic-pituitary-thyroid axis making interpretation of thyroid function tests difficult. Hence the aim of this study was to determine the prevalence and predictors of the entire spectrum of thyroid dysfunction. Overt hypothyroidism, subclinical hypothyroidism, subclinical hyperthyroidism, overt hyperthyroidism, and sick euthyroid syndrome) in stable ambulatory patients with HIV infection.

MATERIALS AND METHODS

This study was a large cross sectional descriptive study conducted in Out Patient Department

(OPD) of a Tertiary care centre. The study was conducted over a period of 12 months. Patients of 18–70 years of age, with serologically documented HIV infection, were included. All those who did not consent for participation in the study, pregnant women and patients with already known thyroid dysfunction before initiating ART, were excluded from the study. The institutional ethics committee approved the study protocol.

Data was collected from the patients and their records regarding the duration of diagnosis of HIV infection and details of HAART and past or current evidence of opportunistic infections (bacterial, viral, and fungal). History of clinical features suggestive of hypothyroidism or hyperthyroidism was taken. All patients underwent detailed clinical assessment, including anthropometry.

All patients in our study were HIV-1 positive and there were no subjects with HIV-2. Data included age, sex, concomitant sexually transmitted infections and vascular risk factors such as hypertension, diabetes and dyslipidemia. Hepatitis B and C coinfection, baseline CD4 cell count at time of ART registration, present CD4 at time of enrolling ,length of time since diagnosis, anti- retroviral therapy, other basic laboratory work up such as haemogram, liver and renal function tests, electrolytes was documented. Patients underwent a clinical evaluation before the study. Patients with a history of any known thyroid disorder were excluded from the study, so as to remove the bias and confounding factors. It was done by an Interview Schedule and a single investigator was involved in the interview. Confidentiality was maintained and there were no conflicts of interests.

Thyroid stimulating hormone (TSH), total thyroxine (T4), and total tri-iodothyronine (T3) were analyzed. In accordance with previous literature, primary overt hypothyroidism was defined as patients having elevated TSH along with low fT4. Subclinical hypothyroidism was defined as patients having elevated TSH along with normal thyroid hormone levels. Subclinical hyperthyroidism was defined as patients having suppressed TSH levels with normal thyroid hormone levels. Overt hyperthyroidism was defined as patients having suppressed TSH levels along with elevated fT4 and/or fT3. Sick euthyroid, was defined as patients having isolated low fT3 or low fT4 with low fT3 levels, along with low or normal TSH levels. Euthyroidism was defined as clinically asymptomatic patients having normal fT3, fT4, and TSH levels. It has been reported that 1.3–6.8% HIV infected patients have isolated low TSH with normal thyroid hormone level. Hence, patients with normal fT3 and fT4 with low TSH were grouped separately.

Statistical considerations

Statistical analysis of the data was performed by SPSS statistical software (version 10.1). Chi-square test, and unpaired‘t’ test was used. Paired‘t’ test was used to test the significance of association in case of paired quantitative data amongst individual groups. Pvalues > 0.05 were not significant and values ≤ 0.05 were significant.

RESULTS

Clinical Information of HIV-Infected Patients

176 HIV-infected patients were included in the study. The mean age of the patients in the study was 37 years. 63% patients were males and 34 % were females. Maximum number of patients, 99patients, (56.25%) belonged to the age group of 30-40 years. The mean duration of HAART was 70 months. 50 % (88) of patients were on TLE regimen. The mean age of the HAART-naive patients was 34 years & patients on HAART was 37 years.86 patients (46.86%) patients were known to be HIV positive since 24-72 months. The duration of HIV infection was significantly longer in the HAART patients (mean- 70.3 months) than in the HAART-naive patients (mean- 31 months). 143 patients (81.25%) had normal BMI .The mean BMI was comparable in both the groups of HAART naïve and the patients on HAART.

51.7% of the study population had baseline CD4 count between 200-500 cu.mm. Only 9.66% patients had CD4 counts less than 200 cu/mm. Mean CD4 count of our study population at first visit is 487cu.mm, while the mean baseline CD4 count was 339 cu.mm. CD4 cell count was higher in the HAART naïve group than in the HAART group. The mean baseline CD4 and present CD4 count in the HAART group are 312cu.mm and 436cu.mm respectively. The respective values for the HAART naïve group were 478cu.mm and 749cu.mm. P- Value for the difference in present CD4 count is significant. (0.038). There were 36 patients diagnosed with OIs, of whom 28 were diagnosed with tuberculosis.

Prevalence of Thyroid Dysfunction in HIV-1-Infected

Out of the 176 study patients, 31 (17.61%) were diagnosed with thyroid dysfunction.17 (54.8%) patients had subclinical hypothyroidism, 2 (6.4%) had overt hypothyroidism, 5 (16.1%) patients had low T4, 7 (22.6%) patients were sick euthyroid syndrome. 12 of the patients with thyroid dysfunction had normal TSH levels. There were no patients with subclinical or overt hyperthyroidism.

Out of the 17 patients of subclinical hypothyroidism, 10 were males, 6 females and 1 transgender. 147 patients were on HAART, of which 28 (19%) patients had thyroid dysfunction, and 119 (81%) were euthyroid. Out of 29 patients who were not on HAART, 3 (10.3%) were diagnosed with thyroid

dysfunction, remaining 26 (89.6%) were euthyroid. The P value (0.2609) was not statistically significant for this association. Of the 28 patients on HAART with thyroid dysfunction, 16 (57.14%) had subclinical hypothyroidism, and 2 (7.1%) had overt hypothyroidism (TABLE 1).

The difference in the values of mean thyroid hormone (TSH, FT3, and FT4) levels in patients on HAART and not on HAART is not statistically significant. The mean baseline CD4 count was 339.5cu.mm in euthyroid group, whereas the mean baseline CD4 count in patients with thyroid dysfunction was 344.94 cu.mm. The mean CD4 count in the first visit is almost the same (492 cu.mm) for all categories of thyroid dysfunction. But we found that the mean of baseline CD4 cell was lowest in case of subclinical hypothyroidism (344.94 cu.mm), followed by sick euthyroid syndrome (349.19 cu.mm), followed by low T4 state (356 cu.mm), and the highest CD4 count was seen in overt hypothyroidism (372 cu.mm).

We also compared the incidence of thyroid dysfunction between patients with and without OIs. The difference in incidence in these two groups was significant with a p value of 0.0002. There were 35 patients with opportunistic infections, 15 patients (42.9%) had thyroid function abnormalities. 6 of them had subclinical hypothyroidism, 1 patient had overt hypothyroidism, 3 patients had sick euthyroid syndrome and 2 patients had isolated low T4. Out of 141 patients without opportunistic infections, 19 patients (13.5%) had thyroid function abnormalities. 11 had subclinical hypothyroidism, 1 had overt hypothyroidism, 3 had isolated low T4, 4 had sick euthyroidism. There was however not much difference between mean values of fT3, fT4 and TSH between these two groups.

Effect of HAART on Thyroid Hormone Levels

The FT3 and FT4 levels in the HAART group were 2.41 ± 0.56 pg/mL and 1.05 ± 0.18 ng/dL, respectively. These values in the HAART-naıve patients were 2.3 ± 0.4 pg/mL and 1.02 ± 0.19 ng/dl respectively. However, the differences were not significant.

The TSH level in the HAART group was 3.79 ±1.4 uIU/ml, in the HAART-naıve group it was 3.65 ± 1.12 uIU/mL. Again, the difference was not significant.

The FT3 and FT4 levels were not significantly related to HAART duration, CD4 cell count

We further studied the effect of different HAART regimens on thyroid function. As only 1 patient was on Abacavir regimen, and 1 patient on Protease inhibitor regimen, we excluded these two patients, and of the remaining patients were divided into 3 groups – ZLE, TLE and ZLN. The mean values of fT3, fT4 and TSH with HAART thyroid hormone levels did not differ among these three subgroups, indicating that there were no significant differences in the effects of these commonly used regimen on thyroid function(TABLE 2).

A logistic regression model of possible variables affecting thyroid function was made, but none of the variables like age, gender, BMI, HAART, baseline and present CD4 significantly affected thyroid function.

During follow-up, FT4, FT3 and TSH values did not differ significantly in both groups of patients- those continuing HAART and those not on HAART, mean CD4 counts were also unmodified; and hypothyroid conditions persisted.

Control group

There were 50 people in the control group. Mean age is 32.6 years. 23(46%) were females and 27(54%) were males. 3 of them had thyroid function abnormalities in the form of subclinical hypothyroidism. The mean fT3, fT4 and TSH levels in the control group were significantly lower than the case group.

Table-1: Comparison between the number of patients belonging to different categories of thyroid function tests in haart naïve patients and patients on haart

Thyroid Function	HAART Naïve	On HAART
Normal	26	119
Subclinical Hypothyroidism	2	15
Low Free T4	1	4
Sick Euthyroid	1	6
Over Hypothyroidism	0	2

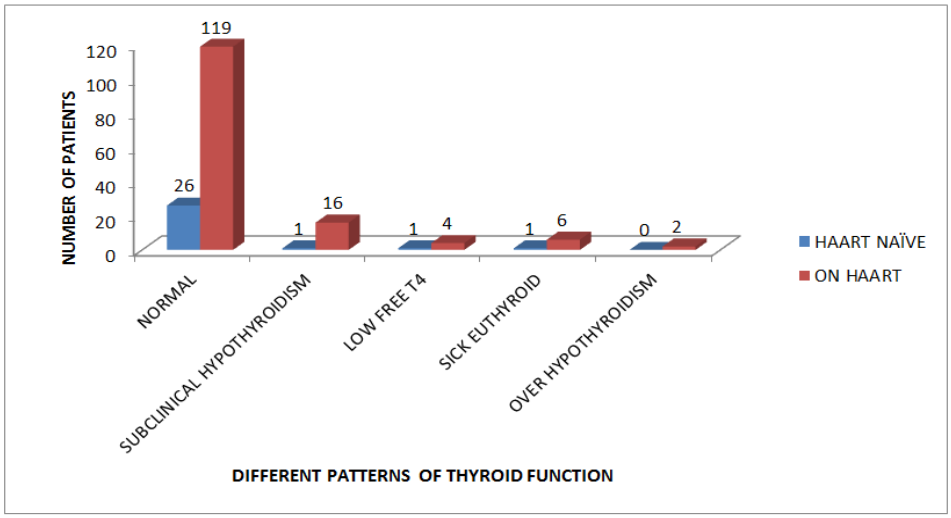

Table-2: Comparison between the frequency of thyroid function patterns in patients on different art regimens (p value- 0.397)

Variables	Nature Of HAART					
	A+LE	TL + PI	TLE	ZLE	ZLN	ART Naive
Normal	1	0	74	21	23	26
Subclinical Hypothyroidism	0	1	6	2	6	2
Low Free T4	0	0	1	2	1	1
Sick Euthyroid	0	0	5	0	1	1
Overt Hypothyroiodism	0	0	2	0	0	0

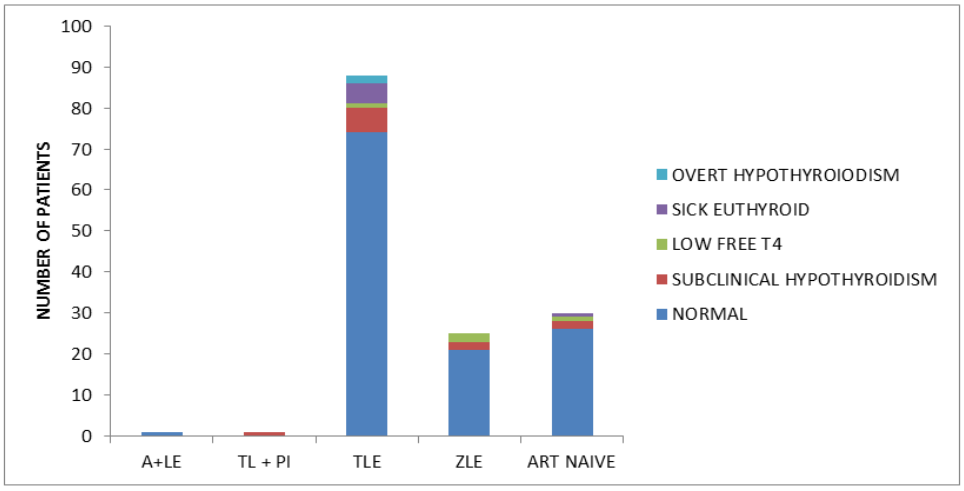

Table-3: Comparison of different variables with thyroid abnormalities

Variables	Euthyroid	Sub Clinical Hypothyroidism	Low Ft4	Sick Euthyroid	Overt Hypothyroidism	P Value
AGE (yrs)	36.27	36.18	41.6	39	37.2	0.647
BMI	23.46	23.32	23.12	24.49	23.74	0.979
Baseline CD4	367.87	159.59	253.80	294.4	368..2	0.003
First Visit CD4	526.19	186.76	478.8	450.8	495.4	0.991
Follow Up CD4	597.29	247.82	512.80	499.7	551.4	0.001
Hb	11.8	10.76	11.8	10.1	11.1	0.687
RBS	126.78	129.18	120.8	124.7	126.3	0.793
AlbumIN	2.68	2.56	2.86	3.07	2.62	0.925
Sodium	138.5	137.82	135	138.8	138.6	0.409
Duration Of Infection (Months)	70.52	56.94	97.6	67.8	111	0.001

Baseline CD4 count and follow up CD4 count is significantly lower in patients with subclinical hypothyroidism. Duration of infection is significantly higher in patients with overt hypothyroidism.

DISCUSSION

Thyroid dysfunction is among the commonest endocrinopathies in HIV. Undiagnosed thyroid dysfunction, even subclinical hypothyroidism, is associated with significant morbidity and poor quality of life [1, 2]. Occurrence of Overt hypothyroidism among the general population, is around 0.3% , and among HIV-infected individuals, small studies have reported a prevalence of 0%–2.6% [3, 4,6,7,8] Overt hypothyroidism is treated with levothyroxine, with the goal of maintaining the TSH level at 0.5–2.5 mU/L.

Subclinical hypothyroidism is common among HIV-infected persons, especially among those who are receiving HAART, prevalence being 3.5%–12.2%) [3-7]. Among patients with HIV infection and subclinical hypothyroidism, anti-thyroid peroxidase antibodies are rarely identified, suggesting that the etiology may not be autoimmune [8,9]. Stavudine use, however, has been associated with subclinical hypothyroidism in some but not all studies [6, 8, 10]. The mechanisms underlying this association are unclear and deserve further investigation.

Current guidelines for the general population recommend treatment if the TSH level is more than 10 mU/L and individualized management of patients with TSH levels of 4.5– 10 mU/L., Determination of the TSH level should be repeated every 6–12 months to monitor for progression [11,12].

In our study, out of the 176 study patients, 31 (17.61%) were diagnosed with thyroid dysfunction, including 17 (9.66%) patients with subclinical hypothyroidism, 2 (1.14%) with overt hypothyroidism. Also, TSH value and CD4 count in the first visit had significant negative correlation. Baseline CD4 is also significantly lower in patients with subclinical hypothyroidism. [TABLE-1,TABLE-3] The inverse relation observed between current CD4 count and TSH even after adjusting for variables, highlights the possible link between increased immunodeficiency and elevated TSH. Further, in the setting of low prevalence of elevated anti-TPO antibody titers, low baseline CD4 count can be taken as a strong independent predictor of subclinical hypothyroidism. This highlights the importance of early immunodeficiency and HIV infection per se having an important role in the genesis of subclinical hypothyroidism later in life. It is likely that patients with lower CD4 counts had higher viral load. However, HIV viral load was not evaluated in our study and is a limitation of this report.

Low FT4 levels with concurrent normal TSH levels are found frequently among HIV-infected individuals, with a reported prevalence of 1.3%–6.8% [3, 4, 7]. An even higher prevalence was reported among children in a pediatric study in which 16 (31%) of 52 children, all of whom were receiving HAART, had this abnormality [13]. In adults, isolated low FT4 levels have been associated with receipt of didanosine, stavudine, and ritonavir [8]. The low FT4 state may be consistent with a centrally mediated process, with failure of the hypothalamus or anterior pituitary. However, in one study, administration of exogenous TSH-releasing hormone identified, neither delayed nor absent TSH response among subjects with low FT4 levels, making either hypothalamic or pituitary insufficiency less likely [8]. An isolated low FT4 level has also been reported in patients who are receiving phenytoin or carbamazepine and was shown to be an artifact related to interference in the free T4 assays. Whether one or more HAART agents cause similar interference has not been evaluated. The clinical significance of a low FT4 level is unclear, because patients with a low FT4 level do not experience a higher frequency of hypothyroid symptoms, compared with control subjects. Furthermore, recent reports have lacked sufficient follow up data to assess the natural history of low FT4 levels [3]. Repeated annual thyroid function testing (of the TSH and FT4 levels) is reasonable, but levothyroxine therapy is not recommended. In our study, 5 patients had low FT4, i.e 0.01% of the study population.

In patients with low thyroid hormone concentrations, the effects of nonthyroidal illness also referred to as “euthyroid sick syndrome,” also need to be considered. During severe illness, including advanced AIDS, 5 -deiodination of T4 declines, leading to decreased T3 production and reverse T3 metabolism, and 5-deiodination of T4 to inactive reverse T3 is increased, creating a pattern of thyroid testing that suggests thyroid dysfunction. This pattern, however, is a result of the physiological response to illness and not a result of abnormal thyroid function. Because chronic HIV infection itself can lead to nonthyroidal illness, this diagnosis should always be considered for patients with uncontrolled HIV infection and abnormal thyroid function test results. The most common thyroid function pattern during nonthyroidal illness is reduced T3 level, elevated reverse T3 level, variable FT4 level, and relatively normal or decreased TSH level [14]. During recovery from illness, the TSH level may increase temporarily, sometimes overshooting the normal range, because both FT4 and T3 level, return to baseline values, which may mimic subclincal hypothyroidism.

The occurrence of sick euthyroid syndrome among HIV infected patients is highly variable ranging from 1.3% to 11.6% in different studies [5, 15, 16]. Stable, ambulatory, asymptomatic patients, with a large majority being on HAART may explain the low occurrence of sick euthyroid syndrome in our study cohort, 7 patients out of 176 patients (3.97%).

Management involves treatment of the underlying condition and not administration of levothyroxine therapy. If the diagnosis of nonthyroidal illness is unclear, repeated thyroid hormone testing is appropriate 4–6 weeks after the resolution of the acute illness or after the control of HIV infection with antiretroviral therapy. The measurement of the reverse T3 level in persons with suspected nonthyroidal illness is not recommended.

In patients with advanced HIV disease, a variety of systemic opportunistic conditions that infect or infiltrate the thyroid can decrease or increase T4 secretion. Cases of thyroiditis have been reported in association with Pneumocystis jiroveci infection, Cryptococcus neoformans infection, visceral leishmaniasis, and suppurative bacterial infection [17, 18]. These infiltrating conditions lead to destructive thyroiditis, which is usually accompanied by neck pain, thyroid enlargement, and increased thyroxine release. A high rate of hypothyroidism (54%) was reported from 69 HIV infected patients with multidrug resistant (MDR) tuberculosis from Mumbai, India [19]. Use of rifampicin, para-aminosalicylate (PAS), and ethionamide for treating tuberculosis has been linked to the increased occurrence of hypothyroidism in these patients [19]. 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. Symptomatic thyroid infection or infiltration has always been uncommon, and in countries where HAART is available, it has become extremely rare.

Graves' disease is the leading cause of hyperthyroidism. In persons with HIV infection, Graves' disease may occur after immune reconstitution from HAART. However, unlike classic immune reconstitution inflammatory syndrome caused by mycobacteria and other pathogens, which develops during the first 3 months of HAART [20, 21], Graves' disease is most commonly diagnosed 12–36 months after HAART initiation. There were no patients with subclinical or overt hyperthyroidism in our study.

CONCLUSION

Thyroid function screening of asymptomatic individuals is an area of controversy, both for HIV-infected patients and for the general population. Although cross-sectional studies have reported a higher prevalence of subclincal hypothyroidism in HIV infected population than in the general population, the pathophysiology of subclincal hypothyroidism may differ in HIV-infected patients. Measurement of the TSH level is appropriate for patients with symptoms suggestive of thyroid dysfunction, reduced bone mineral density, dyslipidemia, depression, or atrial fibrillation. The finding of an abnormal TSH level should prompt the health care provider to measure both the FT4 and the FT3 levels. When testing is performed, nonthyroidal illness should be considered in the differential diagnosis of abnormal thyroid function test results, particularly for patients with advanced AIDS or uncontrolled HIV infection.

REFERENCES

1. Sinha U, Sengupta N, Mukhopadhyay P, Roy KS. Human immunodeficiency virus endocrinopathy. Indian J Endocrinol Metab. 2011;15(4):251–60.
2. Lambert M. Thyroid dysfunction in HIV infection. Baillieres Clin Endocrinol Metab. 1994 Oct;8(4):825–35.
3. Beltran S, Lescure F-X, Desailloud R, et al. Increased prevalence of hypothyroidism among human immunodeficiency virus–infected patients: a need for screening. Clin Infect Dis 2003; 37:579–83.
4. Madeddu G, Spanu A, Chessa F, Calia GM, Lovigu C, Solinas P, Mannazzu M, Falchi A, Mura MS, Madeddu G. Thyroid function in human immunodeficiency virus patients treated with highly active antiretroviral therapy (HAART): a longitudinal study. Clinical endocrinology. 2006 Apr;64(4):375-83.
5. Calza L, Manfredi R, Chiodo F. Subclinical hypothyroidism in HIV-infected patients receiving highly active antiretroviral therapy. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2002 Nov 1;31(3):361-3.
6. Grappin M, Piroth L, Verges B, Sgro C, Mack G, Buisson M, Duong M, Chavanet P, Portier H. Increased prevalence of subclinical hypothyroidism in HIV patients treated with highly active antiretroviral therapy. Aids. 2000 May 26;14(8):1070.
7. Collazos J, Ibarra S, Mayo J. Thyroid hormones in HIV-infected patients in the highly active antiretroviral therapy era. AIDS 2003; 17: 763–5.
8. Beltran S, Lescure FX, El Esper I, Schmit JL, Desailloud R. Subclinical hypothyroidism in HIV-infected patients is not an autoimmune disease. Hormone Research in Paediatrics. 2006;66(1):21-6.
9. Cooper DS. Subclinical hypothyroidism. N Engl J Med. 2001; 345:260–5.
10. Madge S, Smith CJ, Lampe FC, Thomas M, Johnson MA, Youle M, Vanderpump M. No association between HIV disease and its treatment and thyroid function. HIV medicine. 2007 Jan;8(1):22-7.
11. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, Franklyn JA, Hershman JM, Burman KD, Denke MA, Gorman C. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. Jama. 2004 Jan 14;291(2):228-38.
12. Bongiovanni M, Adorni F, Casana M, Tordato F, Tincati C, Cicconi P, Bini T, Monforte AD. Subclinical hypothyroidism in HIV-infected

subjects. Journal of Antimicrobial Chemotherapy. 2006 Sep 1;58(5):1086-9.
13. VIGANÒ A, Riboni S, Bianchi R, Cafarelli L, Vago T, Manzoni P, Di Natale B. Thyroid dysfunction in antiretroviral treated children. The Pediatric infectious disease journal. 2004 Mar 1;23(3):235-9.
14. LoPresti JS, Fried JC, Spencer CA, Nicoloff JT. Unique alterations of thyroid hormone indices in the acquired immunodeficiency syndrome (AIDS). Annals of Internal Medicine. 1989 Jun 15;110(12):970-5.
15. Olivieri A, Sorcini M, Battisti P, Fazzini C, Gilardi E, Sun Y, Medda E, Grandolfo M, Tossini G, Natili S, Gioia C. Thyroid hypofunction related with the progression of human immunodeficiency virus infection. Journal of endocrinological investigation. 1993 Jun 1;16(6):407-13.
16. Grunfeld C, Pang M, Doerrler W, Jensen P, Shimizu L, Feingold KR, Cavalieri RR. Indices of thyroid function and weight loss in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. Metabolism. 1993 Oct 1;42(10):1270-6.
17. Sellmeyer DE, Grunfeld C. Endocrine and metabolic disturbances in human immunodeficiency virus infection and the acquired immune deficiency syndrome. Endocr Rev 2006; 17:518–32.
18. Heufelder AE, Hofbauer LC. Human immunodeficiency virus infection and the thyroid gland. European journal of endocrinology. 1996 Jun 1;134(6):NP-674.
19. Andries A, Isaakidis P, Das M, Khan S, Paryani R, Desai C, Dalal A, Mansoor H, Verma R, Fernandes D, Sotgiu G. High rate of hypothyroidism in multidrug-resistant tuberculosis patients co-infected with HIV in Mumbai, India. PLoS One. 2013 Oct 23;8(10):e78313.
20. Mayer KH, Hirsch HH, Kaufmann G, Sendi P, Battegay M. Immune reconstitution in HIV-infected patients. Clinical Infectious Diseases. 2004 Apr 15;38(8):1159-66.
21. Battegay M, Drechsler H. Clinical spectrum of the immune restoration inflammatory syndrome. Current Opinion in HIV and AIDS. 2006 Jan 1;1(1):56-61.