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General Medicine

A STUDY OF PREVALENCE AND PATTERNS OF THYROID DYSFUNCTION IN HIV INFECTED PATIENTS FROM RURAL BACKGROUND OF EASTERN INDIA .

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ABSTRACT The national prevalence of HIV (Human Immunodeficiency Virus) infection among adults in India is estimated to be 0.22% in the year 2017 . Amongst all endocrine abnormalities , abnormal thyroid function tests are common among HIV infected patients . This study is an attempt to know the magnitude of thyroid dysfunction in HIV infected patient . This observational , cross sectional study was carried out on 153 adult patients attending ART centre of our institution . The gross prevalence of thyroid dysfunction in HIV infected patients and patterns of different thyroid abnormalities were assessed .The serum T3 , Free T4 and TSH were correlated with CD4 count and duration of HAART (highly active anti retroviral therapy) . The prevalence of thyroid dysfunction in HIV infected patient is found to be 30.06% . The most common thyroid disorder , subclinical hypothyroidism was found in 20.26% of the HIV infected patients . Mean CD4 cell count is positively correlated with mean serum T3 and serum free T4 and negatively correlated with mean TSH without any statistical significance in all study population . The correlation of duration of HAART with serum T3 is significantly negative and with serum free T4 , TSH is nonsignificantly negative . So, definitely there is more prevalence of thyroid dysfunction in HIV infected patients than general population . Although there is normal serum free T4 level in subclinical hypothyroid patients , the serum free T4 level decreases within the normal laboratory reference range with severity of HIV infection . The thyroid abnormalities progress further in HIV infected patients who are on HAART . We conclude that more attention to thyroid dysfunction in HIV infected patient should be paid so that timely treatment is done .

KEYWORDS : HIV infection , Thyroid Dysfunction , HAART

INTRODUCTION

There are 2.14 million people living with HIV (Human Immuno deficiency Virus) infection in India, third highest country in the world with people living with HIV / AIDS (PLHIV).[1]The national prevalence of HIV infection among adults in India is estimated to be 0.22% in the year 2017[1]. HIV infection can affect any organ systems directly or indirectly. Prolonged survival in people living with HIV infection after use of highly active anti retroviral therapy (HAART) have increased the chance of detection of several endocrine abnormalities . Abnormalities of endocrine function of the pituitary , thyroid , adrenals , gonads and pancreas are common in patients infected with HIV and becoming the main conditions influencing the long term quality of life in HIV infected patients [2,3]. Abnormal thyroid function tests are common among HIV infected patients [2,4,5] . 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 [5,6] . Undiagnosed thyroid dysfunction , even subclinical hypothyroidism is associated with significant morbidity and poor quality of life [7,8] . Several investigators have used CD4 counts as a marker for assessing the severity of HIV infection in an attempt to identify any correlation with thyroid disease in the HIV-infected patients [2,9,10] . However , other researchers have suggested that the morbidity of overt thyroid dysfunction in patients infected with HIV is similar to that in the general population [2,3,5,11]. Therefore this study is an attempt to know the prevalence and patterns of different thyroid dysfunction and to know the correlation of the CD4 counts and duration of HAART in the HIV infected patients with their serum TSH , T3 , free T4 levels as data in this regard is contradictory , insufficient and inconclusive from Eastern India .

MATERIALS AND METHODS

This observational , cross sectional study was carried out on adult patients attending ART centre of our institution from February 2018 to July 2019 for a total period of 18 months . Our institution is tertiary referral centre in Eastern India for patients of neighbouring seven districts and part of neighbouring state . The Sample size calculated for this study was found to be 144.765 (approximately 145) and considering 10% non-response , the sample size came to 159.24 (approximately 160) . Data were collected from 160 subjects but data from 7 subjects had to be discarded due to incompleteness of reports . So , 153 HIV patients who qualified as per NACO guidelines for diagnosis of HIV infections were enrolled as study subjects by purposive sampling on the basis of inclusion and exclusion criteria . Exclusion criteria for the study were patients with inter-current illnesses (pneumonia , influenza or Herpes simplex infections) , pre existing thyroid disorder , diabetes mellitus , coronary artery disease , chronic liver disease , chronic kidney disease and patient taking drugs like phenytoin , carbamazepine , salicylate , NSAIDs . All participants were provided with written informed consent and the study protocol was approved by the Ethical Committee of the institution. By using structured proforma we recorded clinical symptoms and signs. The patients were asked to attend clinics in next morning in empty stomach and blood sample was taken for CD4 count , thyroid profile , complete blood count , liver and kidney function tests , after taking adequate precaution as per NACO and local hospital guidelines . CD4 Cell count estimation was done by " Partec Flow Cytometer " and " CD4 easy Count Kit " manufactured by Sysmex Partec , Germany . Estimation of thyroid hormone levels was done by means of enzymatic Chemiluminescence 3rd generation T3, free T4 , TSH assays using Cobase 411 (Roche, Switzerland) automated Immuno-assay analyzer system which is calibrated according to " The WHO Reference Standard 80/558 ". The reference range of T3 , free T4 and TSH in our laboratory is 80–220 ng/dl , 0.6–2.2 ng/dl and 0.5–5 mIU/L respectively .

In this study subclinical hypothyroidism was defined as TSH between 4.1 and 10 mIU/ml with normal free T4 concentration , overt hypothyroidism as TSH >10 mIU/L with low free T4 levels , subclinical hyperthyroidism as TSH <0.34 mIU/ml with normal free T4 and/or T3 levels , overt hyperthyroidism as TSH <0.34 mIU/ml with elevated free T4 and/or T3 levels and sick euthyroid syndrome as low T3 , low free T4 , normal TSH levels [5,12] .

All data were analysed by standard statistical methods using SPSS software , 21 version . The comparison of two variables by Karl pearson's coeficient of correlation in linear regression was done. The p value < 0.05 was considered as statistically significant for all tests.

TABLES

Table 1 . Age distribution in HIV patients of present study .

Age group (years)	Number of patients	Percentage (%)
10 – 19	20	13.07
20 – 29	39	25.49

30 – 39	53	34.64
40 –49	33	21.57
50 –59	8	5.23
Total	153	100

Table 2 Sex distribution in HIV patients of present study .

Group	M	F	Sex ratio M:F	Comparison of sex ratio amongst different groups
A (n = 41)	19	22	0.86 : 1	A: B = > 0.05
B (n= 90)	44	46	0.96 : 1	B : C = < 0.05
C (n=22)	17	05	3.4 : 1	C : A = < 0.05
Total (n = 153)	80	73	1.09 :1	

A = (CD4=>500/cumm) B = (CD4= 200-500/cumm)
C = (CD4= <200/cumm) M = Male , F = Female

Table 3 Pattern of various thyroid function abnormalities in HIV patients of present study .

Type of thyroid abnormality	Group A n = 41 (%)	Group B n = 90 (%)	Group C n = 22 (%)	Total n = 153
Subclinical hypothyroidism	7(17.07%)	21(23.33%)	3(13.64%)	31(20.26%)
Overt hypothyroidism	1 (2.44%)	8(8.89%)	2(9.09%)	11(7.19%)
Sick euthyroid syndrome	0	2(2.22%)	0	2(1.31%)
Subclinical hyperthyroidism	1 (2.44%)	0	0	1(0.65%)
Overt hypothyroidism	0	0	1(4.55%)	1(0.65%)
Total abnormality	9 (21.95%)	31(34.44%)	6(27.28%)	46 (30.06%)
Normal thyroid function	32(78.05%)	59 (65.56%)	16 (72.72%)	107 (69.94%)

A = (CD4=>500/cumm) B = (CD4= 200-500/cumm)
C = (CD4= <200/cumm)

Table 4 Correlation of mean serum T3 , T4 , TSH values with CD4 count in HIV patients of present study .

	Thyroid functions	Mean SD	Correlation with CD4 count	
			r	P
All	CD4 count (/cumm)	405.143 208.76		
	Serum T3 (ng/dl)	127.4 25.87	0.0291	> 0.05 (0.721)
	Serum free T4 (ng/dl)	1.0739 0.855	0.118	> 0.05 (0.148)
	TSH (IU /ml)	4.47213.38 5	-0.109	> 0.05 (0.180)
SCH	CD4 count (/cumm)	384.34 84.89		
	Serum T3 (ng/dl)	133.1 28.3	0.0851	> 0.05
	Serum free T4 (ng/dl)	1.46 0 .89	0.4181	< 0.05(0.019)
	TSH (IU /ml)	6.25 0.92	-0.1376	> 0.05

All = All study patients SCH = subclinical hypothyroidism
r =Karl pearson's coefficient of correlation

Table 5 Correlation of mean serum T3 , T4 , TSH values with duration of HAART in HIV patients on HAART of present study .

	Mean SD	Correlation with duration of HAART in months	
		r	P value
Duration of HAART in months	36.65 (39.11)		
Serum T3 (ng/dl)	127.4 25.78	-0.194	< 0.05 (0.016)
Serum free T4 (ng/dl)	1.07390.855	-0.136	>0.05 (0.093)
TSH (IU /ml)	4.47213.385	-0.046	>0.05 (0.564)

HAART = Highly active anti retroviral therapy, Total number of patient on HAART = 122/153 (79.7 %), r =Karl pearson's coefficient of correlation

RESULTS

Majority of the patients in this study are in the age group of 30-39 years (Table 1). Females are affected more than males with higher CD4 count , but opposite is observed with lower CD4 count (Table 2) . The prevalence of thyroid dysfunction in HIV infected patient is found to be 30.06% (46 out of total 153 patients) in this study . The most common thyroid disorder is subclinical hypothyroidism (20.26%) followed by overt hypothyroidism (7.19%) (Table 3) . Mean CD4 cell count is positively correlated with mean serum T3 and serum free T4 and negatively correlated with mean TSH without any statistical significance in total study population . But in subclinical hypothyroidism patient group there is statistically significant positive correlation between mean CD4 cell count and mean serum free T4 level and nonsignificant positive and negative correlation with mean serum T3 and TSH respectively by Karl pearson's coefficient of correlation in linear regression analysis (Table 4) . The correlation of duration of HAART with serum T3 is significantly negative and with serum free T4 , TSH is nonsignificantly negative by Karl pearson's coefficient of correlation in linear regression analysis (Table 5) .

DISCUSSION

The human immunodeficiency virus has been known to affect multiple organ systems . Among all the endocrinological disturbances identified with HIV infection , thyroid dysfunction abnormalities are the commonest [2,4,5]. Thyroid dysfunction reduces the quality of life of patients infected with HIV . The prevalence of thyroid dysfunction in persons with HIV infection in India is much higher i.e. 23- 75.5 % [9,13,14] . This is similar to our study prevalence of 30.06% . However study from the western world reported much lower prevalence of thyroid dysfunction between 10-18 % . The wide variations in prevalence across studies from different part of world is explained by the heterogeneity of study sample with regard to the duration of illness , HAART treatment , severity of immunodeficiency and associated secondary infection [15] . Delayed initiation of HAART and greater prevalence of nutritional iodine deficiency are reasons for more prevalence of thyroid dysfunction in HIV infected patients of our country . In our study , among all patients of thyroid dysfunction in HIV infection , the commonest abnormality is subclinical hypothyroidism (20.26%) . This is almost similar to majority of the studies from different countries [2,4,5,9,13,16] . In contrast , the prevalence of subclinical hypothyroidism in general population is less than 10% . The decreased secretion of thyroid hormones may act as a form of self protection because it decreases energy expenditure in already exhausted HIV infected patient [6, 17] . Isolated abnormal free T4 prevalence was 6.8% in the study by Beltran et al [4] . But in our study , prevalence of sick euthyroid syndrome is 1.31% . Both subclinical hyperthyroidism and overt hyperthyroidism are found in less than 1% of patients in our study , which is similar to Sharma et al [9] . Induction of immune restoration by HAART has been linked to thyroid dysfunction particularly hyperthyroidism and Graves disease [5,14,18] . Graves disease was most commonly been reported 12-36 months after HAART initiation [14, 19] . So, definitely there is more prevalence of thyroid dysfunction in HIV infected patients . There is nonsignificant positive correlation between serum T3 , serum free T4 and CD4 count and nonsignificant negative correlation between serum TSH and CD4 count in our study population . This is similar to Madeddu et al [2] . In subclinical hypothyroidism group , there is statistically significant positive correlation between serum free T4 and CD4 count of our study . Although there is normal serum free T4 level in subclinical hypothyroid patients , the serum free T4 level decreases within the normal laboratory reference range with severity of HIV infection . In our study , the correlations of duration of HAART with serum T3 and serum free T4 are significantly and nonsignificantly negative respectively . This is similar to Madeddu et al , in which subclinical hypothyroidism was the most frequent thyroid dysfunction in HIV patient treated with HAART [2] . Bongiovanni et al concluded that patient who had recently started HAART showed a higher incidence of subclinical hypothyroidism than those who had been on HAART for at least one year [8] .

The reasons for thyroid dysfunction in HIV infection are multifactorial. As thyroid dysfunction in HIV was reported before the introduction of HAART , it was suggested that the thyroid changes are result of direct infection of gland by HIV itself , opportunistic infection such as pneumocystis carini , infiltration of gland by regional tumour

such as Kaposi 's sarcoma , effect of humoral factor such as IL-1 and TNF or serious systemic disease [2,4] . Moreover side effect of antiretroviral drugs such as stavudine or other drugs used in the course of HIV infection such as rifampicin , ketoconazole , steroids etc are linked to thyroid dysfunction in HIV infected patients [2] .

There are several limitations of our study . A study with more number of samples would have produced better result . Prospective cohort study , not cross sectional study like ours can throw better light to identify any dynamic changes of thyroid function in HIV infected patients . The correlation with HIV viral load , anti TPO antibody was not done in our study . In spite of that , with our findings we conclude that more attention to thyroid dysfunction in HIV infected patient should be paid so that timely treatment is done and future large scale studies are required for routine recommendation of periodic thyroid testing in HIV infected patients .

REFERENCES

1. National AIDS Control Organisation , India . HIV Estimations 2017 Technical Report . New Delhi : Ministry of Health & Family Welfare, Government of India ; 2018 .
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 (HAART) : a longitudinal study . Clinical Endocrinology . 2006 :64(4) 375–383 .
3. Tang WW , Kaptein EM. Thyroid hormone levels in the acquired immunodeficiency syndrome (AIDS) or AIDS-related complex . West J Med . 1989 Dec ;151 (6): 627–631.
4. 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. 2003 Aug ;37(4):579--83.
5. Mayer KH , Hoffman CJ , Brown TT . Thyroid Function Abnormalities in HIV-Infected Patients . Clin Infect Dis. 2007Aug ;45(4):488-94.
6. Silva GA , Andrade MC , Sugui DA , Nunes RF , Pinto JF , Silva WA , et al . Association between antiretrovirals and thyroid diseases : a cross-sectional study . Arch. Endocrinol. Metab. 2015 Apr ; 59 (2) : 116–22 .
7. Quirino T , Bongiovanni M , Ricci E , Chebot E , Carradori S , Martinelli C , et al . Hypothyroidism in HIV infected patients who have or have not received HAART . Clin Infect Disease . 2004 Feb :38(4):596-7.
8. Bongiovanni M , Adorni F, Casana M , Tordato F , Tincati C , Cicconi P, et al . Subclinical hypothyroidism in HIV-infected subjects . J Antimicrob Chemother. 2006 Sept ; 58(5):1086- 9.
9. 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[Internet]. 2015; 2015:517173. Available from: https:// hindawi.com/ journals/ jtr/ 2015/517173. doi: 10.1155/2015/517173.
10. Jain G , Devpura G , Gupta BS . Abnormalities in the thyroid function tests as surrogate marker of advancing HIV infection in infected adults. J Assoc Physicians India 2009 Jul;57:508–10 .
11. Weetman AP . Thyroid abnormalities . Endocrinology and Metabolism Clinics of North America 2014 Jun ; 43(3): 781–90.
12. Melmed S , Polonsky KS , Larsen PR , Kronenberg HM . Williams textbook of endocrinology E-Book . Pittsburgh : Elsevier Health Sciences; 2015 Nov 11.
13. 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 Nov;26(13):965–70.
14. Meena LP, Rai M , Singh SK , Chakravarty J , Singh A, Goel R , et al. Endocrine changes in male HIV patients. J Assoc Physicians India 2011;59:365--71.
15. Sebastian SA , Sumithra S, Kurian J, Mathew V, Idiculla JM. Thyroid dysfunction in patients on antiretroviral therapy: A perspective from southern India. The National Medical Journal of India 2018 May 1; 31(3): 136-39 .
16. Calza L , Manfredi R , Chiodo F. Subclinical hypothyroidism in HIV-infected patients receiving highly active antiretroviral therapy. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2002 Nov 1;31 (3) :361-3.
17. Brown TT. The effects of HIV-1 infection on endocrine organs . Best Practice and Research Clinical Endocrinology & Metabolism.2011 Jun 1;25 (3):403–13 .
18. Rasul S , Delapenha R , Farhat F, Gajjala J , Zahra SM . Graves' disease as a manifestation of immune reconstitution in HIV-infected individuals after initiation of highly active antiretroviral therapy . AIDS research and treatment . 2011 Oct;2011.
19. Crum NF , Ganesan A , Johns ST , Wallace MR .Graves disease: an increasingly recognized immune reconstitution syndrome . Aids.2006 Feb 14; 20(3): 466–9.