



THYROID DYSFUNCTION IN HIV INFECTED PATIENTS - A CROSS SECTIONAL PREVALENCE STUDY IN TERTIARY CARE HOSPITAL

General Medicine

Vinod Angadi* Junior Resident, Dept of General Medicine, AIMS B G Nagara, Mandya, Karnataka
*Corresponding Author

Inbanathan J Professor & HOD, Dept of General Medicine, AIMS B G Nagara, Mandya, Karnataka

Anand L Assistant Professor, Dept of General Medicine, AIMS B G Nagara, Mandya, Karnataka

ABSTRACT

Background: Thyroid dysfunction is becoming more common in HIV infected patients. However, there is no enough data to suggest routine thyroid monitoring for those who are asymptomatic. Therefore, this study was conducted in an effort to find a solution to these problems. **Methods:** A cross sectional observational study was conducted on 50 adult HIV positive patients with no comorbidities. A detailed history taking and examination was done and necessary investigations were done to make diagnosis. FT3, FT4, TSH and CD4 were done in all the patients. **Results:** Overt Hypothyroidism was noted in 2%(1), subclinical hypothyroidism in 10% (6), isolated low FT4 noted in 2%(1) and sick euthyroidism in 22%(14) patients. FT3, FT4 levels found decreasing, as the stage of HIV advanced whereas TSH levels did not correlate with stage of infection. A direct correlation was found FT3 and CD4 counts and an inverse correlation between TSH and CD4 counts. TSH levels in patients on HAART were significantly higher when compared to those not on HAART. **Conclusion:** Majority of HIV infected patients with thyroid dysfunction did not have any symptoms. Serum FT3 and FT4 were directly correlated with WHO clinical infection stage. As CD4 counts dropped, TSH level was rising. Subclinical hypothyroidism was prevalent among HAART patients. Due to short sample size, no association could be shown between opportunistic infections and thyroid dysfunction.

KEYWORDS

HIV, Thyroid dysfunction, Subclinical hypothyroidism, Sick euthyroidism

INTRODUCTION

Patients with human immunodeficiency virus (HIV) frequently have abnormal thyroid function testing^{1,2}. In fact, one of the most prevalent endocrinopathies in HIV is thyroid dysfunction³. Although overt thyroid disease does not appear to be more common in HIV infected people than in general population, subtle thyroid dysfunction is common and is thought to affect up to 35% of all HIV infected people⁴. T4 secretion is affected in variety of systemic opportunistic infections, in patients with advanced HIV disease⁵. Sick euthyroid syndrome was found to be more prevalent in AIDS patients, probably due to hypothalamic-pituitary deficit. During ART, prevalence of subclinical hypothyroidism and isolated low FT4 levels is increased².

The data on thyroid dysfunction in HIV from India is minimal. There is insufficient evidence to recommend routine thyroid screening in asymptomatic HIV infected individuals. Hence this study was conducted, to evaluate various thyroid abnormalities in subset of HIV positive patients.

MATERIALS AND METHODS

This cross sectional prevalence study was conducted on HIV positive patients admitted to Department of Medicine at AIMS B G Nagara, Mandya, India over a period of 18 months.

Inclusion Criteria

The Institutional Ethical committee approval was obtained and a properly written informed consent was taken from all 50 patients. These 50 adult HIV infected patients comprising both males and females admitted for various indications, were the study subjects.

Exclusion Criteria

Patients who are pregnant, known thyroid disorder, known Hypertension, diabetes, coronary artery disease, or those who are on medications that influence thyroid function like amiodarone, propranolol, corticosteroids and oral contraceptives were excluded.

Detailed history was obtained and examination was performed, both for the current admission and for thyroid related problems. Patients were categorised according to WHO clinical stage for HIV. All routine investigations along with specific biochemical, microbiological and radiological investigations (such as sputum studies, blood culture, chest x ray, Ultrasound abdomen, CT chest or brain) in order to reach to a diagnosis. FT3, FT4, TSH and CD4 counts were done in all patients. Anti thyroid peroxidase (anti-TPO) antibodies were done in all cases. Thyroid scan was not required for any of the study subjects.

Statistical Analysis

Frequency and descriptive analysis were done using IBM SPSS version 22 statistical software.

RESULTS

50 adult HIV infected patients who were admitted to wards for various indications, were included in the study. There were 36 males (mean age 38.8 ± 10.04) and 14 females (mean age 34.77 ± 7.74). Majority of the patients were in age group 30 to 50 years. 32 patients (64%) presented with opportunistic infections (OIs), which was the commonest presentation. 7 patients (14%) were asymptomatic and were admitted for social reasons. Table 1 shows the distribution of the patients based on clinical presentation.

Table 1: Distribution of patients according to clinical presentation.

clinical presentation	N	%
Opportunistic Infections	32	64
No symptoms	7	14
Severe anemia	3	6
ATT induced liver injury	1	2
Idiopathic Thrombocytopenic Purpura (ITP)	2	4
Organophosphorus poisoning	2	4
Lactic acidosis	2	4
ART induced rash	1	2

Out of 50 patients, overt hypothyroidism was found in 2(2%) patients, sub clinical hypothyroidism was seen in 6(10%) patients, isolated low FT4 levels was seen in 1(2%) patients and sick euthyroidism was noticed in 13(22%) patients. Anti-thyroid peroxidase antibodies were negative in all patients and none of them had hyperthyroidism.

Table2: Thyroid dysfunction in HIV infected patients in the present study

Thyroid dysfunction	N	%	Males	Females
Hyperthyroidism	0	0	0	0
Overt Hypothyroidism	2	2	1	1
Subclinical hypothyroidism	6	10	3	3
Isolated low FT4	1	2	0	1
Sick euthyroidism	13	22	9	3
Euthyroidism	28	64	22	6
Total	50	100	36	14

Table3: Distribution of Thyroid dysfunction according to WHO clinical stage

Stages	Overt Hypo-thyroidism	Subclinical Hypo-thy-roidism	Isolated low FT4	Sick euthy-roidism	Total
I	0	0	0	2	2
II	0	1	0	2	3
III	1	2	0	1	4

IV	1	3	1	8	13
Total	2	6	1	13	22

Table4: Correlation between clinical stage and FT3 levels

FT3 (1.7-4.2ng/dl)	N	Mean±SD
stage I	12	2.5±0.6
stage II	4	2.5±0.4
stage III	8	2.4±0.5
stage IV	26	1.8±0.6

One way Anova test; F value= 8.011, p value= 0.001

Difference is significant

Table5 : Correlation between clinical stage and FT4 levels

FT4 (0.8-1.8ng/dl)	N	Mean±SD
stage I	12	1.3±0.3
stage II	4	1.2±0.2
stage III	8	1.1±0.33
stage IV	26	1.04±0.27

One way Anova test; F value= 2.732, p value= 0.050

Difference is significant

This is our modest attempt to study correlation between WHO clinical stage and thyroid dysfunction by categorising patients in the 4 clinical stages and comparing the mean TSH levels, FT4 and FT3 levels in each stage with each other. There were 12 (24%) patients in stage I, 4 (8%) in stage II, 8 (16%) in stage III and 26 (52%) in stage IV.

Out of 12 patients in stage I, only 2 had hypothyroidism which was sick euthyroidism. None of them had overt or subclinical hypothyroidism or isolated low FT4 levels. Out of 4 patients in stage II, 2 had sick euthyroidism and 1 had subclinical hypothyroidism. Out of 8 patients in stage III, 2 had subclinical hypothyroidism, 1 had overt hypothyroidism and 1 had subclinical hypothyroidism. Out of 26 patients in stage IV, 8 had sick euthyroidism, 3 had subclinical hypothyroidism, 1 had overt hypothyroidism and 1 had isolated low FT4 levels.

After distributing 50 cases from stage I to stage IV, mean FT3, FT4 and TSH were calculated and results were analysed using ANOVA test. It was noticed that levels of FT3 and FT4 went on decreasing from stage I to stage IV. But levels of TSH did not show any correlation with WHO clinical stage. (Table 4-6)

Table6 : Correlation between clinical stage and TSH levels

TSH (0.3-5.5 mIU/L)	N	Mean±SD
stage I	12	2.8±0.9
stage II	4	3.9±2.1
stage III	8	4.5±3.6
stage IV	26	3.85±2.85

One way Anova test; F value=1.032, p value= 0.268

Difference is not significant

CD4 count, being the most important marker of severity of HIV infection and AIDS, we studied correlation of FT3, FT4 and TSH levels with CD4 count. We divided 50 patients into three groups according to CD4 count, randomly. Group A: 0-200 cells/cumm, Group B: 201-350 cells/cumm and Group C: >350 cells/cumm. (Table7)

Out of 24 patients in group A, 11 had thyroid dysfunction. 6 (25%) patients had sick euthyroidism, 3 (12.5%) had subclinical hypothyroidism, 1 (4.16%) of them had overt hypothyroidism and other one (4.16%) showed isolated low FT4 levels.

Out of 18 patients in group B, 5 had thyroid abnormalities. 2 (11.11%) had subclinical hypothyroidism, 2 (11.11%) had sick euthyroidism and 1 (5.55%) had overt hypothyroidism, none of them showed isolated low FT4 levels.

Out of 8 patients in group C, only 1 had thyroid dysfunction i.e sick euthyroidism. None had overt hypothyroidism, subclinical hypothyroidism or low FT4 levels (Table8). In our study we found out that there is direct correlation between FT3 and CD4 count ($r=0.2034$ and $p=0.0133$).

It means that as CD4 count decreases, FT3 levels go on decreasing and TSH levels go on increasing. The relation between CD4 and FT4 levels

was not significant.

Table7 : Distribution of cases according to CD4 counts

CD4 count (cumm.)	Male	Female	Total	%
Group A	18	6	24	48
Group B	12	6	18	36
Group C	6	2	8	16
Total	36	14	50	100

Table8 : Distribution of thyroid dysfunction according to CD4 counts

CD4 (cumm)	Overt Hypo-thyroidism	Subclinical Hypothyroidism	Isolated low FT4	Sick euthyroidism	Total
Group A	1	3	1	6	11
Group B	1	2	0	2	5
Group C	0	0	0	1	1
Total	2	5	1	9	17

Out of 50 patients, 29 were on HAART and 24 were not on HAART. The difference in the FT3 and TSH levels between the two groups i.e patients on HAART and patients not on HAART was found to be significant ($p=0.02$ for FT3 and 0.01 for TSH)

DISCUSSION

Thyroid gland dysfunction is one of the most common endocrine abnormalities described in HIV. Subtle abnormalities in thyroid function are due to multiple causes such as opportunistic infections or tumours occurring in patients at the symptomatic stage of infection, defective function of the immune system or due to antiretroviral therapy or direct effect of HIV itself. Here we have tried to study the correlation between HIV infection and thyroid dysfunction in our rural tertiary care hospital using a cross sectional prevalence study for a period of 18 months. 50 HIV positive individuals were our study subjects. There were 36 males (mean age 38.8 ± 10.04) and 14 females (mean age 34.77 ± 7.74). Majority of the patients were in the age group 30 to 50 years.

Overt Hypothyroidism was noted in 2%(1), subclinical hypothyroidism in 10%(6), isolated low FT4 noted in 2%(1) and sick euthyroidism in 22%(14) patients. FT3, FT4 levels found decreasing, as the stage of HIV advanced whereas TSH levels did not correlate with stage of infection. A direct correlation was found FT3 and CD4 counts and an inverse correlation between TSH and CD4 counts. TSH levels in patients on HAART were significantly higher when compared to those not on HAART.

Our study had certain limitations. Study is conducted at a tertiary care hospital, study group does not show population characteristics. Other limitations are due to its cross sectional nature, it is limited in terms of deriving deterministic conclusions. Small sample size is another limitation that fails to support/ to draw any meaningful conclusions.

CONCLUSION

Majority of HIV infected patients with thyroid dysfunction did not have any symptoms. Serum FT3 and FT4 were directly correlated with WHO clinical infection stage. As CD4 counts dropped, TSH level was rising. Subclinical hypothyroidism was prevalent among HAART patients. Hence, patients on HAART may need regular monitoring of thyroid function tests. Due to short sample size, no association could be shown between opportunistic infections and thyroid dysfunction. Larger studies are needed for the epidemiology and health consequences of mild thyroid dysfunction in HIV infected patients.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

Study	Madge et al	Beltran et al	Raffi et al	Quirino et al	Kaneria MV et al	Our study
Overt Hypothyroidism	2.5%	2.6%			2.67%	2%
Subclinical Hypothyroidism	4%	6.6%		7.42%	13.33%	10%
Sick euthyroidism			16%		25.33%	22%
Isolated low FT4 levels		6.8%			2.67%	2%
Overt Hyperthyroidism	< 1%				0	0

REFERENCES

1. Kaneria MV, Kahalekar VV. A study of thyroid dysfunction in HIV infected patients in a tertiary care hospital. *Int J Adv Med* 2016;3:708-15.
2. Madeddu G, Spanu A, Chessa F, Calia GM, Lovigu C, Solinas P, et al. Thyroid function in human immunodeficiency virus patients treated with highly active antiretroviral therapy. *Clin Endocrinol (Oxf)*. 2006;64:375-83.
3. Hoffman CJ, Brown TT. Thyroid Function Abnormalities in HIV-Infected Patients *Clin Infect Dis*. 2007;45(4):488-94.
4. Calza L, Manfredi R, Chiodo F. "Subclinical hypothyroidism in HIV-infected patients receiving highly active antiretroviral therapy," *Journal of Acquired Immune Deficiency Syndromes*. 2002;31(3):361-3.
5. Pearce EN. Diagnosis management of thyrotoxicosis. *BMJ*. 2006;332:1369-73.
6. Sharma N, Sharma LK, Dutta D, Gadpayle AK, Anand A, Gaurav K, et al. "Prevalence and Predictors of Thyroid Dysfunction in Patients with HIV Infection and Acquired Immunodeficiency Syndrome: An Indian Perspective," *Journal of Thyroid Research*. 2015(2015).
7. Raffi F, Brisseau JM, Planchon B, Rémi JP, Barrier JH, Grolleau JY. Endocrine function in 98 HIV-infected patients: a prospective study. *AIDS*. 1991;5:729-33.
8. Quirino T, Bongiovanni M, Ricci E. Hypothyroidism in HIV infected patients who have or have not received HAART. *Clin Infect Disease*. 2004;38:596-7.
9. Madge S, Smith C, Lampe F, et al: No association between HIV disease and its treatment and thyroid function. *British HIV Association HIV Medicine* 2007;8:22-7.