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**Original Research Article**

# Thyroid dysfunction in human immuno-deficiency virus infected patients: a non-randomized, cross-sectional, single-center study

**Vaheed U. Mujawar[1], Anilkumar C. Byakod[1], Lakshmi Devi P. P.[2]*, Basavaraj N. Walikar[2], Tai A. Usmangani[2]**

[1]Department of General Medicine, [2]Department of ENT, Al Ameen Medical College Hospital, Vijayapur, Karnataka, India

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***Correspondence:**
Dr. Lakshmi Devi P. P.,
E-mail: laxmyravy99@gmail.com



## ABSTRACT

**Background:** Increasing prevalence of thyroid dysfunction has been reported in human immuno-deficiency virus (HIV)-infected patients. However, there is insufficient evidence to recommend routine thyroid screening of asymptomatic individuals. Hence, this study was undertaken in an attempt to resolve these issues. Objectives of this non-randomized, cross-sectional, single-center study was to study thyroid function in HIV positive patients at various stages of disease.
**Methods:** This single-center study was carried out at Al-Ameen Medical College Hospital and Government District Hospital Bijapur, Karnataka, India from December 2020 to December 2022. The final selected study population included newly diagnosed adult and adolescent (17-60 years) HIV+ patients was composed of 100 participants of either gender. Patients were interviewed and enrolled in the study after examining in detail according to the proforma and then by taking their written consent and explaining the purpose of the study. The thyroid hormone assays (S. TSH, FT3 and FT4) were done by chemiluminescence immuno assay (CLIA) using ADVIA Centaur-equipment.
**Results:** Overall mean age was 36 years (range in years: 17–66 years) and 66 patients (66%) were males. Male: female ratio of 1.94:1 was recorded. In the 50 patients having acquired immuno-deficiency virus (AIDS), FT3 levels ranged from 0.230 to 4.0 picogram/ml with a mean of 2.131+0.9826 picogram/ml. In 50 patients having AIDS, the FT4 levels ranged from 0.30 to 1.90 nanogram/dI with a mean 1.179±0.4484 nanogram/dl.
**Conclusions:** All forms of thyroid dysfunction were observed.

**Keywords:** Thyroid dysfunction, HIV, India, Sub clinical hypothyroidism

## INTRODUCTION

Abnormal thyroid function tests are common among human immunodeficiency virus (HIV)–infected patients.[1] In fact, thyroid dysfunction is among the commonest endocrinopathies in HIV.[2] Although the prevalence of overt thyroid disease does not appear to be significantly increased as compared to the general population, subtle thyroid dysfunction is common, believed to occur in as many as 35% of all HIV infected individuals.[3]

In patients with advanced HIV disease, variety of systemic opportunistic conditions that infect or infiltrate the thyroid can decrease or increase T4 secretion.[4] Less frequently, hypothalamic pituitary failure caused by central nervous system infections such as *Cryptococcosis* or *Toxoplasmosis* has been reported.[5] Thyroid dysfunctions in HIV-positive individuals can result from gland destruction by opportunistic pathogens (*Pneumocystis jirovecii* or *Cytomegalovirus*).[6]

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 immunodeficiency and cachexia. During antiretroviral therapy, the prevalence of 2 generally asymptomatic conditions (sub clinical hypothyroidism, which is characterized by isolated elevated thyroid-stimulating hormone levels, and isolated low free thyroxine levels) is increased. In addition, Graves' disease may occur during immune reconstitution. The data on the prevalence of thyroid dysfunction in HIV infected patients from India is scant.[7]

Testing for thyroid disease among symptomatic patients should begin with measurement of the thyroid-stimulating hormone level.[8,9]

However, there is insufficient evidence to recommend routine thyroid screening of asymptomatic HIV-infected individuals. In view of the above, the objective of this study was to study thyroid function in HIV positive patients at various stages of disease.

## METHODS

Patients visiting the Al-Ameen Medical College Hospital and Government District Hospital Bijapur, Karnataka, India between December 2020 to December 2022 were invited to participate and were included in this non-randomized, cross-sectional, single-center study after obtaining their written informed consent. The final selected study population included newly diagnosed adult and adolescent (17-60 years) HIV+ patients was composed of 100 participants of either gender.

Patients were interviewed and enrolled in the study after examining in detail according to the proforma and then by taking their written consent and explaining the purpose of the study. Patients with past history s/o thyroid illness, clinically evident thyroid enlargement, or signs of thyroid disease; on drugs known to interfere with thyroid hormone metabolism for e.g. rifampicin, steroids, ketoconazole, anti-epileptics; with abnormal liver function tests i.e. SGOT or SGPT levels greater than three times the upper normal limit; with abnormal renal function tests i.e. serum creatinine level greater than 1.6 mg°/0; and who could not provide informed consent were excluded from the study. The Institutional Ethics Committee approved this study.

### *Patient population*

100 consecutive HIV+ cases were studied in two groups.

Group A included 50 HIV+ patients having AIDS. A HIV+ patient is said to have AIDS if the patient fulfils any of the following criteria: CD4+ cell count of <200/l, regardless of the presence of opportunistic infections or neoplasms; or CD4+cell count of >200/l with at least one of the following: pulmonary or extra pulmonary tuberculosis, candidiasis of lower airways and/or esophagus, cryptococcosis extra pulmonary, chronic intestinal cryptosporidiosis (>1 months duration), invasive cervical cancer vi. Kaposi's sarcoma, primary brain lymphoma or Burkitt's lymphoma, HIV related encephalopathy, cytomegalovirus retinitis, pneumocystis jiroveci pneumonia, herpes simplex: chronic ulcer (s) (>1 month's duration) or bronchitis, pneumonia, or esophagitis, progressive multifocal leukoencephalopathy, pneumonia recurrent, Salmonella septicemia recurrent, and wasting syndrome due to HIV.

Group B included 50 HIV+ patients having CD4+ cell count >200/l without any opportunistic infection or complication. CD4+ cell count was noted which was determined by flow-cytometry with fluorescence activated cell sorter (FACS) Calibur count system (Beckton Dickinson, USA).

### *Blood analysis*

A single blood sample drawn between 8 am to 12 noon was subjected for laboratory analysis. Patients were evaluated for free thyroxin (FT-4), free tri-lodothyronine (FT-3) and serum thyroid stimulating hormone (S. TSH) levels. The principle of free thyronines assay is a solid-phase, chemiluminescent, competitive analogue immunoassay while that of S. TSH estimation is a solid-phase, two site chemiluminescentimmunometric assay. In all patient's liver function test (LFT), kidney function test (KFT) and haemogram were done.

### *Thyroid function tests*

The thyroid hormone assays (S.TSH, FT3 and FT4) were done by chemiluminescencelmmuno assay (CLIA) using ADVIA Centaur-equipment. Definitions used are as per recommendations of consensus statement by the American Association of clinical endocrinologists, the American thyroid association, and The Endocrine Society.[10]

### *Statistical methods*

The data was collected on an excel sheet and descriptive statistical analysis was performed. Analytical method of statistical analysis was undertaken through Pearson's correlation coefficient.

## RESULTS

In total, 100 patients were enrolled for the study. Overall mean age was 36 years (range in years: 17–66 years) and 66 patients (66%) were males. Table 1 summarizes the age group and gender characteristics of study population.

Out of 100 HIV+ cases studied, 66 (66%) were males and 34 (34%) were females, with male: female ratio of 1.94:1 was recorded. The age in these cases ranged from 17 years to 66 years with a mean of 36.22±9.07. Of these 100 cases, 6 (6%) were below 25 years, 37 (37%) were between 25-34 years, 37 (37%) were between 35-44 years and 20

(20%) were above 44 years. Mean age for a male patent was 37.95±9.26 years and for a female patient was 32.85±7.75 years.

**Table 1: Age group and gender characteristics of study population.**

| Age groups in years | Male | Female | Frequency |
|---|---|---|---|
| **17-24** | 1 | 5 | 6 |
| **25-34** | 24 | 13 | 37 |
| **35-44** | 25 | 12 | 37 |
| **>44** | 16 | 4 | 20 |
| **Total** | 66 | 34 | 100 |

In the 50 patients having AIDS, FT3 levels ranged from 0.230 to 4.0 picogram/ml with a mean of 2.131+0.9826 picogram/ml. 34 (68%) patients had normal FT 3 levels while FT3 levels were below normal in 16 (32%) patients. In the 50 HIV positive patients studied FT3 levels ranged from 1.71 to 4.10 picogram/ml with a mean of 2.828+6406 pico gram/ml 48 (96%) patients had normal FT3 values while 2 (4%) patients had FT3 levels below the normal range (Table 2).

**Table 2: Tabulation showing free trilodothyronine (FT3) in 50 AIDS patients (group A) and free trilodothyronine (FT3) in 50 HIV+ patients (group B).**

| Observation FT3 (pico gram/ml) | Frequency (%) of group A patients (%) | Frequency (%) of group B patients (%) | Observa-tion (%) |
|---|---|---|---|
| **Normal (1.8-4.2)** | 34 (68) | 34 (68) | 34 (68) |
| **Elevated (>4.2)** | 0 (0) | 0 (0) | 0 (0) |
| **Decreased (<1.8)** | 16 (32) | 16 (32) | 16 (32) |

In 50 patients having AIDS, the FT4 levels ranged from 0.30 to 1.90 nanogram/dl with a mean 1.179±0.4484 nanogram/dl. 39 (78%) patients had normal FT4 levels while FT4 levels were below normal in 11 (22%) patients. Elevated FT 4 level was not observed in any patient. In the 50 HIV+ patients the FT4 levels ranged from 0.66 to 2.41 nanogram/dl with a mean of 1.310±0.3183 nanogram/dl. 48 (96%) patients had normal FT 4 values, 1 (2%) patient had FT 4 level below normal range and 1 (2%) patient had FT 4 level above normal range (Table 3).

In the 50 AIDS patients the S. TSH value ranged from 1.11 to 15.0 µIU/ml with a mean of 5.622±3.616 µIU/ml. 27 (54%) patients had normal S. TSH levels while S. TSH levels were above normal in 23 (46%) patients. No patient had decreased S. TSH level. The patients with increased S. TSH levels had no clinical examination of hypothyroidism. In the 50 HIV+ patients the S. TSH levels ranged from 0.25 to 6.030 µIU/ml with a mean of 2.43±1.115 µIU/ml. 47 (94%) patients had normal S. TSH levels while 2 (4%) patients had S. TSH levels above normal range (Table 4).

**Table 3: Tabulation showing free thyroxine (FT4) in 50 AIDS patients (group A) in 50 HIV+ patients (group B).**

| Observation FT4 (ng/ml) | Frequency (%) of group A patients | Frequency (%) of group B patients |
|---|---|---|
| **Normal (0.8-1.9)** | 39 (78) | 48 (96) |
| **Elevated (>1.9)** | 0 (0) | 1 (2) |
| **Decreased (<0.8)** | 11 (22) | 1 (2) |

**Table 4: Tabulation showing serum thyrotropin (S. TSH) in 50 AIDS patients (group A) in 50 HIV+ patients (group B).**

| Observation TSH (µIU/ml) | Frequency (%) of group A patients | Frequency (%) of group B patients |
|---|---|---|
| **Normal (0.4-4.0)** | 27 (54) | 47 (94) |
| **Elevated (>4.0)** | 23 (46) | 2 (4) |
| **Decreased (<0.4)** | 0 (0) | 1 (2) |

## DISCUSSION

Endocrine system is one of the important systems involved in HIV, and in this, thyroid gland involvement is most commonly described.[11] Subtle abnormalities in thyroid function is common in HIV positive individuals. The cause of this is multifactorial *viz.* opportunistic infections or tumors occurring in patients at the symptomatic stage of infection, defective function of the immune system, antiretroviral drugs used or a direct effect of HIV itself.[12]

There are many studies showing correlation between HIV infection and its associated conditions like stage of infection, CD4 count, OIs, HAART and thyroiddysfunction.[13-17] However, these correlations are unclear.

In present study, clinical (overt) hypothyroidism was seen in 25 (25%) patients, 74 (74%) had sub clinical hypothyroidism, 1 (1%) had isolated low TSH levels. Beltran[18] in a similar study reported overt hypothyroidism in 26%, sub clinical hypothyroidism in66% and an isolated low TSH level in 6% of 350 subjects studied.

Low free T4 levels and sub clinical hypothyroidism which correlated with low CD4 counts were reported in a Spanish population. In a similar study by Raffi et al, the main abnormalities were sick euthyroid syndrome with low tri-idothyronine and/or thyroxine in 16% of patients.[19] In a study by Quirino et al, out of total 687 patients, 51(7.42%) were sub-clinically hypothyroid.[20] Madge et al reported that out of 1565 patients, thirty-nine (2.5%) were found to

have overt hypothyroidism, and eight had overt hyperthyroidism.[21] Sixty-one (4%) had sub clinical hypothyroidism, five (had sub clinical hyperthyroidism and 263 (17%) had a non-thyroidal illness. A normal TFT was obtained in 1118 patients (75.5%). Prevalence of overt primary hypothyroidism in the general population and HIV infected individuals from different studies across the globe has been reported to be 0.3% and 0–2.6%, respectively. Our study had a number of strengths. First, we included consecutive patients resulting in a cohort generalizable to general practice. Second, the study design ensured sufficiently large sample size (here n=100).

Regarding the limitations of our study, we must emphasize that it was carried out in a single center. Another potential limitation of this study was that it was conducted in a tertiary care hospital, the study group does not show the population characteristics and the patients in the study could not be equally distributed for HIV associated conditions like stage of infection, CD4 count, and HAART. Finally, clinical data over opportunistic infections could not be extrapolated. Therefore, the results may not adequately represent the results that would be observed in the HIV population.

## CONCLUSION

Abnormal thyroid function test results are common among HIV-infected individuals. Currently, there is insufficient evidence in favor of screening for thyroid abnormalities among asymptomatic HIV-infected individuals. Patients on HAART have high prevalence of sub clinical hypothyroidism as compared to patients naïve to HAART. Hence, patients on HAART may need regular monitoring of thyroid function tests. Larger studies are needed to examine the epidemiology and health consequences of mild thyroid dysfunction in HIV-infected patients and to better inform screening and treatment guidelines.

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## REFERENCES

1. Micali C, Russotto Y, Celesia BM, Santoro L, Marino A, Pellicanò GF, Nunnari G, VenanziRullo E. Thyroid diseases and thyroid asymptomatic dysfunction in people living with HIV. Infect Dis Rep. 2022;14(5):655-67.
2. Himanshu D, Tandon R, Kumar S, Sawlani KK, Verma SK, MisraR, Atam V. Is International HIV Dementia Scale good enough to diagnose HIV-associated neurocognitive disorders? J Fam Med Prim Care. 2022;11(9):5060-4.
3. Sethi Y, Uniyal N, Maheshwari S, Sinha R, Goel A. Thyroid Function Abnormalities in the Acute Phase of COVID-19: A Cross-Sectional Hospital-Based Study From North India. Cureus. 2022;14(5).
4. Sah UK, Ansari M, Sah AK, Chaudhary P, Gupta S, Kumar P, Sah JP. Study of thyroid dysfunction in people living with HIV in Nepalese population undergoing antiretroviral therapy: a cross-sectional study. Int J STD AIDS. 2023;09564624221147963.
5. Kornete L, Terauda R, Sausa S, Dzivite-Krisane I, Melderis I, Sitkare V, et al. Graves' disease as a manifestation of immune reconstitution inflammatory syndrome in an HIV-1-infected adolescent patient: A case report. J Clin Transl Endocrinol. 2022;100118.
6. Raguthu CC, Gajjela H, Kela I, Kakarala CL, Hassan M, Belavadi R, et al. Cardiovascular Involvement in Thyrotoxicosis Resulting in Heart Failure: The Risk Factors and Hemodynamic Implications. Cureus. 2022;14(1).
7. Deb N, Roy P. Human immunodeficiency virus-associated nephropathy with hypothyroidism. Apollo Med. 2022;19(4):282.
8. Razvi S, Bhana S, Mrabeti S. Challenges in interpreting thyroid stimulating hormone results in the diagnosis of thyroid dysfunction. J Thyroid Res. 2019;4106816.
9. Saidi S, Jaafar SN, Daud A, Musa R, Ahmad NN. Relationship between levels of thyroid stimulating hormone, age, and gender, with symptoms of depression among patients with thyroid disorders as measured by the Depression Anxiety Stress Scale 21 (DASS-21). Enfermeriaclinica. 2018;28:180-3.
10. Hennessey JV, Garber JR, Woeber KA, Cobin R, Klein I, Thyroid Scientific Committee. American association of clinical endocrinologists and American college of endocrinology position statement on thyroid dysfunction case finding. Endocrine Practice. 2016;22(2):262-70.
11. Turk MC, Bakker CJ, Spencer SM, Lofgren SM. Systematic review of sex differences in the relationship between hormones and depression in HIV. Psychoneuroendocrinology. 2022;105665.
12. Ayeni OA, O'Neil DS, Pumpalova YS, Chen WC, Nietz S, Phakathi B, et al. Impact of HIV infection on survival among women with stage I-III breast cancer: Results from the South African breast cancer and HIV outcomes study. Int J Cancer. 2022;151(2):209-21.
13. Kaneria MV, Kahalekar VV. A study of thyroid dysfunction in HIV infected patients in a tertiary care hospital. Int J Adv Med. 2016;3(3):708-15.
14. Verma RK, Giri R, Gupta C, Srivastava V. Study of thyroid profile in seropositive HIV adults patients on HAART regimen. Int J Adv Med. 2017;4(4):1092.
15. 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. J Thyroid Res. 2015;517173.
16. Roszkiewicz J, Smolewska E. Kaleidoscope of autoimmune diseases in HIV infection. Rheumatol Int. 2016;36(11):1481-91.

17. Dev N, Sahoo R, Kulshreshtha B, Gadpayle AK, Sharma SC. Prevalence of thyroid dysfunction and its correlation with CD4 count in newly-diagnosed HIV-positive adults–a cross-sectional study. Int J STD AIDS. 2015;26(13):965-70.
18. Beltran S, Lescure FX, Desailloud R, Douadi Y, Smail A, El Esper I, et al. Increased prevalence of hypothyroidism among human immunodeficiency virus—infected patients: A need for screening. Clin Infect Dis. 2020;37(4):579-83.
19. Raffi F, Brisseau JM, Planchon B, Rémi JP, Barrier JH, Grolleau JY. Endocrine function in 98 HIV-infected patients: a prospective study. AIDS (London, England). 2019;5(6):729-33.
20. Quirino T, Bongiovanni M, Ricci E, Chebat E, Carradori S, Martinelli C, et al. Hypothyroidism in HIV-infected patients who have or have not received HAART. Clin Infect Dis. 2019;38(4):596-7.
21. Madge S, Smith CJ, Lampe FC, Thomas M, Johnson MA, Youle M, et al. No association between HIV disease and its treatment and thyroid function. HIV Med. 2007;8(1):22-7.

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