Section: General Medicine

Original Research Article

A STUDY ON THYROID DYSFUNCTION IN PEOPLE LIVING WITH HIV/AIDS (PLWHA)

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ABSTRACT

Background: People with HIV appear to have a greater likelihood of disorders of the thyroid. During HIV infections, overt clinical manifestations are less common, whereas subtle changes in thyroid function are found more commonly in several studies. **Objective:** To study the prevalence of thyroid dysfunction in people with HIV/AIDS. (PLWHA) and to compare thyroid dysfunction in pre-ART HIV individuals with individuals on HAART.
Materials and Methods: This Cross Sectional Study was conducted in Department of Medicine, Andhra Medical College, and King George Hospital, Visakhapatnam in collaboration of ART centre and Department of Biochemistry. Duration of the study was July 2021 to June 2022.
Results: Majority of thyroid abnormality was found in the age group of 25 – 35 years. There was a significant inverse correlation between CD 4count and Thyroid abnormalities. Heterosexual route was the common route of transmission. Tuberculosis was the most common opportunistic infection. Thyroid abnormality, especially subclinical hypothyroidism, was common in the HAART group.
Conclusion: Thyroid abnormality, especially subclinical hypothyroidism, was common in the HAART group. Screening of thyroid parameters is warranted in this population in view of the increasing prevalence in the Study Population.
Keywords: Thyroid abnormality, People Living with HIV/AIDS, HAART.

INTRODUCTION

Human Immuno Deficiency Virus was identified from a lymphadenopathy patient in1983 and was proven scientifically in 1984 to be the causal agent of AIDS.[1] India's earliest case of AIDS was recognized in 1986 in Chennai.[2]

HIV infection can lead to multiple organ involvement, including the endocrine system. An endocrine function may be altered in these subjects because of the possible relationship between the immune and endocrine systems, direct involvement of the glands by the HIV itself, opportunistic infections or malignancies.[3,4]

Abnormal thyroid functions in these patients may be caused by the stress of advanced disease or concomitant morbidities. They may manifest as the classic sick euthyroid syndrome, probably due to a hypothalamic- pituitary deficit related to the progress of immunodeficiency and cachexia.[3] Cytokines such as IL-6 and TNF- can acutely decrease TSH and T3 and increase rT3 levels. LoPresti et al. studied thyroid functions in HIV-positive patients to evaluate if they could be used to predict their progression and outcome.

Jain et al. reported abnormal thyroid levels correlated with the CD4 counts and disease severity.[5]

Screening studies have demonstrated an increased prevalence of primary hypothyroidism in HIV-infected patients. Beltran,[4] reported overt hypothyroidism in 2.6%, subclinical hypothyroidism in 6.6%, and an isolated low T4 level in 6.8% of 350 subjects studied. Low free T4 levels (1.3%) and subclinical hypothyroidism (3.5%) correlated with low CD4 counts were reported in a Spanish population.[6]

A proposed explanation for autoimmune illness is an infection trigger for autoimmunity (through molecular mimicry). However, hypothyroidism is

not related to autoimmunity in HIV-infected people. So far, one incidence of Hashimoto's hypothyroidism has been recorded following the start of highly active antiretroviral treatment (HAART).[7]

Subclinical hypothyroidism is more prevalent in the HIV-infected population compared to HIV-negative individuals.[8,9] Quirino reported a similar prevalence of subclinical hypothyroidism in both naive and HAART- treated subjects,

Beltran et al,[12] found that subclinical hypothyroidism was associated with stavudine and lower CD4+ cell count; the cumulative daily dose of both stavudine and lamivudine was significantly related to the presence of hypothyroidism in Grappin's series.[9] Didanosine and ritonavir were associated with a low free T4.

Madge et al,[10] found the prevalence of hypothyroidism to be 2.5% (overt) and 4% (subclinical). Hyperthyroidism (overt and subclinical) l occurred in <1%.of patients.

Nelson's study,[11] revealed a higher-than-expected incidence of overt hypothyroidism in patients receiving HAART, and they recommend universal screening of subjects on therapy.

Given abnormal TFT often encountered in HIV-positive individuals and HIV patients on HAART, it was decided to study thyroid function in HIV-infected patients at Andhra Medical College, King George Hospital Visakhapatnam.

MATERIALS AND METHODS

This Cross Sectional Study was conducted in Department of Medicine, Andhra Medical College, and King George Hospital, Visakhapatnam in collaboration of ART centre and Department of Biochemistry. Duration of the study was July 2021 to June 2022.

Study Population

In the study mentioned above period, 100 patients will be chosen. Randomly they were either pre-ART HIV positive individuals (n=50) or HIV. Patients on HAART (n=50) strictly adhere to inclusion and exclusion Criteria.

Inclusion Criteria

- All HIV-infected patients, both Pre ART and individuals on HAART.
- Patients of more than 18 years

Exclusion Criteria

- Patients less than 18 years of age
- Patients with known thyroid dysfunction
- Patients on drugs known to cause thyroid dysfunction
- Pregnancy
- Severely ill patients
- Patients with renal and hepatic dysfunction
- Pituitary and hypothalamic disorders

Consent

All patients gave written informed consent.

Methodology

Detailed history, symptoms and signs of thyroid dysfunction were noted. A standard proforma pointed out a history of medication and anthropometric measurements like height, weight, and waist circumference. All patients were examined, and routine urine and blood investigations were taken to rule out comorbid conditions. Patients were staged by WHO guidelines and grouped accordingly.

The following investigations were done

- Thyroid profile (Free T4, FreeT 3, and TSH)
- Renal Function Test (Sugar, Urea, Creatinine, and Electrolytes)
- Liver Function Test (S.Bilirubin, SGOT, SGPT, SAP, Total Protein, and Albumin)
- Complete Blood Count (Total Count, Differential Count, ESR, Hemoglobin, PCV, and Platelets)
- Electrocardiogram and Chest X-Ray – PA view
- CD4 Count

Detection of HIV infection

The detection of HIV infection was done by ELISA (Enzyme-Linked Immuno Sorbent Assay). The kit contains antigens for both HIV- 1 and HIV-2. These kits use both natural and recombinant antigens.

CD4 cell count

CD4 cell count was done by flow cytometry. The FACS count method was used, and the laser principle technique was applied.

Thyroid Hormone Assay

The thyroid hormone assay (TSH and FT4) was done by Chemiluminescence Immuno Assay (CLIA) using ADVIA Centaur- equipment.

Statistical Analysis

Statistical analysis was done by using windows SPSS software (version 11.5). The Chi-square test was applied for significance. A "P" value less than 0.05 was considered significant.

RESULTS

A total of 100 seropositive were taken as a study group which included 50 patients on HAART and 50 patients who were PRE-ART.

The following sociodemographic factors and clinical profiles of the patients were analyzed.

The mean age of the study population is 33.80±7.45, the Minimum age is 22 years, and the maximum age is 59 years.

The population under the study shows a normal distribution with respect to age.

For the purpose of study analysis, patients were categorized based on age groups into <25 years,25 -35 years, 36 -45 years,>45 years.

Among them majority(46%) of them were between 25 -35 years age group.

Table 1: Department-Wise distribution of prescriptions and antibiotic utilization pattern

AGE GROUP	HAART	FREQUENCY	PERCENTAGE
< 25 Years	CATEGORY		
	PRE ART	8	53.3
	HAART	7	46.7
	TOTAL	15	100
25 -35 Years	PRE ART	28	60.9
	HAART	18	39.1
	TOTAL	46	100
36 -45 Years	PRE ART	12	37.5
	HAART	20	62.5
	TOTAL	32	100
>45 Years	PRE ART	2	28.6
	HAART	5	71.4
	TOTAL	7	100

Under the age group <25 years, the majority were pre- ART I.e.53.3%, Under the age group 25 -35 years, the majority were pre- ART I.e.60.9%. Under the age group 35 -45 years, the majority were pre-ART, I.e.62.5% Under the age group >45 years, the majority were pre-ART, I.e.71.4%.

Table 2: Gender distribution of the study population

GENDER		FREQUENCY	PERCENTAGE
FEMALE	PRE ART	25	56.8
	HAART	19	43.2
	TOTAL	44	100
MALE	PRE ART	25	44.6
	HAART	31	55.4
	TOTAL	56	100

Pictorial representation of gender distribution among females pre -ART were 25 in members and HAART were 19 members. Among males pre -ART were 25 in members and HAART were 31 members. Among the study of population, unskilled labour constitutes the majority of the population in pre-ART.68%, and HAART 54%.

Least number of individuals (2%) in the pre -ART category were office workers, and there was no office Workers in the HAART category.

- Out of 100 study populations, the heterosexual route was the most prevalent method of HIV transmission.
- Patients were about 97%. Among heterosexual transmission individuals, a nearly equal Percentage of pre-ART and HAART categories were seen.

Table 3: Distribution of oppurtunistic infections in study population

OPPORTUNISTIC INFECTION	FREQUENCY	PERCENTAGE (%)
ORAL CANDIDA	7	7
OTHER CANDIDA	2	2
HERPES	1	1
TUBERCULOSIS	13	13
NO INFECTIONS	77	77
TOTAL	100	100

Most of the study population (77%) has no opportunistic infection. Opportunistic infections were observed in 23% of patients. the commonest opportunistic infection was tuberculosis, followed by oral candidiasis and herpes zoster.

Mean TSH levels among the study population – 3.21 ± 2.00 Mean FT3 levels among the study population – 3.14 ± 0.816 Mean FT4 levels among the study population – 1.1± 0.272.

TSH levels were found to be more abnormal among pre-ART individuals (52.2%), whereas 47.8% of TSH Abnormalities were observed in HAART individuals.

The correlation between TSH levels and people between HAART & Pre ART was found to be statistically insignificant. P value is-0.812

Table 4: Distribution of ft3 levels among pre-art & heart individuals

TYPE OF TREATMENT	FT3 LEVELS	
	NORMAL (n,%)	ABNORMAL (n,%)
PRE ART	45(50%)	05(50%)
HAART	45(50%)	05(50%)
TOTAL	90(100%)	10 (100%)

FT3 levels were found to be equally abnormal among pre-ART individuals and HAART individuals which Were about 50%.

Table 5: Distribution of ft4 levels among pre-ART & ART individuals

TYPE OF TREATMENT	FT4 LEVELS	
	NORMAL (n,%)	ABNORMAL (n,%)
PRE ART	47(50%)	03(50%)
HAART	47(50%)	03(50%)
TOTAL	94(100%)	06(100%)

FT4 levels were found to be equally abnormal among pre-ART individuals and HAART individuals which Were about 50%.

Most of the patients in the study were euthyroid i.e.77 members. Fewer members in the pre-ART category had subclinical hypothyroidism, i.e., 12 members, and the majority were euthyroid, i.e., 38 members. Significantly fewer members in the HAART category had subclinical hypothyroidism, i.e., 10 members. And the majority were euthyroid, i.e., 39 members..

Table 6: Total thyroid profile in pre-art and art individuals

THYROID PROFILE	NORMAL RANGE	PRE-ART (Mean ±SD)	HAART (Mean±SD)
TSH	0.34 -4.25	3.232 ±1.8	3.2 ±2.18
FT 3	2.4 -4.2	3.13±0.837	3.15±0.804
FT 4	0.80 -1.70	1.11±0.27	1.15±0.27

Table 7: Who staging of HIV individuals on HAART with thyroid dysfunction

WHO STAGE	TSH		TOTAL	FT3		TOTAL	FT4		TOTAL
	NORMAL	ABNORMAL		NORMAL	ABNORMAL		NORMAL	ABNORMAL	
I	23	2	25	23	2	25	24	1	25
	-92%	-8%	-100%	-92%	-8%	-100%	-96%	-4%	-100%
II	28	9	37	36	1	37	36	1	37
	-75.70%	-24.30%	-100%	()97.3%	-2.70%	-100%	-97.30%	-2.70%	-100%
III	21	8	29	22	7	29	26	3	29
	-72.40%	-27.60%	-100%	-75.90%	-24.10%	-100%	-89.70%	-10.30%	-100%
IV	5	4	9	9	0	9	8	1	9
	-55.60%	-44.40%	-100%	-100%		-100%	-88.90%	-11.10%	-100%

The majority (9) members of the TSH abnormalities are seen in individuals with WHO stage -II. least (2) Members were seen in WHO stage -I. The majority (7) members of the FT3 abnormalities are seen in individuals with WHO stage -III. No Individuals were found with FT3 abnormalities in WHO stage -IV. The majority (3) members of the FT4 abnormalities are seen in individuals with WHO stage -III.

Among the HAART individuals, the majority (42%) of the patients were having CD4 count in the range of 200 -350. Among the pre-ART individuals, the majority (48%) of the patients had a CD4 count in the range of 200 -350.

The thyroid dysfunction compared to the CD4 category majority of members was euthyroid. very few members were hypothyroid. The correlation between CD4 count and thyroid dysfunction was found to be statistically significant. P - value 0.010.

DISCUSSIONS

The present study was undertaken based on the above observation in our hospital, Andhra Medical College, and King George Hospital, Visakhapatnam. Our study population consisted of 100 patients chosen randomly attending the ART center adhering to inclusion and exclusion criteria (both pre-ART = 50 and patients on HAAR T=50). Patients were categorized based on age groups into <25 years,25 - 35 years, 36- 45 years, and>45 years.

Under the age group <25 years, majority of them were pre ART I.e.53.3% Under the age group 25 - 35 years, majority of them were pre ART I.e.60.9% Under the age group 35 - 45 years, majority of them were ART I.e.62.5% Under the age group >45 years, majority of them were ART I.e.71.4%

In our study, HIV infection was more common in the age group of 25 - 35 years. Grappin et al. showed thyroid dysfunction was more common in the age group between 38.14±12.5.[12]

Gender Distribution In our study, the overall male population was more than Their female counterpart, with a sex ratio of 1.27 in favor of males. The prevalence of thyroid dysfunction was found to be more in males than females. There was no statistical correlation between gender and thyroid dysfunction.

The gender distribution demonstrated 56 (56%) and 44females (44%) in our Study population.

In our study group, unskilled laborers and housewives constituted The majority of the population, 68% and 26%, respectively,4% were Skilled office workers, and 2% were. Statistically, the nature of the work was not related. Significantly to thyroid dysfunction.

Heterosexual contact (97%) was the commonest route of transmission in our study, which correlates well with other studies. NACO reported a more than

80% rate of heterosexual transmission. (87.1%) and Rangna (95%).[13,14]

National AIDS Control Organization (NACO) data reveal that tuberculosis is the commonest infection in AIDS patients, followed by candidiasis, cryptosporidiosis, and others.[15]

In our study, Opportunistic infections were observed in 23% of patients. the commonest opportunistic infection was tuberculosis (13%), followed by oral candidiasis (7%), followed by other candida(2%), and herpes zoster (1%).

Quirino et al. reported a similar prevalence of sub-clinical. Hypothyroidism in both pre-ART and HAART individuals.[16]

In our study, TSH was found to be abnormal in 23 patients among 100 study group population, which constitutes about 23%.

Among 23 patients11 were patients on HAART, and 12 were pre-ART individuals.

All 23 patients had elevated TSH values .

Mean TSH levels among the study population are 3.21 ± 2.00 Mean TSH levels among pre-ART individuals are 3.232 ± 1.8 Mean TSH levels among ART individuals is 3.2 ± 2.18

The TSH abnormality was found to be statistically significant, with a p-value is 0.010.

Lo Presti et al. correlated low T3 levels with the severity of critical illness and mortality among hospitalized patients with HIV (AIDS),[17]

Chiarelli et al. also found that FT3 levels were significantly reduced in HIV children. Compared with controls, TSH and TBG were increased and suggested Thyroid dysfunction.[18]

In our study, FT3 levels were found to be decreased in 10 patients (10%) among 100 patients; it was found to be equally abnormal among pre-ART individuals And ART individuals, which were about 50%.

Chiarelli et al. also found that FT4 levels were significantly reduced in HIV children. Compared With controls, TSH and TBG were increased, suggesting thyroid dysfunction.[18]

In our study, FT4 levels were found to be decreased in 6 patients (6%) among 100 Patients. It was found to be equally abnormal among pre-ART individuals and HAART individuals, which was about 50%.

Meena et al. found abnormal thyroid function in 40.66% (30% sub-clinical Hypothyroidism, 10.66% primary hypothyroidism). This could be due to the more patients with lower CD4 counts were in their study. There was a highly Significant positive correlation between CD4 count and TSH, which means that The probability of thyroid dysfunction increases as CD4 decreases or as the disease progresses.[19]

In another Indian study, there was a direct correlation between CD4 count and free T3 (FT3) and FT4 values (r=0.357 with P < 0.05; r=0.650 with P < 0.05, respectively). An inverse correlation of CD4 counts with serum TSH levels was also noted (r = −0.470 with P < 0.0 50).[10]

In our study, CD 4 count was < 200 in 24 %, 200 - 350in 42% under the ART group, Whereas in the pre-ART group, 48 % had a CD 4 count of 200 - 350, and 40 % had CD 4 Count> 350. Overt hypothyroidism and subclinical hypothyroidism were found Mostly in patients with h CD 4, Count between 200 - 350.

WHO staging

Of the 100 study population, 50 patients were on HAART, and 50 patients were In the pre-ART group.

- 25 patients (25%) belong to WHO stage I
- 37patients (37%) belong to WHO stage II
- 29 patients (29%) belong to WHO stage III
- 9 patients (9%) belong to WHO stage IV

TSH ABNORMALITY

The majority (9) members of the TSH abnormalities are seen in individuals with WHO Stage- II. Least (2) members were seen in WHO stage - I.

FT3 ABNORMALITY

The majority (7) members of the FT3 abnormalities are seen in individuals with WHO Stage- III. No individuals were found with FT3 abnormalities in WHO stage - IV.

FT4 ABNORMALITY

The majority (3) members of the FT4 abnormalities are seen in individuals with WHO Stage- III.

CONCLUSION

Thyroid abnormality, especially subclinical hypothyroidism, is more prevalent in HIV-positive individuals. There is no significant Thyroid dysfunction was observed between patients on HAART and PART individual Thyroid abnormality was found more in males in ourn study group. Majority of thyroid abnormality was found in the age group of 25 –35 years. There was a significant inverse correlation between CD 4count and Thyroid abnormalities. The decline in CD 4 count was associated with an Increased incidence of thyroid abnormalities.Thyroid abnormality was found more in the advanced stage of the disease who were in WHO stages III and IV? Heterosexual route was the common route of transmission. Tuberculosis was the most common opportunistic infection. Thyroid abnormality, especially subclinical hypothyroidism, was common in the HAART group. Screening of thyroid parameters is warranted in this population in view of the increasing prevalence in the Study Population.

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