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The Prevalence of Thyroid Disorders in Patients with Type 2 Diabetes Mellitus in Saudi Community Based Hospital

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Abstract

Background and objective: The association between diabetes and thyroid dysfunction were reported. Thus, the present study was conducted to find out the relationship between T2DM and thyroid dysfunction in patients with T2DM in a cohort of Saudi population.

Design: A cross-sectional study was conducted in the Diabetes centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia from January 2018 to December 2018. Thyroid stimulating hormone (TSH), free thyroxin (FT4) and HBa1c were measured.

Results: A total of 2069 subjects with T2DM were included in this study. Average age of the study population was 51.3 ±16.4 years. 1511 (73%) were euthyroid, primary hypothyroid was present in 229 (11.1%) and subclinical hypothyroidism was present in 3 (3%) patients. Hyperthyroidism was present in 33 (1.6%), and subclinical hyperthyroidism was present in 125 (6%) patients. Patients with primary hypothyroid were statistically non-significant older compared to subclinical hypothyroidism, hyperthyroidism and subclinical hyperthyroidism (P=0.6), and included statistically non-significant difference between thyroid dysfunctions in younger compared to older than 50 years subjects (P=0.3).

Moreover, there was a statistically non-significant difference between thyroid dysfunctions in males compared to females (P<0.0001). In addition, there was a statistically non-significant difference between thyroid dysfunctions in males compared to females (P<0.0001). Patients with primary hypothyroid were statistically significant have higher HbA1c compared to subclinical hypothyroidism, hyperthyroidism and subclinical hyperthyroidism (P=0.004). In addition, there was a statistically significant difference between HbA1c below and above 7% in correlation to thyroid dysfunctions (P=0.02).

Keywords: Hypothyroidism; Type 2 Diabetes; Thyroid dysfunctions; Endocrine diseases; Diabetes; Human body; Radioimmunoassay; Hypothalamic control; Thyroxin; Triiodothyronine

Abbreviation: T2DM: Type 2 Diabetes Mellitus; TSH: Thyroid Stimulating Hormone; T4: Thyroxin; T3: Triiodothyronine; CMIA: Chemiluminescent Immunoassay Method; FT4: Free Thyroxine; SD: Standard Deviation; TT4: Total Thyroxine; TRH: Thyrotropin Releasing Hormone

Introduction

Thyroid gland is one of the important organs in human body and the burden of thyroid diseases in the general population is enormous specially in females [1,2]. Thyroid disorders have increased recently and are considered the commonest endocrine diseases [3]. Several studies have been reported from different parts of the world showing the prevalence of hypothyroidism between 1% and 2%, and it is ten times more common in women than in men [4].

Type 2 diabetes mellitus (T2DM) is the commonest endocrine disorder [5]. The World health organization estimated diabetes prevalence was 2.8% in 2000 and 4.4% in 2030 [6]. Saudi Arabia is the seventh of the top ten countries in terms of the prevalence of diabetes among the adult population aged 20-79 [7].

The association between diabetes and thyroid dysfunction were first published in 1979 [8]. Since then a number of studies have estimated the prevalence of thyroid dysfunction among diabetes patients to be varying from 2.2 to 17 % [9,10]. However, fewer studies have estimated much higher prevalence of thyroid dysfunction in diabetes i.e. 31 % and 46.5% respectively [11,12]. The prevalence of thyroid dysfunction among Saudi diabetic patients was reported to be 16-28.5% of which 25.3% had hypothyroidism [13,14]. Thyroid dysfunction is a disorder of the

thyroid gland which manifests either as hyper or hypothyroidism and is reflected in the levels of thyroid stimulating hormone (TSH) [15].

T2DM appears to influence thyroid function in two sites; at the level of hypothalamic control of TSH release and at peripheral tissue by converting thyroxin (T4) to triiodothyronine (T3). Hyperglycemia causes reduction in hepatic concentration of T4-5 deiodinase, low serum concentration of T3, raised levels of reverse T3 and low, normal, or high level of T4. Thyroid hormone regulate metabolism and diabetes can alter metabolism [16].

Epidemiological studies of thyroid dysfunction have limitations, for example the definition of overt hypothyroidism and subclinical hypothyroidism, the selection criteria of the sample used, the influence of age, sex, genetic, environmental factor, the different techniques used for the measurement of thyroid hormones and the relative paucity of incidence data [5]. Thus, the present study was conducted to find out the relationship between T2DM and thyroid dysfunction in patients with T2DM in a cohort of Saudi population.

Methods

A cross-sectional study was conducted in the Diabetes centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia from January 2018 to December 2018 for a period of 12 months which included 2069 patients who were diagnosed as T2DM on the basis of ADA criteria [17]. Patients who are pregnant were excluded. TSH was measured with a chemiluminescent immunoassay method (CMIA) (Architect i2000 system, Abbott, USA). Serum free thyroxine (FT4) was estimated by radioimmunoassay. The assays have intra- assay precision of 4.3%. TSH levels between 0.22-4.2 mIU/L and Free T4 12.0-22.0 pmol/L were regarded normal [18]. High performance liquid chromatography was used. HbA1c was expressed as percentage. Hypothyroidism was defined as a clinical syndrome of hypothyroidism associated with elevated TSH >4.2 mIU/l and decreased serum levels of FT4. Subclinical hypothyroidism was defined as elevated TSH >4.2 mIU/l and normal circulating FT4. Hyperthyroidism was defined as TSH <0.22 mIU/l with elevated FT4. Subclinical hyperthyroidism was defined as TSH <.22 mIU/l and normal circulating FT4 [19].

Statistical analysis

Data are presented as means ± standard deviation (SD) or numbers (%). Quantitative variables were compared between two groups by using the Student's test. Differences in categorical variables were analyzed using the chi-square test. The relationship between continuous variables was assessed using coefficients of correlation. The statistical analysis was conducted with SPSS version 23.0 for Windows.

Results

A total of 2069 subjects with T2DM were included in this study. Average age of the study population was 51.3 ±16.4 years (Table 1). 24.5% were male and 75.5% were female. Mean HbA1c (%), TSH and FT4 were 7.5±2, 3.4 ±8.8 mIU/l and 14.0±5 pmol/L respectively. 1511 (73%) were euthyroid, primary hypothyroid was present in 229 (11.1%) and subclinical hypothyroidism was present in 3 (3%) patients (Figure 1). Hyperthyroidism was present in 33 (1.6%), and subclinical hyperthyroidism was present in 125 (6%) patients.

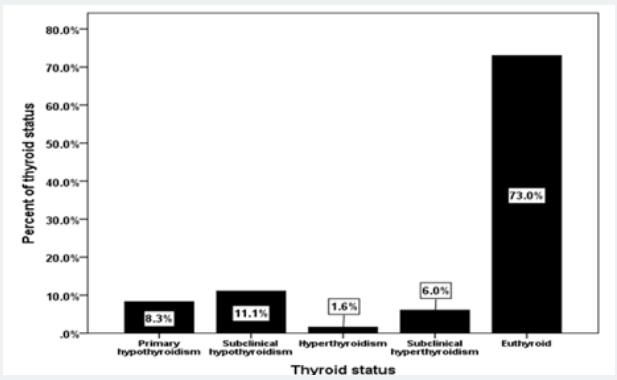

Figure 1: Distribution of Thyroid Status.

Table 1: Base Line Characteristic of Total Population.

Parameters		Total
Age (years)		51.3±16.4
Gender	Male	506 (24.5)
	Female	1563 (75.5)
HbA1c		7.5±2.0
TSH (mIU/l)		3.4±8.8
FT4 (pmol/l)		14.0±5.0

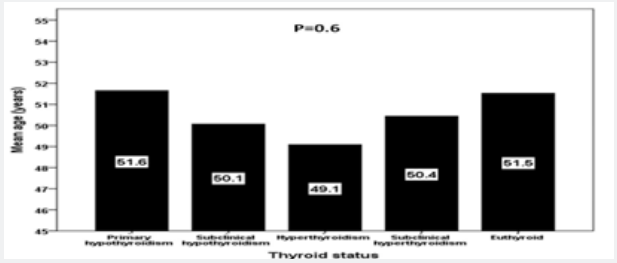

Figure 2: Age Distribution in Relation Thyroid Status.

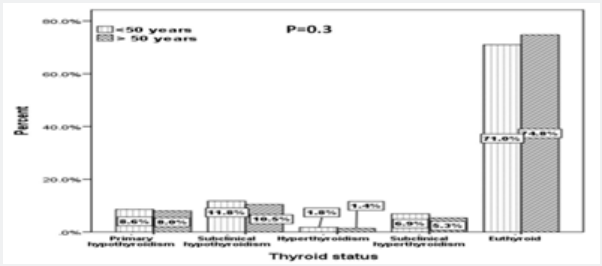

Figure 3: Age Groups Distribution in Relation Thyroid Status.

Patients with primary hypothyroid were statistically non-significant older compared to subclinical hypothyroidism, hyperthyroidism and subclinical hyperthyroidism (mean age:

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51 years versus 50, 49 and 50 years respectively; P=0.6) (Figure 2), and included statistically non-significant difference between thyroid dysfunction in younger compared to older than 50 years subjects (P=0.3) (Figure 3).

Moreover, there was a statistically non-significant difference between thyroid dysfunctions in males compared to females (P<0.0001) (Figure 4). In addition, there was a statistically non-significant difference between thyroid dysfunctions in males compared to females (P<0.0001) (Figure 4).

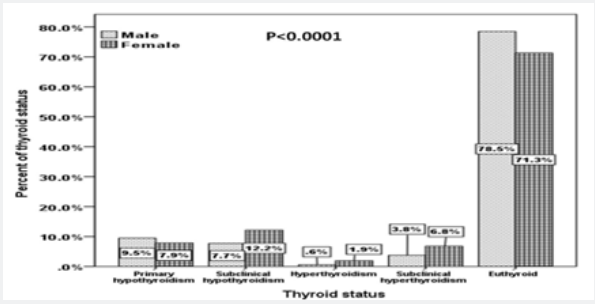

Figure 4: Gender Distribution in Relation Thyroid Status.

Patients with primary hypothyroid were statistically significant have higher HbA1c compared to subclinical hypothyroidism, hyperthyroidism and subclinical hyperthyroidism (mean HbA1c (%): 7.8 versus 7.7, 6.2 and 6.8% respectively; P=0.004) (Figure 5). In addition, there was a statistically significant difference between HbA1c below and above 7% in correlation to thyroid dysfunction (P=0.02) (Figure 6).

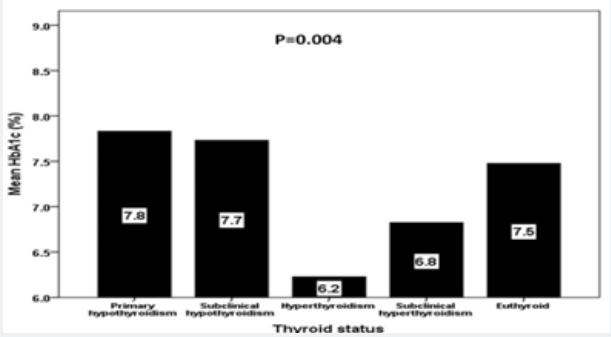

Figure 5: HbA1c Distribution in Relation to Thyroid Status.

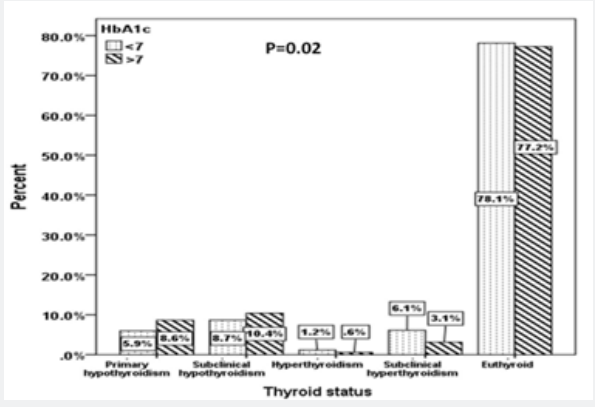

Figure 6: HbA1c Groups in Relation to Thyroid Status.

Discussion

There is a complex interaction between thyroid dysfunction and diabetes mellitus. In the present study among the 2069 subjects with T2DM, thyroid dysfunction was found in 27%. Primary hypothyroid was present in 11.1% and subclinical hypothyroidism was present in 3% patients. Moreover, hyperthyroidism was present in 1.6%, and subclinical hyperthyroidism was present in 6% patients. Brijesh et al found 26% of patients with T2DM have thyroid dysfunction [20]. Pasupathi et al in their study found that prevalence of thyroid dysfunction was 45% among type 2 diabetics.

Hypothyroidism was present in 28% and 17% had hyperthyroidism [21]. Udiong et al in their study from Nigeria found that prevalence of thyroid dysfunction was 46.5%. Hypothyroidism was present in 26.6% and 19.9% had hyperthyroidism [12]. A prevalence of 12.3% was reported among Greek diabetic patients and 16% of Saudi patients with type 2 diabetes were found to have thyroid dysfunction [13,22]. In Jordan, a study reported that thyroid dysfunction was present in 12.5% of type 2 diabetic patients [23]. Perros et al demonstrated an overall prevalence of 13.4% of thyroid diseases in diabetics [9].

It has been suggested that altered thyroid status in T2DM is linked toleration of hypothalamo-pituitary- thyroid axis causing decreased formation of total thyroxine (TT4). Also, there is less activation of AMPK (5'-Adenosine Mono Phosphate activated Protein Kinase) in T2DM that also causes decreased formation of thyroid hormones [24]. Decrease levels of thyroid hormones cause increased TSH release from anterior pituitary gland by feedback mechanism [25-27]. Most of the T2DM patients were obese who might have increased level of leptin. This increased level of leptin develops leptin resistance centrally that causes decreased formation of thyroid hormones and increase TSH secretion [24]. Moreover, the binding affinity of TT4 is increased in T2DM that causes decrease formation of FT4 in blood [26,27]. T2DM are also associated with obesity, stress, infection that caused changes in hypothalamo-pituitary thyroid axis lead to decrease level of FT4 and increased TSH level in T2DM [24].

The presence of both raised and low levels of thyroid hormones in diabetic may be due to modified thyrotropin releasing hormone (TRH) synthesis and release [21]. The hyperglycaemia seen in type- 2 diabetics is known to have negative effect on thyroid function precisely blunting the pituitary TSH response to stimulation by hypothalamic TRH. This may be due to possible alteration of post translational glycosylation of TRH hence affecting its biological activity [28]. T2DM is associated with increased insulin level and C-peptide level. Insulin is an anabolic hormone known to enhance TSH turnover, which is protein in nature. Recently, C-peptide has been shown to enhance Na+/K+- ATPase activity, an action that may also increase protein synthesis. Such an action would induce increased turnover of TSH, a protein hormone [29,30].

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Our results showed a different frequency between thyroid dysfunction in both males and females. Still, detailed molecular mechanisms remain unclear, because sex hormones (such as estrogen, and testosterone) can regulate the thyroid function [31]. Boucai the difference in sex hormones may partly explain the sex-difference in the relationship between thyroid dysfunction. However, because levels of sex hormones such as testosterone and estrogen were not measured in this study, further research is needed to explore this issue. In addition, because the sample size was smaller for males (24.5%) than in females (75.5%), the precision and statistical power of the analysis may be lower for males. Further large-scale population studies are required to confirm the above findings.

In our study we found that diabetic patients with primary and subclinical hypothyroidism have higher uncontrolled diabetes HbA1c > 7 when compared to patients with HbA1c < 7 (8.6 vs. 5.9% and 10.4 vs. 8.7%) respectively whereas patients with hyperthyroidism and subclinical hyperthyroidism have lower uncontrolled diabetes HbA1c > 7 when compared to patients with HbA1c < 7 (0.6 vs. 1.2% and 3.1 vs. 6.1%) respectively. In addition, patients with primary hypothyroid were statistically significant have higher HbA1c compared to subclinical hypothyroidism, hyperthyroidism and subclinical hyperthyroidism (mean HbA1c (%): 7.8, 7.7, 6.2 and 6.8% respectively; P=0.004). These findings are supported by various studies [32-34]. Hypothyroidism falsely raises HbA1c due to decreased erythropoiesis. Thyroid hormone replacement is associated with decrease in HbA1c level, which is influenced by increased erythropoiesis rather than by changes in glucose level [35].

We aimed to identify the frequency of thyroid dysfunction in patients with T2DM in hospital-based health care setting. Furthermore, due to the cross-sectional nature of this study, the observed population reflects a selected yet comprehensive group of patients rather than the general population. In addition, the current study population may appear limited in size and therefore may underestimate the true frequency of thyroid dysfunction in patients with T2DM [36].

We conclude that despite the limitations of this hospital-based retrospective study, hypothyroidism is highly prevalent in cohort of Saudis with T2DM. The majority of our patients with primary hypothyroidism were predominantly males. These two observations remain to be validated by population-based studies. In the absence of registry data, larger cooperative studies involving diverse population samples from multiple centers could help to provide further information on the true frequency nationally. Based on a high prevalence of hypothyroidism among Saudi T2DM patients, routine screening for hypothyroidism is highly recommended in Saudi diabetic population.

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