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# TO STUDY THYROID DYSFUNCTION AND ITS CORRELATION WITH CD4 COUNTS IN PEOPLE LIVING WITH HIV

General Medicine

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## ABSTRACT

**Background -** HIV is a retrovirus which targets T lymphocytes, thereby affecting the immune system of the body causing immunosuppression. Multiple organ involvement including endocrine dysfunction can be seen in HIV infected people. Recent studies have suggested that high levels of TSH are associated with disease progression. **Aim:** To estimate thyroid dysfunction in people with HIV and to correlate TSH levels with absolute CD4 cell count. **Material and Method:** This Cross sectional study was performed between February 2021 to August 2022 at hospitals attached to Bangalore Medical College and Research Institute. HIV positive patients fulfilling inclusion criteria were evaluated as per proforma. TSH, T3,T4 levels and CD4 counts were estimated and correlated. **Result:** The study population consisted of 136. The majority of participants (47.10%) were classified as WHO Stage 1, while 28.70% were classified as Stage 4. Tuberculosis was the most common opportunistic infection observed. Hypothyroidism was the most common comorbiditiy. Other laboratory values measured in the study population, including total protein, globulin, creatinine, hemoglobin, total leukocyte count, platelet count, and liver function tests, were within normal limits. TSH levels and CD4 counts inversely correlated in this study. This suggested that thyroid dysfunction is common among HIV patients. **Conclusion:** It was concluded that there was inverse correlation between TSH levels and CD4 counts in HIV patients.

## KEYWORDS

TSH, T3, T4, CD4 counts, Immune suppression.

## INTRODUCTION

Human immunodeficiency virus (HIV) infection is characterized by decreased CD4 cell count and immunodeficiency, leading to opportunistic infections (OIs) and tumors(1). In recent years, increasing number of patients with HIV infection are able to survive for long periods because of the extensive application of highly active antiretroviral therapy (HAART) for the repression of viral replication as well as because of the emergence of new medicines and therapeutic regimens. Thyroid hormone, an important hormone regulating metabolism, can also be affected by HIV infection. Numerous studies have reported that the incidence of thyroid dysfunction is much higher (about 36%-37%) in patients infected with HIV than in the general population (2,3). Patients who have been infected with the human immunodeficiency virus (HIV) frequently have abnormal thyroid function test findings. Subclinical hypothyroidism is seen especially in those on highly active anti-retroviral therapy (HAART).(4–7) Nonthyroidal disease (also known as euthyroid unwell syndrome) is prevalent in people with advanced AIDS. Subclinical hypothyroidism, which is characterised by isolated elevated thyroid-stimulating hormone levels, and isolated low free thyroxine levels, are two largely asymptomatic disorders that are more common with antiretroviral therapy.

A US screening study in general population, showed a prevalence of 0.4% and 9% for overt and subclinical hypothyroidism, respectively, with the latter increasing to over 20% among women 75 years of age or older(8). In a meta-analysis from Europe, the prevalence of overt and subclinical hypothyroidism in general population was 0.37% and 3.8%, respectively, including both diagnosed and undiagnosed cases, and the estimated incidence of hypothyroidism was 226 cases per 100,000 individuals per year(9).

When diagnosing thyroid diseases in patients exhibiting thyroid-related symptoms or generalised symptoms without a known cause, thyroid function testing is acceptable. However, there is debate over whether to screen asymptomatic people for thyroid function, both for HIV patients and the general public. The significant frequency of subclinical hypothyroidism and the potential benefit of levothyroxine medication in this population may justify evaluating older patients regardless of their HIV status. The pathophysiology of subclinical hypothyroidism may be different in HIV-infected patients, despite the fact that cross-sectional studies have shown a higher prevalence of the condition than is typically seen in the general population.

Currently, there is insufficient evidence to support routine screening of thyroid function in all HIV-infected people (10).This study was performed to know the prevalence of thyroid dysfunction in HIV patients and to correlate CD4+ counts and TSH in HIV patients.

## METHODOLOGY

This cross sectional study was conducted in hospitals attached to Bangalore Medical College and Research Institute. Inclusion criteria included patient willing to give valid written informed consent, age more than 18years and less than 60 years, HIV positive patients diagnosed by ELISA method. After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled for the study. Patients with renal dysfunction, chronic liver disease and infections altering thyroid function were excluded from the study.

Clinical examination and investigations was done as per the Performa. Routine investigations (CBC, LFT, RFT) and Thyroid stimulating hormone (TSH), total thyroxine (T4), and total tri-iodothyronine (T3) were measured using standard laboratory techniques. Data from the case record proforma was entered into Microsoft Excel spreadsheet version 2021 and analyzed using IBM-SPSS version 26.

## RESULTS

A total of 136 individuals participated in the study. Out of 136 total participants, 64 (47.10%) were classified as WHO Stage 1, which indicates that they had asymptomatic HIV infection with a CD4 count >500 cells/mm3. 4 (2.90%) were classified as Stage 2, indicating mild symptoms with a CD4 count of 350-500 cells/mm3. 29 (21.30%) were classified as Stage 3, indicating advanced symptoms with a CD4 count of 200-350 cells/mm3. 39 (28.70%) were classified as Stage 4, indicating severe symptoms with a CD4 count <200 cells/mm3. (Fig.1 & Table.1)

Out of 136 total participants, 32 (24%) had tuberculosis, 18 (13%) had candidiasis, 7 (5%) had herpes zoster (shingles), 6 (4%) had PCP pneumonia, 4 (3%) had peripheral neuropathy, 2 (1%) had tinea infection, 2(1%) had HIV retinopathy, 2 (1%) had genital warts, and 1 (1%) had CSOM (chronic suppurative otitis media).The high proportion of participants with tuberculosis (24%) is notable, as tuberculosis is a common opportunistic infection in people living with HIV. (Fig.2 & Table 2)

Out of 136 total participants, 93 (69%) had no comorbidities, while the remaining participants had one or more comorbidities. The most common comorbidities in this study population was hypothyroidism,

present in 20(15%) of patients. Hypertension and diabetes both of which were present in 19 participants (14%). Ischemic heart disease was present in 5 (4%) participants. The remaining comorbidities (seizure disorder, bronchial asthma, hyperthyroidism, and cardiomyopathy) each affected 2 participants (1%) or fewer. (Fig.3 & Table.3)

The mean total protein level in the study population was 5.4 g/dL, with a standard deviation of 1 g/dL. The mean globulin level in the study population was 3 g/dL, with a standard deviation of 0.8 g/dL. (Fig.4 & Table.4) The mean urea level in the study population was 28.3 mg/dL, with a standard deviation of 13.6 mg/dL. The mean creatinine level in the study population was 0.96 mg/dL, with a standard deviation of 0.53 mg/dL.. (Fig.5 & Table.5)

The mean HB level in the study population was 11.1 g/dL, with a standard deviation of 2.2 g/dL. The mean TC in the study population was 7012 cells/mm3, with a standard deviation of 3801 cells/$mm^3$. The mean PLT count in the study population was 2.57 x 10^5 cells/mm3, with a standard deviation of 0.77 x 10^5 cells/$mm^3$. (Table.6)

The mean albumin level in the study population was 2.4 g/dL, with a standard deviation of 0.4 g/dL. The mean TB level in the study population was 0.7 mg/dL, with a standard deviation of 0.3 mg/dL. The mean DB level in the study population was 0.31 mg/dL, with a standard deviation of 0.2 mg/dL. The mean AST level in the study population was 36 U/L, with a standard deviation of 17 U/L. The mean ALT level in the study population was 34.1 U/L, with a standard deviation of 18.2 U/L. The mean ALP level in the study population was 88 U/L, with a standard deviation of 35 U/L. (Fig. 6&Table.7)

The correlation between TSH and CD4 count was 0.489, with p value of <0.001 indicating a negative correlation between these 2 variables. (Fig.7)

The mean value of TSH is 3.68 with a standard deviation of 2.74. The mean value of T4 is 7.78 with a standard deviation of 2.27. The mean value of T3 is 154.9 with a standard deviation of 28.93. (Fig.8 & Table.8)

## DISCUSSION

In our study, we found that the prevalence of hypothyroidism in HIV patients was 15%. This is higher than the prevalence of hypothyroidism in general population which is 8% as shown by Merenich et al., he also reported FT3 levels were also marginally lower than those of healthy control participants but remained within the normal range.(11)

According to a recent study by Beltran et al., persons with HIV infection have a higher frequency of subclinical hypothyroidism than people in the general population. This distinction was especially significant for male patients. Additionally, the investigators noted a statistically significant connection between subclinical hypothyroidism, receiving stavudine-containing medication, and the patients' level of immunodeficiency.(12)

In a French study of 212 HIV-positive individuals, thyroid function testing revealed that 12.3% of the participants had aberrant results, including 1.9% with overt hypothyroidism, 8.5% with subclinical hypothyroidism, and 1.9% with significant levels of anti-thyroperoxidase antibodies.(13). Also, Calza et al. found that HAART-using HIV patients had a significant prevalence (12.2%) of subclinical hypothyroidism. (14)

A German study found an even greater rate of subclinical hypothyroidism (17.4%), but only a few patients were included in that study (15). In contrast, Collazos et al. (16) reported a lower prevalence, of 3.5%, in a Spanish population of 202 patients. According to Sonia et al., screening is necessary for HIV-positive patients, especially for those using stavudine and those with low CD4 cell counts, because hypothyroidism is more common in this population.(12)

Low T3 levels were linked by LoPresti et al. to AIDS hospitalised patients' critical disease severity and fatality.(17) Thyroid dysfunction is associated with disease severity and can be seen early in the course of perinatal HIV infection and worsen over time, according to Chiarelli et al. They also discovered that T3, T4, FT4, and TBG were significantly reduced in HIV children compared with controls while TSH and TBG were increased. (18)

Thyroid stimulating hormone (TSH), total thyroxine (T4), total tri-iodothyronine (T3), and CD4 counts have all been compared in HIV-positive individuals, and the results have generally demonstrated that a higher TSH is associated with a lower CD4 count. This finding supports the hypothesis that thyroid dysfunction can be a valuable predictor of better clinical outcomes in terms of immunosuppression in HIV-positive people.

| | | Count | Column N % |
|---|---|---|---|
| WHO STAGING | 1 | 64 | 47.10% |
| | 2 | 4 | 2.90% |
| | 3 | 29 | 21.30% |
| | 4 | 39 | 28.70% |

Table 1: WHO staging among HIV patients

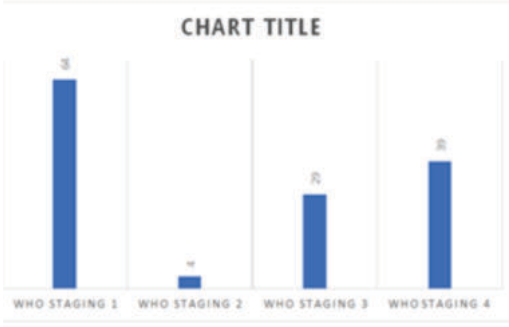



Fig 1: WHO staging among HIV patients

| OPPORTUNISTIC INFECTIONS | N | % |
|---|---|---|
| TUBERCULOSIS | 32 | 24% |
| CANDIDIASIS | 18 | 13% |
| HERPES ZOSTER | 7 | 5% |
| PCP PNEUMONIA | 6 | 4% |
| PERIPHERAL NEUROPATHY | 4 | 3% |
| TINEA INFECTION | 2 | 1% |
| HIV RETINOPATHY | 2 | 1% |
| GENITAL WARTS | 2 | 1% |
| CSOM | 1 | 1% |

Table 2: Distribution of opportunistic infection among HIV patients

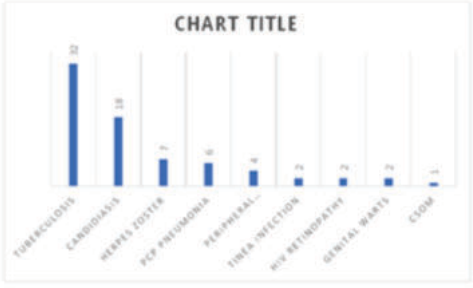



Fig 2: Distribution of opportunistic infection among HIV patients

| COMORBIDITIES | N | % |
|---|---|---|
| NIL | 93 | 69% |
| HYPERTENSION | 19 | 14% |
| HYPOTHYROIDISM | 20 | 15% |
| DIABETES | 19 | 14% |
| ISCHEMIC HEART DISEASE | 5 | 4% |
| SEIZURE DISORDER | 2 | 1% |
| BRONCHIAL ASTHMA | 2 | 1% |
| HYPERTHYROIDISM | 1 | 1% |
| CARDIOMYOPATHY | 1 | 1% |

Table 3: Distribution of Co-morbidities among HIV patients

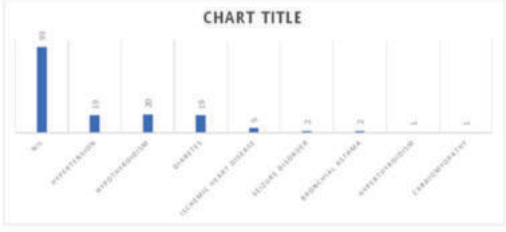



Fig 3: Distribution of Co-morbidities among HIV patients

| | Mean | Standard Deviation |
|---|---|---|
| TOTAL PROTEINS | 5.4 | 1 |
| GLOBULIN | 3 | 0.8 |

Table 4: Mean and standard deviation of total protein and globulin among HIV patients

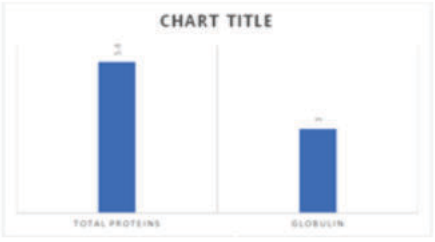



Fig 4: Mean and standard deviation of total protein and globulin among HIV patients

| | Mean | Standard Deviation |
|---|---|---|
| UREA | 28.3 | 13.6 |
| CREATININE | 0.96 | 0.53 |

Table 5: Mean and standard deviation of urea and creatinine among HIV patients

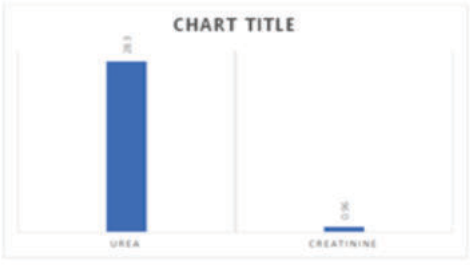



Fig 5: Mean and standard deviation of urea and creatinine among HIV patients

| | Mean | Standard Deviation |
|---|---|---|
| HB | 11.1 | 2.2 |
| TC | 7012 | 3801 |
| PLT | 2.57 | 0.77 |

Table 6: Mean and standard deviation of Haemoglobin, total counts and platelet

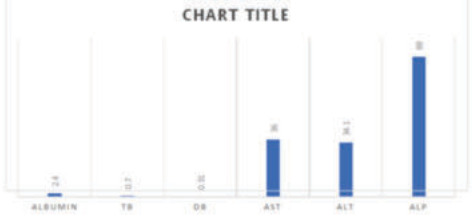
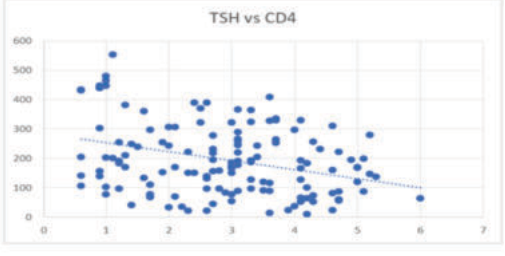



Fig 6: Mean and standard deviation of albumin, total bilirubin, direct bilirubin, AST, ALT,

| | Mean | Standard Deviation |
|---|---|---|
| ALBUMIN | 2.4 | 0.4 |
| TB | 0.7 | 0.3 |
| DB | 0.31 | 0.2 |
| AST | 36 | 17 |
| ALT | 34.1 | 18.2 |
| ALP | 88 | 35 |

Table 7: Mean and standard deviation of albumin, total bilirubin, direct bilirubin, AST,ALT, ALP.




Pearson correlation, r= -0.489, p<0.001

**Fig 7 : Correlation between TSH and CD4 counts among HIV patients**

| | Mean | Standard Deviation |
|---|---|---|
| TSH | 3.68 | 2.74 |
| T4 | 7.78 | 2.27 |
| T3 | 154.9 | 28.93 |

Table 8: Mean and standard deviation of TSH, T3, T4 among HIV patients

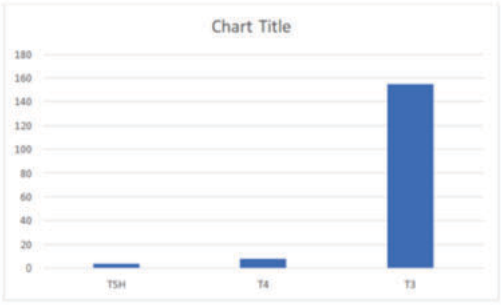



Fig 8: Mean and standard deviation of TSH, T3, T4 among HIV patients

## CONCLUSION

Based on the findings of the study, it can be concluded that thyroid dysfunction and CD4 counts are correlated inversely in people living with HIV. This suggests that prevalence of thyroid dysfunction increases as the disease progresses.

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