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RESEARCH ARTICLE

THYROID DYSFUNCTION IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED PATIENTS AND THEIR CORRELATION WITH CD4 COUNT - A NON-RANDOMIZED, CROSS-SECTIONAL, SINGLE-CENTER STUDY

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Abstract

Background: Thyroid dysfunction has been reported in human immunodeficiency virus (HIV)-infected individuals.

Objective: Objectives of this non-randomized, cross-sectional, single-center study was to study thyroid function in HIV positive patients at various stages of disease and to correlate the results obtained with CD4+ counts.

Materials and Methods: This single-center study was carried out at Al-Ameen Medical College Hospital and Government District Hospital Bijapur, Karnataka, India from November 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 &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 Chemiluminescencelmmuno Assay (CLIA) using ADVIA Centaur-equipment.The CD4+ T-cell count was completed using FACS Calibur, Beckton Dickinson, USA27.

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. Among 50 cases having CD4+ count <200/pl there were 38(76%) males and 12(24%) females. Among 50 cases having CD4 count >200/pl there were 28(56%) males and 22(44%) females.The CD4+ count ranged from 5 to 773/pl with a mean of 223±190.9/pl. This study observed that abnormalities of thyroid function are more common among patients having CD4+ count <200/pl. Clinically evident hyperthyroidism was not observed in any case.Direct correlation was observed between CD4 count and FT3 and FT4 values

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and Inverse correlation was observed when CD4+ counts were compared with serum TSH levels.
Conclusion: All individuals with CD4 count less than 200 should be screened for hypothyroidism.An inverse correlation was seen between TSH and CD4 count indicating trend for hypothyroidism as HIV disease progress.

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Introduction:-

Several endocrinopathies have been reported to be associated with HIV infection when the CD4 count is low.[1] Abnormal thyroid function tests are commoner in HIV patients than the general population.[2] These include Sick Euthyroid state, Subclinical hypothyroidism, Hypothyroidism, Grave's disease, and Thyroiditis. Subclinical hypothyroidism is seen especially in those on Highly Active Anti-Retroviral Therapy (HAART).[3]

The two parameters giving a reliable index of disease activity in monitoring patients with HIV infection are CD4+ T cell counts and HIV RNA level assay.[4] These tests can be performed at the disease onset and in regular periods thereafter.[5] The CDC guidelines recommend that ART is started when the CD4 count is <500/µl. Drugs can be changed if the patient does not improve CD4 counts by at least 25% after starting therapy.[6]

Post-HIV infection, there is a steady decline in CD4 count.[7] The count decreases by approximately 50 per year. Patient may be clinically silent even for a decade. But it is not microbiological or immunological latency. There is a continual destruction of immune system as well as progressive increase in viral load as the years advance even though patient is asymptomatic.[8]

There is an enhanced lymphocyte turnover rate and destruction in HIV.[9]The depletion of CD4+ cells occur by various mechanism like Gp120 self-fusion with CD4 intracellularly, interference with RNA processing, formation of syncytia, viral budding causing loss plasma of membrane intergrity and accumulation of unintergrated pro viral DNA.[10,11]

Thus far, the relationship between thyroid dysfunction and HIV infection with respect to CD4 count is obscure. In view of the above, the objective of this study was to study thyroid function in HIV positive patients at various stages of disease and to correlate the results obtained with $CD4^+$ counts.

Method:-

Patients visiting the Al-Ameen Medical College Hospital and Government District Hospital Bijapur, Karnataka, India between November 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 &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 a) with past history s/o thyroid illness, clinically evident thyroid enlargement, or signs of thyroid disease, b) on drugs known to interfere with thyroid hormone metabolism for e.g. rifampicin, steroids, ketoconazole, anti-epileptics etc. c) with abnormal liver function tests i.e. SGOT or SGPT levels greater than three times the upper normal limit, d) with abnormal renal function tests i.e. serum creatinine level greater than 1.6 mg°/0 and e) 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: 50 HIV + patients having AIDS.

A HIV + patient is said to have AIDS if the patient fulfils any of the following criteria:
1) A CD4+ cell count of < 200/L, regardless of the presence of opportunistic infections or neoplasms. Or

2) A CD4+cell count of >200/L with at least one of the following:
a. Pulmonary or extra pulmonary tuberculosis.
b. Candidiasis of lower airways and / or esophagus.
c. Cryptococcosis, extra pulmonary.
d. Chronic intestinal cryptosporidiosis (> 1months duration)
e. Invasive cervical cancer vi. Kaposi's sarcoma.
f. Primary brain lymphoma or Burkitt's lymphoma.
g. HIV related encephalopathy.
h. Cytomegalovirus retinitis.
i. Pneumocystis jiroveci pneumonia.
j. Herpes simplex: Chronic ulcer (s) (>1 month's duration); or bronchitis, pneumonia, or esophagitis.
k. Progressive multifocal leukoencephalopathy.
l. Pneumonia, recurrent.
m. Salmonella septicemia, recurrent.
n. Wasting Syndrome due to HIV.

Group B:
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 8am 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 patients LFT, 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.[12]

CD4+ count:
The CD4+ T-cell count is the laboratory test generally accepted as the best indicator of the immediate state of immunologic competence in a patient with HIV infection. This measurement was determined by Flow Cytometry. A single test required one convenient ready-to-use reagent [EDTA] tube pair. One tube determined the absolute number of helper T-lymphocytes and other tube determined absolute number of cytotoxic T-lymphocytes. When whole blood was added to reagent tubes, fluorochrome-labeled antibody in the reagents bound specifically to lymphocytes surface antigens. After a fixative solution was added to the reagent tubes the sample was run on instrument FACS Calibur, Beckton Dickinson, USA27. Within FACS, the cells came in contact with laser light that caused the fluorochrome labeled cells to fluoresce, whose information was necessary for the instrument to count the cells.[13]

Statistical methods
The data was collected on an excel sheet and descriptive statistical analysis was performed. Analytical method of statistical analysis was undertaken through ANOVA, T-test and 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. Below **Table 1** summarizes the Age group and gender characteristics of study population.

Table 1:- Age group and gendercharacteristics 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

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 2:- Tabulation showing age and gender distribution in 100 HIV positive patients studied according to CD4+ count.

Age groups in years	CD4+ count					
	Group A (<200/pl)			Group B (>200/pl)		
	Male	Female	Total	Male	Female	Total
15-24	1(2%)	1(2%)	2(4%)	0	4(8%)	4(8%)
25-44	27(54%)	9(18%)	36(72%)	21(42%)	16(32%)	37(74%)
>44	10(20%)	2(4%)	12(24%)	7(14%)	2(4%)	9(18%)
Total	38(76%)	12(24%)	50	28(56%)	22(44%)	50

In our study, 100 cases studied were divided in to two groups according to CD4+ count as, >200/pl and < 200/pl. Among 50 cases having CD4+ count <200/pl there were 38(76%) males and 12(24%) females. Around 36(72%) patients belonged to the age group of 25-44 years, only 2(4%) patients were <25 years of age and 2 (4%) were >44 years of age.

Among 50 cases having CD4 count >200/pl there were 28(56%) males and 22(44%) females. Around 37(74%) patients belonged to the age group of 25-44 years, 4(8%) patients were <25 years of age and 9(18%) were >44 years of age.

No statistically significant difference was observed (P=0.570) in age and gender distribution in Group A (CD4+ count <200/pl). In Group B (CD4+ count>200/pl), the difference observed in age and gender distribution was statistically significant (P=0.030).

Table 3:- Tabulation showing distribution of CD4+ according to age group.

CD4+ count (in pl)	Age groups in years				
	17-24 n(%)	25-34 n(%)	35-44 n(%)	>44 n(%)	Total
0-100	2(2%)	14(14%)	17(17%)	6(6%)	39(39%)
101-200	0	3(3%)	3(3%)	5(5%)	11(11%)
201-300	1(1%)	10(10%)	8(8%)	3(3%)	22(22%)
301-400	0	5(5%)	4(4%)	0	9(9%)
401-500	2(2%)	2(2%)	0	3(3%)	7(7%)
501-600	0	5(5%)	0	1(1%)	6(6%)
601-700	1(1%)	2(2%)	0	2(2%)	5(5%)
701-800	0	1(1%)	0	0	1(1%)
Total	6(6%)	42(42%)	32(32%)	20(20%)	100

In our study, the CD4+ count was studied in the 100 HIV+ cases. The CD4+ count ranged from 5 to 773/pl with a mean of 223±190.9/pl. When CD4+ count was correlated with the age of patients, the difference observed was not found to be statistically significant (P=0.1443 by ANOVA test).

Table 4:- Tabulation showing Free Triiodothyronine (FT3) in Group A (<200/pl) and Group B (>200/pl).

Observation	Frequency (%) of Group A patients with (<200/pl)	Frequency (%) of Group B patients (>200/pl)
Normal FT3 (1.8-4.2 Pico gram/ml)	34 (68%)	48 (96%)
Elevated T3 (>4.2 Pico gram/ml)	0 (0%)	0 (0%)
Decreased FT3 (< 1.8 Pico gram/ml)	16 (32%)	2 (4%)
Total	50 (100%)	50 (100%)

In our study, 34 patients from Group A and 48 patients from Group B had normal FT3 values. 16 patients from Group A and 2 patients from Group B had FT3 values below normal. The difference observed in FT3 values in the two groups was statistically significant (P=0.001).

Table 5:- Tabulation showing Free Thyroxine (FT4) in Group A (<200/pl) and Group B (>200/pl).

Observation	Frequency (%) of Group A patients with (<200/pl)	Frequency (%) of Group B patients with (>200/pl)
Normal FT4 (0.8-1.9 ng/ml)	39 (78%)	48 (96%)
Elevated FT4 (>1.9 ng/ml)	0 (0%)	1 (2%)
Decreased FT4 (<0.8 ng/ml)	11 (22%)	1 (2%)
Total	50 (100%)	50 (100%)

In 39 patients from Group A and 48 patients from Group B had normal FT4 values. 11 patients from Group A and 1 patient from Group B had FT4 values below normal and 1 patient from Group B had elevated FT4 value. The difference observed in FT4 values in the two groups was statistically significant (P=0.001).

Table 6:- Tabulation showing serum thyrotropin (S.TSH) in Group A (<200/pl) and Group B (>200/pl).

Observation	Frequency (%) of Group A patients with (<200/pl)	Frequency (%) of Group B patients with (>200/pl)
Normal TSH (0.4-4.0 µIU/ml)	27 (54%)	47 (94%)
Elevated TSH (>4.0 µIU/ml)	23 (46%)	2 (4%)
Decreased TSH (<0.4 µIU/ml)	0 (0%)	1 (2%)
Total	50 (100%)	50 (100%)

In 27 patients from Group A and 47 patients from Group B had normal S.TSH values. 23 patients from Group A and 2 patients from Group B had elevated S.TSH values. 1 patient in Group B had S.TSH value below normal range. The difference observed in S.TSH values in the two groups was statistically significant (P=0.001).

Table 7:- Tabulation showing Thyroid function according to CD4 count (n=100).

CD4+ count (no. of pt.) (n=100)	FT3 (p-0.0345, significant)			FT4 (p-0.0215, significant)			S.TSH (p-0.0314, significant)		
	T	4	Normal	T	4	Normal	T	4.	Normal
>500 (12)	0	0	12	1	0	11	0	0	12
500-200 (38)	0	2	36	0	1	37	2	1	35
<200 (50)	0	16	34	0	11	39	23	0	27
Total (100)	0	18	82	1	12	87	25	1	74

Evaluation of Thyroid functions in 100 HIV + cases were compared with CD4+ counts. Out of 12 patients with CD4+ count >500/p1 only 1(8.33%) patient had increased FT4 value.Out of 38 patients with CD4+ count between 200-500/pl, 2(5.24%) patients had decreased FT3 value, 1(2.62%) patient had decreased FT4 value, 2(2.62%) patients had

increased S.TSH and 1(5.24%) patient had decreased S.TSH.Out of 50 patients who had CD4+ count <200/pl, 16(32%) patients had decreased FT3 level, 11(22%) patients had decreased FT4 and 23(46%) had increased S.TSH. It is observed that abnormalities of thyroid function are more common among patients having CD4+ count <200. The difference observed was statistically significant (P<0.05 by ANOVA test).

Table 8:- Tabulation showing pattern of Thyroid abnormalities according to CD4+ count.

Type of Thyroid abnormalities	CD4+ count		Total (n=100)	P value
	<200 (n-50) (Group A)	>200 (n-50) (Group B)		
Euthyroidism	13(13%)	44(44%)	57(57%)	P-0.0001, significant
Subclinical Hypothyroidism	17(17%)	2(2%)	19(19%)	P-0.0001, significant
Hypothyroidism	6(6%)	0	6(6%)	NS
Subclinical hyperthyroidism	0	1(1%)	1(1%)	NS
Hyperthyroidism	0	0	0	NS
Isolated low FT3	10(10%)	2(2%)	12(12%)	NS
Isolated low FT4	4(4%)	1(1%)	5(5%)	NS
Total	50(50%)	50(50%)	100	NS
Isolated low FT3/FT4	14(14%)	3(3%)	17(17%)	P-0.0001, significant

Among the 100 cases studied 57 patients had normal Thyroid function tests. Of the 43 patients with abnormal Thyroid function tests subclinical hypothyroidism was noticed in 19 patients, 6 patients were found to have hypothyroidism and 1 patient had subclinical hypothyroidism. Clinically evident hyperthyroidism was not observed in any case. Isolated low FT3 was observed in 12 patients and isolated FT4 was observed in 5 patients.When Thyroid abnormalities were compared in the group A and B, 13 patients in group A were found to be Euthyroid as compared to 44 patients in group B. the difference observed was statistically significant (P<0.05).17 patients in group A and 2 patients in group B had subclinical hypothyroidism. The difference observed in the two groups was statistically significant (P<0.05).One patient in group B had subclinicalhyperthyroidism. Isolated FT3/FT4 was observed in 14 patients in group A and 3 patients in group B. The difference was observed significant (P<0.05).

Table 9:- Tabulation showing correlation between CD4+ counts and Thyroid function tests in study group (n=100).

Parameters	R value	P value	Significance
CD4 vs. FT3	0.4261	<0.05	significant
CD4 vs. FT4	0.2266	<0.05	significant
CD4 Vs.S.TSH	-0.4683	<0.05	significant

When the results were statistically analyzed for the 100 patients enrolled in our study using Pearson's correlation coefficient, direct correlation was observed between CD4 count and FT3 and FT4 values (r=0.4261 with P<0.05 and r=0.2266 with P<0.05 respectively). Inverse correlation was observed when CD4+ counts were compared with serum TSH levels (r=0.4683 with p<0.05).

Discussion:-

In our study the results were statistically analyzed for the 100 HIV+ patients enrolled using Pearson's Correlation coefficient. We recorded a direct correction between CD4+ count and FT3 and FT4 value. Also, we recorded an inverse correlation of CD4+ counts with serum TSH levels. Similar results were obtained by other researchers.

According to Hirschfeld et al[14] there was a positive correlation between FT4 level and CD4+ cell counts. Jain et al[15] studied 50 patients infected with HIV. They found that there was a direct correlation between CD4+ count and FT3 and FT4 values. There was an inverse correlation of CD4+ counts with serum TSH levels.

Thyroid dysfunction was more common in the HAART group. Clinical hypothyroidism was the most common thyroid dysfunction in HIV-infected patients, which is consistent with the findings of Beltran et al.[16] However, Madeddu et al[17] reported that subclinical hypothyroidism was the most frequent thyroid dysfunction in HIV patients treated with HAART.

The differences in the incidence of thyroid dysfunction in HIV-infected patients may be related to differences in disease course, criteria of hypothyroidism, subclinical hypothyroidism, and so forth.

Beltran et al[16] found that stavudine and low CD4 cell counts were associated with hypothyroidism. FT3 and FT4 levels have been reported to be related to the state of HIV infection and are potential biomarkers of HIV progression. Beltran et al[16] reported that compared with HIV-infected patients with normal thyroid function, patients with hypothyroidism were older, had HIV infection for a longer duration, had lower CD4 cell count.

Collazos et al[18]found a correlation between FT4 levels and CD4 cell counts in patient treated with HAART. Majority of the patients had CD4 count >200 cells/mm^3.This study reported no significant correlation between thyroid dysfunction and patients on HAART.

Meena et al[19] studied 150 patients infected with HIV divided into three groups according to CD4+ count. They observed subclinical hypothyroidism in 45(30%) cases out of 150 HIV infected patients. In group of 50 patients with CD4+ count <200/pl i.e. AIDS 15 (30%) patients had subclinical hypothyroidism and among 100 patients with CD4+ count >200/pl i.e. non AIDS 40 (40%) patients were detected as subclinical hypothyroid.

Vigano et al[20] in their study on a cohort of 52 vertically HIV-1 infected patients. Among the patients with low FT4 value, regression analysis showed a positive correlation between FT4 value and CD4+ cell percentage.

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, HAART, et. 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:-

The present study shows that the biochemical abnormality of thyroid function is quite common among HIV patients. An inverse correlation was seen between TSH and CD4+ count indicating trend for hypothyroidism as HIV disease progress. However, it will require further longitudinal study with larger number of patients of different groups of CD4+ counts and with more thyroid function parameters like free T4, free T3, TBG to confirm the need of regular thyroid function study in the management of HIV patients.

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Conflict of interest:
None declared

Ethical approval:
The study was approved by the Institutional Ethics Committee

References:-

1. Meek M, Kabengele C, Kamanga B. Autoimmune polyglandular syndrome type 2 in an HIV-positive man managed at the University Teaching Hospitals Lusaka, Zambia: a case report. The Pan African Medical Journal. 2022;41.
2. Hu H, Liang L, Ge Q, Jiang X, Fu Z, Liu C, Long J. Correlation between Peripheral T Cell Subsets and the Activity of Thyroid-Associated Ophthalmopathy. International Journal of Endocrinology. 2022 Mar 8;2022.
3. Kalogeris N, Herolidi E, Moustaki M, Dermetzoglou A, Loi V, Vakali E, Lioni A, Sakka V, Mangafas N, Chini M, Vryonidou A. Thyroid Dysfunction in patients with HIV infection. InEndocrine Abstracts 2020 Aug 21 (Vol. 70). Bioscientifica.

4. Mulyani S, Pramudianti MD, Ariningrum D. The Association of CD4, CD8, and CD4/CD8 Ratio with Thyroid Dysfunction in HIV/AIDS. Indonesian Journal Of Clinical Pathology And Medical Laboratory. 2021 Sep 21;27(3):326-32.
5. Gupta PK, Taneja RS, Chauhan L, Vijayshri SL, Tyagi S, Meena RC, Gupta A, Khatak M. Prevalence and Predictors of Thyroid Dysfunction in Human Immunodeficiency Virus (HIV)-Infected Individuals. Journal, Indian Academy of Clinical Medicine. 2020 Jul;21(3-4):107.
6. Ekouévi DK, Avettand-Fènoël V, Tchounga BK, Coffie PA, Sawadogo A, Minta D, Minga A, Eholie SP, Plantier JC, Damond F, Dabis F. Plasma HIV-2 RNA according to CD4 count strata among HIV-2-infected adults in the IeDEA West Africa Collaboration. PLoS One. 2015 Jun 25;10(6):e0129886.
7. Akbar RZ, Hatta SF, Noh RM, Shah FZ, Rahman TH, Ghani RA, Ismail Z. Endocrinopathies in HIV Infected Patients. Journal of Clinical and Health Sciences. 2020 Nov 1;5(2):39-45.
8. Lane KL, Moin T. Autoimmune diabetes in a patient with human immunodeficiency virus on anti-retroviral therapy with literature review. AACE Clinical Case Reports. 2020 Sep 1;6(5):e201-6.
9. Sharan R, Bucşan AN, Ganatra S, Paiardini M, Mohan M, Mehra S, Khader SA, Kaushal D. Chronic immune activation in TB/HIV co-infection. Trends in microbiology. 2020 Aug 1;28(8):619-32.
10. Peng X, Ouyang J, Isnard S, Lin J, Fombuena B, Zhu B, Routy JP. Sharing CD4+ T cell loss: when COVID-19 and HIV collide on immune system. Frontiers in immunology. 2020 Dec 15;11:3307.
11. Grossman Z, Meier-Schellersheim M, Sousa AE, Victorino RM, Paul WE. CD4+ T-cell depletion in HIV infection: are we closer to understanding the cause?. Nature medicine. 2022 Apr 1;8(4):319-23.
12. 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 Feb 1;22(2):262-70
13. Hunt PW, Martin JN, Sinclair E, Bredt B, Hagos E, Lampiris H, Deeks SG. T cell activation is associated with lower CD4+ T cell gains in human immunodeficiency virus-infected patients with sustained viral suppression during antiretroviral therapy. The Journal of infectious diseases. 2020 May 15;187(10):1534-43.
14. Hirschfeld S, Laue L, Cutler Jr GB, Pizzo PA. Thyroid abnormalities in children infected with human immunodeficiency virus. The Journal of pediatrics. 2020 Jan 1;128(1):70-4.
15. Jain G, Devpura G, Gupta BS. Abnormalities in the thyroid function tests as surrogate marker of advancing HIV infection in infected adults. The Journal of the Association of Physicians of India. 2020 Jul 1;57:508-10.
16. Beltran S, Lescure FX, Desailloud R, Douadi Y, Smail A, El Esper I, Arlot S, Schmit JL, Thyroid and VIH (THYVI) Group. Increased prevalence of hypothyroidism among human immunodeficiency virus—infected patients: A need for screening. Clinical Infectious Diseases. 2020 Aug 15;37(4):579-83.
17. 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. 2020 Apr;64(4):375-83.
18. Collazos J, Ibarra S, Mayo J. Thyroid hormones in HIV-infected patients in the highly active antiretroviral therapy era: evidence of an interrelation between the thyroid axis and the immune system. Aids. 2020 Mar 28;17(5):763-5.
19. Meena LP, Rai M, Singh SK, Chakravarty J, Singh A, Goel R, Pathak A, Sundar S. Endocrine changes in male HIV patients. JAPI. 2020Jun;59:1-3.
20. 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. 2020 Mar 1;23(3):235-9.