

RESEARCH ARTICLE

Prevalence of Thyroid Abnormalities among Adults with HIV Infection in Oman

Al Qassabi SS¹, Kamble B^{2*}, D'Souza MS³, Al Shehi NI⁴, Kurup PM⁵ and Elgalib A⁶

¹Senior Consultant Endocrinology, Al Nahda Hospital, Ministry of Health, Oman

²Senior Specialist Internal Medicine, Al Nahda Hospital, Ministry of Health, Oman

³College of Nursing, Sultan Qaboos University, Muscat, Oman

⁴Al Nahda Hospital, Ministry of Health, Oman

⁵Communicable Disease Surveillance & Control Directorate General of Health Services, Muscat, Oman

⁶Consultant Physician (HIV medicine), Department of communicable disease, Ministry of health, Oman

***Corresponding author:** Kamble B, Senior Specialist Internal Medicine, Al Nahda Hospital, Ministry of Health, Oman, Tel: +96892942934, E-mail: binakamble63@gmail.com

Citation: Al Qassabi SS, Kamble B, D'Souza MS, Al Shehi NI, Kurup PM, et al. (2017) Prevalence of thyroid abnormalities among adults with HIV infection in Oman. J Hormonal Dis Endocrine Res 1: 101

Abstract

Context: Thyroid dysfunction is a common endocrinopathy in HIV and occurs in 35% of all HIV infected adults.

Aims: The aim was to find out prevalence of thyroid abnormalities among adults with HIV infection in Oman.

Settings and Design: A retrospective cross-sectional design was used for the study. Adults with HIV infection attending the infectious disease clinic were selected from a public hospital in Oman.

Methods and Material: HIV-infected adults, aged 13-75 years old, attending the ID clinic at our hospital were identified. We reviewed electronic patient record (EPR) from January 2003 to December 2015 for those with clinical data of at least 1 visit to ID clinic. TSH and free T4 were measured by sandwich ELISA method on Cobas analyzer.

Statistical analysis used: Chi-square was used to analyse the group difference. A p value of <0.05 was considered significant.

Results: Among 151 patients who met the inclusion criteria, 50 patients (33.1%) had abnormal thyroid function. Out of 105 males, 29 (27.6%) had thyroid dysfunctions while out of 45 females, 21 (45.7%) had abnormal thyroid functions. There were 85 (56.3%) patients with initial CD4>200 cells/uL and 66 (43.7%) patients with initial CD4<200 cells/uL. Among patients with initial CD4>200cells/uL, 29 (34.1%) patients had thyroid function abnormalities compared to 21 (31.8%) with CD4<200 cells/uL.

Conclusion: The prevalence of thyroid functional abnormalities was 33.1% among adults with HIV in our cohort. Isolated low T4 followed by Subclinical hypothyroidism were the most common abnormalities found in our study.

Keywords: Thyroid abnormalities; HIV infection; Prevalence; Thyroid dysfunction; Oman

Introduction

Multiple endocrine and metabolic abnormalities have been observed in patients infected with human immunodeficiency virus (HIV) and among them thyroid function abnormalities are common [1-3]. There are various mechanisms for thyroid function abnormalities in HIV patients. It can be due to infiltration of the gland by tumours like Kaposi sarcoma, infection of the gland with opportunistic infections like Pneumocystis Jirovecii, and direct infection of the gland with the HIV virus [4]. Other potential causes for thyroid dysfunction in HIV patients include side effects of the drugs used in the course of the HIV infection, which includes highly active antiretroviral therapy (HAART), anti-tubercular, and antifungal drugs, and euthyroid sick syndrome [4]. A recent study from India examined 158 autopsies from AIDS patients observed a wide range of fungal, bacterial and viral as causes of thyroid dysfunction; Hashimoto's thyroiditis and lymphocytic thyroiditis were also seen [5].

Prevalence of thyroid dysfunction in HIV-infected adults was reported as high as 40% [6-9]. Such abnormalities include overt thyroid disease (1-2%) and subtle changes in thyroid function tests (TFT) [8,10-14]. The prevalence of overt hypothyroidism in HIV-infected adults and overt primary hypothyroidism in general population have been reported as 0-2.6% and 0.3%, respectively [8,11,15].

Subclinical hypothyroidism was the commonest thyroid dysfunction reported in HIV patients (14.7%), followed by sick euthyroid syndrome (5.29%) and isolated low thyroid stimulation hormone (TSH) (3.1%) [16,17]. Data about the prevalence of thyroid function abnormalities in HIV-infected patients in Oman are lacking. In order to inform local practice and future operational research directions, we sought to estimate the prevalence of thyroid dysfunction in HIV positive patients attending an HIV clinic in Muscat, Oman.

Methods

We conducted a retrospective cross-sectional study of adult, aged 13-75 years old, HIV-infected patients attending the outpatient clinic at Alnahda Hospital, Muscat, Sultanate of Oman. We included patients who had stable clinical condition and at least one test for free tetraiodo thyronine (FT4) and TSH in the period between January 2003 and December 2015. Severely ill patients, including inpatients, were excluded. Patients were identified from the HIV clinic database. Electronic patient records (EPR) of patients attending the outpatient clinic at least once in the study period were reviewed for inclusion criteria.

Data collected included initial available CD4 cell count, FT4, TSH and Free tri-iodothyronine (FT3), where available. Laboratory reference ranges for FT4 and TSH were (12-22) pmol/L, (0.27-4.2) mU/L, respectively.

Thyroid dysfunctions were classified as follows:

- Overt hypothyroidism: If free T4 level was <12 pmol/L and TSH level was >4.2 mU/L.
- Overt hyperthyroidism: If free T4 measurement was >22 pmol/L and TSH level was <0.27 mU/L.
- Subclinical hypothyroidism: If FT4 level was between 12 and 22 pmol/L and TSH level was >4.2 mU/L.
- Subclinical hyperthyroidism: If FT4 level was FT4 level was between 12 and 22 pmol/L and TSH level was <0.27 mU/L.
- Isolated low FT4 level: If FT4 level was <12 pmol/L and TSH level was between 0.27 and 4.2 mU/L.
- Normal thyroid function: If FT4 level was between 12 and 22 pmol/L and TSH level was between 0.27 and 4.2 mU/L.

The hospital's ethical committee approved the study protocol and a written consent was deemed unnecessary. Chi-square was used to analyse the group difference. A p value of <0.05 was considered significant.

Results

EPR for a total of 204 patients were reviewed; 151 met the inclusion criteria and included in the final analysis. The median interquartile (IQR) age was 43 (35-50). The majority (69.5%, 105/151) were male. The median (IQR) baseline CD4 count was 232 (95-416). All patients were on HAART. Abnormal thyroid function was observed in 33.1% (50/151) of the total cohort; out of those 50, 29 were male and 21 were female. Isolated low T4 was the commonest abnormality, seen in 16.6% (25/151) of the patients, followed by subclinical hypothyroidism, seen in 11.3% (17/151). There were 5 (1.3%) cases of overt hypothyroidism, 2 (1.3%) cases of subclinical hypothyroidism and 1 (0.7%) case of overt hyperthyroidism.

Subclinical hypothyroidism, overt hyperthyroidism and isolated low T4 were more prevalent in females, while males had higher prevalence of subclinical hyperthyroidism and overt hypothyroidism (Table 1). Thyroid abnormalities among patients with initial CD4 count of <200 stratified by gender and among patients with initial CD4 count of >200 stratified by gender are shown in Table 2 and 3, respectively.

	Male, N=105	Female, N=46	P value
Thyroid abnormality	n (%)	n (%)	
Overt hypothyroidism	4 (3.8)	1 (2.1)	0.12
Overt hyperthyroidism	0 (0.0)	1 (2.1)	0.23
Subclinical hypothyroidism	10 (9.5)	7 (15.2)	0.43
Subclinical hyperthyroidism	2 (1.9)	0 (0.0)	0.53
Isolated low T4 level	12(11.4)	13 (28.2)	0.23
Normal thyroid function	77(73.3)	24 (52.2)	0.34

Table 1: Thyroid abnormalities among all cohort stratified by gender

There were 85 (56.3%) patients with CD4 >200 and 66 (43.7%) patients with CD4 <200 among our cohort (Table 4). Among patients with CD4 >200, 34% (29/85) had thyroid function abnormalities compared to 31% (21/66) in patients with CD4<200; p value=0.77. Isolated low T4 in was seen in 17.6% (15/85) of patients with CD4>200 compared to 15.2% (10/66) in patients with CD4<200. Subclinical hypothyroidism was observed in 10.7% (9/85) and 12.1% (8/66) in patients with CD4>200 and patients with CD4<200, respectively.

	Male, N=45	Female, N=21	P value
Thyroid abnormality	n (%)	n (%)	
Overt hypothyroidism	2 (4.4)	0 (0.0)	0.23
Overt hyperthyroidism	0 (0.0)	0 (0.0)	0.57
Subclinical hypothyroidism	4 (8.9)	4 (19.0)	0.47
Subclinical hyperthyroidism	1 (2.2)	0 (0.0)	0.67
Isolated low T4 level	6 (13.3)	4 (19.0)	0.82
Normal thyroid function	32 (71.1)	13 (61.9)	0.72

Table 2: Thyroid abnormalities among patients with initial CD4 count of <200 stratified by gender

	Male, N=60	Female, N=25	P value
Thyroid abnormality	n (%)	n (%)	
Overt hypothyroidism	2 (3.33)	1 (4.0)	0.25
Overt hyperthyroidism	0 (0.0)	1 (4.0)	0.34
Subclinical hypothyroidism	6 (10.0)	3 (12.0)	0.23
Subclinical hyperthyroidism	1 (1.7)	0 (0.0)	0.16
Isolated low T4 level	6 (10.0)	9 (36.0)	0.41
Normal thyroid function	45 (75.0)	11 (44.0)	0.32

Table 3: Thyroid abnormalities among patients with baseline CD4 count of >200 stratified by gender

	CD4 >200, N=85	CD4<200, N=66	P value
Thyroid abnormality	n (%)	n (%)	
Overt hypothyroidism	3 (3.5)	2 (3.0)	0.21
Overt hyperthyroidism	1 (1.2)	0 (0)	0.13
Subclinical hypothyroidism	9 (10.6)	8 (12.1)	0.57
Subclinical hyperthyroidism	1 (1.2)	1 (1.5)	0.68
Isolated low T4 level	15 (17.6)	10 (15.2)	0.48
Normal thyroid function	56 (65.9)	45 (68.2)	0.92

Table 4: Thyroid abnormalities among all cohort stratified by baseline CD4 count

Discussion

In this study, 33.1% of our cohort had thyroid abnormalities which were comparable to previous reports where thyroid dysfunction was found in 35% of HIV-infected patients [8-11]. The commonest dysfunctions we observed were the isolated low FT4 (16.6%) and subclinical hypothyroidism (11.3%). Our data show that females had higher prevalence for subclinical hypothyroidism, isolated low T4 and overt hyperthyroidism compared to males; while males had higher prevalence for overt hypothyroidism, which is usually higher in females in HIV-negative individuals. One study conducted for thyroid dysfunction among adult males with HIV shows higher incidence of thyroid and gonadal dysfunction [3].

There was no significant difference in prevalence of thyroid abnormalities in patients with CD4<200 (31%) when compared to those with CD4>200 cells/uL (34%); p value=0.77. Recent study shows burden of thyroid dysfunction in chronic HIV infection with stable immune function is lower compared to pre HAART era and severe immunodeficiency at disease onset, thyroperoxidase antibodies (TPOAb) positivity and tuberculosis were best predictor of subclinical hypothyroidism [17,18]. We could not correlate thyroid function abnormalities and severity in immune dysfunction. In our study, thyroid function was not checked at the same time frame of initial CD4 cell count.

Isolated low FT4 with normal TSH levels are found frequently among HIV-infected individuals, with reported prevalence of 1.3%-6.8% [8,11,20]. In one study 16% of the patients are affected with non-thyroid illness with HIV infection [19]. We could not categorize patients for non-thyroidal illness due to non-availability of the data for free T3 level, reverse T3 level. Isolated low T4 can be part of severe non-thyroidal illness but in our study we did not include severely sick individuals. Isolated central

hypothyroidism is a very rare entity and we did not investigate patients to exclude this cause for low T4. There are few case reports of isolated idiopathic central hypothyroidism in adult [20]. Isolated low T4 is also associated with receipt of didanosine, stavudine, and ritonavir [21]. Drugs like phenytoin and carbamazepine can interfere with free T4 assays, though similar effect of antiretrovirals (ARV) has not been proved [22]. Clinical significance of low FT4 level remains unclear and our patients with this dysfunction did not report any symptoms of hypothyroidism; none of them was started on levothyroxine.

Overt hypothyroidism was found in 1.3% in our study population, which was slightly lower than previous reports. One cross-sectional multicentre study of 350 HIV-infected patients reported a prevalence of overt hypothyroidism of 2.6% [8]. The risk of hypothyroidism increased among patients with lower CD4 counts. Adults with HIV infection go through significant stresses, which affects hypothalamic-pituitary-thyroid axis.

Subclinical hypothyroidism among adults with HIV infection had been reported in the range of 3.5-14.76% [8,10,15,17,18]. Antithyroid peroxidase antibodies are rarely positive among these patients suggesting that mechanism may not be autoimmune [10,21]. The clinical significance of the 11.3% prevalence of subclinical hypothyroidism we report is uncertain; several studies among general population showed that most patients with subclinical hypothyroidism did not require treatment and in many cases TFT normalised spontaneously; however, some authors reported that 19 to 27.3% of patients required replacement therapy with levothyroxine [23,24]. In addition, the prevalence of subclinical hypothyroidism in our patients was higher than what was reported in HIV negative counterparts, including data from countries in the Asian Continent (4.2% in Japan) and Arab World (6.18% in Libya) [25-30]. Indeed, some authors have advocated routine screening of TFT in HIV patients, particularly in certain subgroups [9,31]. It is worth noting that the treatment and prevention of thyroid dysfunctions in HIV patients, regardless of geographical location, is similar to the general population [4]. The only special consideration in HIV would be the potential for drug-to-drug interactions [32,33].

One limitation of our study is its retrospective nature and the small size. Also, we were not able to address correlates of thyroid abnormalities among our cohort. Furthermore, the study did not analyse the follow up thyroid function tests to assess the pattern of the thyroid dysfunction over time; some of the reported abnormalities, such as subclinical hypothyroidism, could have been very transient.

Conclusion

To our knowledge, this is the first study to examine the thyroid dysfunction in HIV patients in the Middle East and North Africa. The prevalence of thyroid function abnormalities was high among our patients. Isolated low T4 followed by Subclinical hypothyroidism were the most common abnormalities found in our study. Females had higher prevalence of all forms of abnormal thyroid function except subclinical hyperthyroidism and overt hypothyroidism. Initial CD4 count had no effect on prevalence of thyroid abnormalities in our patients.

To conclude, routine screening of TFT may help in detecting thyroid abnormalities in asymptomatic HIV patients; however, the clinical significance of subtle thyroid abnormalities identified is not entirely clear. Findings from our small descriptive study do not support routine screening for thyroid dysfunction in asymptomatic HIV patients; however, larger longitudinal studies may be required to better inform clinical practice.

Key Message: Findings from our small study do not support routine screening for thyroid dysfunction in asymptomatic HIV patients; however, larger longitudinal studies may be required to better inform clinical practice.

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