

# Abnormalities in the Thyroid Function Tests as Surrogate Marker of Advancing HIV Infection in Infected Adults

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## Abstract

**Objective:** To study thyroid function tests in patients infected with human immunodeficiency virus (HIV) infection at various stages of the illness and to correlate the results with the disease progression.

**Methods:** In a prevalence study of 50 HIV infected patients at various stages of illness thyroid function tests consisting of free-thyroxin (FT-4), free tri-iodothyronine (FT-3), and serum thyroid stimulating hormone (s. TSH) were done. Subjects belonged to both sexes and all subjects were newly diagnosed HIV+ patients and were not receiving antiretroviral therapy (ART) when enrolled in the study. Patients were studied in two groups: Group-1 had 25 patients having AIDS and Group-2 had 25 patients who were HIV+ but were not having AIDS as per 1993 revised CDC classification for HIV infection in adolescents and adults. The results were statistically analyzed and correlation of abnormalities in thyroid function tests with the disease progression was studied.

**Results:** Out of 50 cases, thyroid function abnormalities were observed in substantial number of patients. Nine (18%) patients had FT-3 levels below the normal range, ten (20%) patients had decreased FT-4 levels and twelve (24%) patients had s. TSH levels above the normal range.

When the results were statistically analyzed for the 50 patients enrolled in our study using Pearson's correlation coefficient, there was a direct correlation between CD4 count and FT3 and FT4 values ( $r=0.357$  with  $p < 0.05$ ;  $r = 0.650$  with  $p < 0.05$  respectively). There was an inverse correlation of CD4 counts with serum TSH levels ( $r = -0.470$  with  $p < 0.050$ ).

**Conclusion:** Thyroid dysfunction is frequent in HIV infection and with progression of disease there is a primary hypothyroid like stage that occurs in patients with HIV infection.

FT3 /FT4 / serum TSH can be used as a surrogate marker of the progression of the disease.

## Introduction

Acquired immunodeficiency syndrome (AIDS) resulting from infection with human immunodeficiency virus (HIV) may directly or indirectly affect any organ system. Increasing experience with this syndrome has led to the recognition of a variety of HIV related endocrine disorder that occurs during both the early and late stages of the disease. Among these disorders a high prevalence of abnormalities in thyroid function tests is reported in previous cross-sectional studies. Unique abnormalities of thyroid function tests were reported by Lambert M et al.<sup>4</sup> They described a progressive elevation in serum thyroxin binding globulin (s. TBG) but not in other binding proteins such as cortisol binding globulin (CBG) that accompanies a decline in CD4+ count with advancing HIV infection. Feldt-Rasmussen U et al<sup>2</sup> reported elevation of s. TSH and s. TBG concentration in conjunction with low FT-4 that occurs frequently and correlates with CD4+ cell depletion in AIDS patients. In addition this thyroid dysfunction correlated with the degree of immunosuppression and viral replication and preceded the worsening of the disease.

Subtle alterations in thyroid function tests (TFT) are more common in HIV infection and are sometimes already detectable in the early phase of disease. The changes in thyroid function

tests are HIV specific and are consistent with an abnormal response to acute illness. Various mechanisms have been proposed to explain such abnormalities in TFT. These include direct infection of thyroid gland by opportunistic organisms such as *Pneumocystis carinii*, infiltration of the gland by tumors such as Kaposi sarcoma, effect of humoral factors such as IL-1 $\beta$  and TNF- $\alpha$ , side effect of the drugs used in the course of HIV infection for e.g. rifampicin, ketoconazole, steroids etc. and direct infection of gland by HIV.

Usefulness of TFT as a biochemical predictor of the disease progression in HIV infection has not been studied in Indian subjects. Thus we studied a spectrum of newly diagnosed HIV+ patients from asymptomatic to AIDS who were not receiving HAART.

## Materials and Methods

Subjects belonged to both sexes and all subjects were newly diagnosed HIV+ patients who were not receiving antiretroviral therapy (ART) at the time of enrollment in the study. All the cases included were interrogated and were examined. Informed consent was obtained from all subjects.

Inclusion criteria:

1. Subject having HIV serology positive by ELISA test. We used Micro ELISA, Comb AIDS-RS, and HIV Tri-dot antigen kits. Patients included were HIV+ by all three kits.

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Table 1 : Comparison of laboratory parameters between HIV positive non-AIDS and AIDS patients

Parameter	HIV positive non-AIDS patients (n=25)	AIDS patients (n=25)
A) CD 4 – Count		
> 500/ $\mu$ L	4	None
200 – 500/ $\mu$ L	21	None
<200/ $\mu$ L	None	25
Mean CD4 count	358.20 $\pm$ 138.305	97.20 $\pm$ 56.178
B) Thyroid function tests		
Mean FT3 (picogram/ml)	2.826 $\pm$ 0.702	2.518 $\pm$ 0.868
Mean FT4 (nanogram/ml)	1.352 $\pm$ 0.371	0.925 $\pm$ 0.264
Mean serum TSH ( $\mu$ IU/ml)	2.134 $\pm$ 1.127	4.135 $\pm$ 3.231

Table 2 : Distribution of TFT results in 25 HIV+ non-AIDS patients

	Normal	Elevated	Decreased
FT-3 (picogram/ml)	22	0	03
FT-4 (nanogram/ml)	23	01	01
s. TSH ( $\mu$ IU/ml)	22	02	01

#### Exclusion criteria:

1. History s/o thyroid illness, clinically evident thyroid enlargement, or signs of thyroid disease.
2. Use of drugs known to interfere with thyroid hormone metabolism for e.g. rifampicin, steroids, ketoconazole, anti-epileptics etc.
3. Abnormal liver function tests i.e. SGOT or SGPT levels greater than three times the upper normal limit.
4. Abnormal renal function tests i.e. serum creatinine level greater than 1.6 mg%.

Cases were studied in two groups.

#### Group-1

It consisted of 25 HIV+ patients having AIDS. A HIV+ patient was said to be having AIDS if the patient belonged to 1993 revised CDC classification for HIV infection Category A-3, B3, C1-3.

#### Group-2

It consisted of 25 HIV+ patients belonging to 1993 revised CDC classification for HIV infection Category A1-2, B1-2.

Free thyroxin (FT-4), free tri-iodothyronine (FT-3), and serum thyroid stimulating hormone (s. TSH) levels were measured by IMMULITE-2000. The principle of free thyronine assay was solid-phase, chemiluminescent, competitive analog immunoassay while that of s. TSH estimation was solid-phase, two-site chemiluminescent immunometric assay. CD4 count, CD8 count and CD4-CD8 ratio apart from routine biochemistry and pathological investigations were also done. CD-4 count was determined by flow cytometry, FACS count system (Beck ton Dickinson).

A single fasting blood sample drawn between 8 a.m. to 10 a.m. was sent for lab analysis to various labs.

## Results

On the basis of CD4 count distribution; 4 (8%) patients had CD4 > 500/ $\mu$ L, 21 (42%) patients had CD4 between 200-500/ $\mu$ L and 25 (50%) patients had CD4 < 200/ $\mu$ L. Mean CD4 count in HIV positive non-AIDS patient was 358.20  $\pm$  138.305, while in AIDS patients it was 97.20  $\pm$  56.178. Thyroid function tests were

Table 3 : Distribution of TFT results in 25 AIDS patients

	Normal	Elevated	Decreased
FT-3 (picogram/ml)	19	0	06
FT-4 (nanogram/ml)	16	0	09
s TSH ( $\mu$ IU/ml)	15	10	0

compared in both HIV+ non-AIDS and AIDS patients. Mean FT-3 and mean FT-4 values were 2.826 $\pm$ 0.702 pg/ml and 1.352 $\pm$ 0.371 ng/ml in non-AIDS patients while it was 2.518 $\pm$ 0.868 pg/ml and 0.925 $\pm$ 0.264 ng/ml respectively in AIDS patients. S. TSH was 2.134 $\pm$ 1.127  $\mu$ IU/ml and 4.135 $\pm$ 3.231  $\mu$ IU/ml in non-AIDS and AIDS patient respectively (Table 1).

Among 25 HIV+ patients who were not having AIDS, 3 (12%) patients had FT-3 levels below the normal range, 1 (4%) patient had FT-4 level below the normal range and 1 (4%) patient had FT-4 level above the normal range. Two (8%) patients had s. TSH levels above the normal range. Serum TSH was decreased in one (4%) patient (Table 2).

In 25 patients having AIDS, FT-3 levels were below the normal in 6 (24%) patients, FT-4 levels were below the normal in 9 (36%) patients and s. TSH levels were above normal in 10 (40%) patients (Table 3).

As the 50 patients were distributed during the course of the disease from less severe to more severe according to CD4 count, the results were statistically analyzed for the all 50 patients enrolled in our study using Pearson's correlation coefficient. We found that there was a direct correlation between CD4 count and FT3 and FT4 values ( $r=0.357$  with  $p < 0.05$ ;  $r = 0.650$  with  $p < 0.05$  respectively). There was an inverse correlation of CD4 counts with serum TSH levels ( $r = -0.470$  with  $p < 0.050$ ).

## Discussion

During HIV infection abnormalities in thyroid include both pathological changes and disturbances in its function.<sup>3-8</sup> Our present study shows that thyroid dysfunction is frequent in HIV infection and with progression of disease there is a subclinical hypothyroid like stage that occurs in patients with advancing HIV infection. Various thyroid function tests such as FT3 /FT4 /serum TSH can be used as a surrogate marker as these correlate with the progression of the disease. One should not start upon the replacement therapy for hypothyroid like state in HIV infection as the state may be responsive to highly active antiretroviral therapy. Our present study may not be giving the true picture of thyroid abnormality in HIV-AIDS as structural correlates of thyroid dysfunction could not be done in patients with hypothyroid like state. Beside this, serum reverse-triiodothyronine, serum thyroxin binding globulin levels and TRH stimulation test could also not be done because of non-availability of these tests in our set up. Further studies are needed in to solve the issue of management of thyroid dysfunction in AIDS.

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## Swine Flu Update

H1N1 Influenza Update as on 24<sup>th</sup> June, 2009

WHO declared the Influenza A (H1N1) pandemic on June 11, 2009. The Director-General of WHO raised the influenza pandemic alert to the highest level - Phase 6 - on the guidance and advice from an Emergency Committee established for this purpose under the International Health Regulations (IHR).

More than 100 countries have reported cases with over 55,867 confirmed cases and 238 deaths. In India, 64 laboratory confirmed cases have been detected. No deaths have been reported from India.



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