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**Research Article** 

# The Prevalence of Hypothyroidism in Patients with Type 2 Diabetes Mellitus in Saudi Community based Hospital a Retrospective Single Centre Study

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#### **Abstract**

#### **Background and Objective**

The association between diabetes and thyroid dysfunction were studied. To estimate retrospectively the frequency of hypothyroidism in patients with type 2 diabetes (T2DM) in Saudi community-based hospital.

#### Design

We analyzed retrospectively 3760 participants whom are between the age 20 to 98 years. All patients were from the population of the Primary health centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. All data were collected on the basis of a review of electronic medical data. Patients with TSH above the normal range of TSH for our laboratory reference (4.2 MIU/L, history of hypothyroidism and taking thyroid replacement therapy were included. Patient who are pregnant were excluded.

#### Results

Out of the initial screening of 6023 subjects, 3760 subjects were included. There were 861 (22.9%) male and 2899 (77.1%) were female with mean age  $44.9\pm15.8$ . The mean TSH value was  $4.3\pm8.1$ . Among them we found 1521 (40.7%) and 1086 (28.9%) cases with T2DM and hypothyroidism respectively. Among cases of T2DM, there were 467 (30.7%) with hypothyroidism. There were 86 (18.4%) cases were male and 381 (81.6%) were female with male to female ratio of 1 to 4.4, p<0.0001. Cases with hypothyroidism were nonsignificantly older than cases with no hypothyroidism,  $55.2\pm12.6$  vs.  $54.9\pm13.2$  respectively, p=0.6. Cases with hypothyroidism were nonsignificantly showed no differences in HbA1c than cases with no hypothyroidism,  $7.9\pm2.3$  vs.  $8.1\pm2.1$  respectively, p=0.2. Hypothyroidism was more prevalent in the sixth decade (32%), figure 1. Hypothyroidism was significantly more prevalent in females between the third to the seventh decades as compared to males. Male was no significantly more prevalent than females in the eighth and ninth decades.

#### Conclusion

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 females. 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.

Keywords: Hypothyroidism; Type 2 Diabetes; Saudi Arabia

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## 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 dysfunctions 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. The prevalence of spontaneous hypothyroidism is between 1% and 2%, and it is more common in older women and ten times more common in women than in men [4]. Diabetes Mellitus is the commonest endocrine disorder, leading cause of death worldwide [5]. The World health organization estimated diabetes prevalence was 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million 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]. The strong link between diabetes and thyroid diseases encouraged the American Diabetes Association (ADA) to propose that people with diabetes must be checked periodically for thyroid dysfunction [9]. Thyroid disease should be screened annually in diabetic patients to detect asymptomatic thyroid dysfunction [10]. A number of studies estimated prevalence of thyroid dysfunction among diabetes patients ranging from 2.2-17% [11-13]. However, fewer studies have estimated higher prevalence of thyrodiabetics i.e. 31% and 46.5% respectively. [14,15] The prevalence of thyroid dysfunction among Saudi diabetic patients was reported to be 16-28.5% of which 25.3% had hypothyroidism [16,17]. 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 and environmental factor and 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 type 2 DM and hypothyroidism in patients with type 2 diabetes (T2DM) in a cohort of Saudi population.

#### **Methods**

We analyzed retrospectively 3760 participants whom are between the age 20 to 98 years. All patients were from the population of the Primary health centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. All data were collected on the basis of a review of electronic medical data. Patients with Thyrotropin level (TSH) above the normal range of TSH for our laboratory reference, history of hypothyroidism and taking thyroid replacement therapy were included. Patient who are pregnant were excluded. The study designed to investigate hypothyroid in T2DM by estimation of TSH among Saudi adult males and females

to determine the prevalence hypothyroidism in studies population in order to compare the result to other population worldwide. The reference range values of TSH 0.22-4.2 MIU/L, Free T4 12.0-22.0 pmol/L. Participants were defined as having T2DM according to self-report, clinical reports, use of antidiabetic agents and HbA1c (≥6.5). [18] HbA1c was expressed as percentage. High performance liquid chromatography was used. The total number of cohorts were separated on basis of age values into eight groups: <20 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years and ≥80 years.

## Statistical Analysis

Continuous variables were described using means and Standard Deviations. Univariate analysis of baseline demography both between groups, were accomplished using unpaired t-test and Chi square test were used for categorical data comparison. P value <0.05 indicates significance. The statistical analysis was conducted with SPSS version 22.0 for Windows.

## Results

Table 1: Base line characteristic of total population.

Parameters		Total (3760)	
Age (years)		44.9±15.8	
Gender	Male	861 (22.9)	
	Female	2899 (77.1)	
Type 2 diabetes		1521 (40.5)	
Hypothyroidism		1086 (28.9)	
HbA1c		7.4 ±2.2	
TSH (mIU/l)		4.3 ±8.1	
FT4 (pmol/l)		14.9 ±3.1	

**Table 2:** Base line characteristic and comparison between patients with type 2 diabetes with and without hypothyroidism.

Parameters		Type 2 diabetes with hypothy- roidism 467 (30.7)	Type 2 diabetes without hypothy- roidism 1054 (69.3)	P value
Age (y	rears)	55.2±12.6	54.9±13.2	0.6
Gender	Male	86 (18.4)	337 (32.0)	<0.0001
	Female	381 (81.6)	717 (68.0)	
HbA1c		7.9±2.3	8.1±2.1	0.2
TSH (mIU/l)		9.6±13.3	2.1±0.9	<0.0001
FT4 (pmol/l)		14.6±3.0	15.4±2.6	<0.0001

Out of the initial screening of 6023 subjects, 3760 subjects were included. There were 861 (22.9%) male and 2899 (77.1%) were female with mean age  $44.9\pm15.8$  (Table 1). The mean TSH value was  $4.3\pm8.1$ . Among them we found 1521 (40.7%) and 1086 (28.9%) cases with T2DM and hypothyroidism respectively. Among cases of T2DM, there were 467 (30.7%) with hypothyroidism (Table 2). There were 86 (18.4%) cases were male and 381 (81.6%) were female with male to female ratio of 1 to 4.4, p<0.0001. Cases with

hypothyroidism were nonsignificantly older than cases with no hypothyroidism,  $55.2\pm12.6$  vs.  $54.9\pm13.2$  respectively, p=0.6. Cases with hypothyroidism were nonsignificantly showed no differences in HbA1c than cases with no hypothyroidism,  $7.9\pm2.3$  vs.  $8.1\pm2.1$  respectively, p=0.2. Hypothyroidism was more prevalent in the

sixth decade (32%) (Figure 1). Hypothyroidism was significantly more prevalent in females between the third to the seventh decades as compared to males (Figure 2). Male was nonsignificantly more prevalent than females in the eighth and ninth decades (Figure 2).

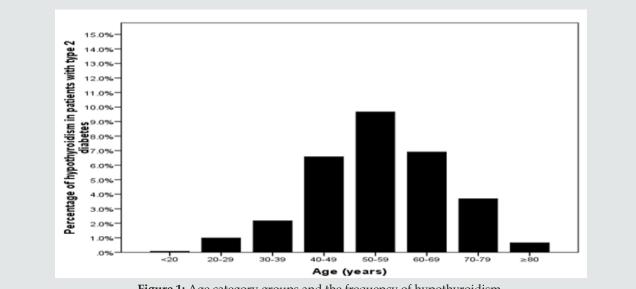


Figure 1: Age category groups and the frequency of hypothyroidism.

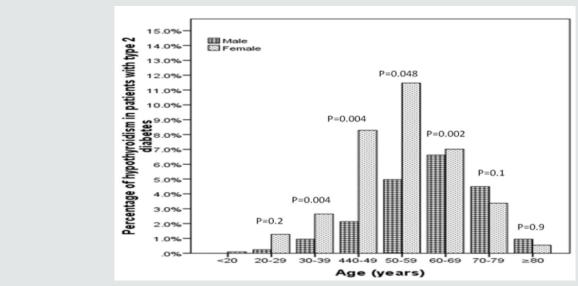


Figure 2: Age category groups and the frequency of hypothyroidism in correlation to gender.

# Discussion

The current study revealed that hypothyroidism was found in 30.7% in patients with T2DM. The association between diabetes and thyroid disease is well known. Thyroid diseases are also common in the general population. Diseases of the thyroid are of great importance because most are amenable to medical management. There is a great difference in the prevalence of the thyroid diseases in the general population, ranging from6.6% to 13.4% [19,20]. Large scale studies of thyroid dysfunction in the United States have reported prevalence of 6.6% in the general population [21,22].

The first studies were published in year 1997 [23]. Therefore, several studies in different countries were conducted to estimate the prevalence of thyroid disease in diabetic patients. Some studies estimated the prevalence to be 10–24% [24]. Our finding is more than that has been reported by Akbar et al. [16] and Al-Geffari et al. [17] of 16% in 2006 and 25.3% in 2013 respectively. In this study, we report the highest prevalence of thyroid dysfunction in T2DM patients when compared with other communities, shown by the Scotland study to be 13.4% among both Type 1 diabetes and T2DM or by the Jordanian study, where it was 12.5% among Type 2 diabetes. [11,13] Studies from Libya and Oman showed the

prevalence of hypothyroidism to be 2.3% and 406% respectively [25]. A meta-analysis data in a study of 10920 patients with diabetes which revealed a mean frequency of thyroid disease of 11% [26].

In general population, it was documented by many authors that hypothyroidism is more common in females [27-32]. In the present study, the prevalence of thyroid disorders was more in females as compared to males (81.6% versus 18.4%). This was statistically significant, P value of <0.0001. Our results are consistent with studies of Celani, et al. [14], Papazafiropoulou et al. [23], Babu et al. [33] and Michalek et al. [34], Vondra, et al. [35] but our findings seemed to be relatively higher [36]. Thus, the prevalence of thyroid disorders in diabetic patients is influenced by female gender. Interestingly, the present study observed nonsignificant higher in TSH among T2DM females in compression with males, 10.0±14.3 vs. 7.7±6.8, p=0.1. In concurrent with previous finding that, estrogen hormone has direct role in thyroid follicular cells, and its role in thyroxine binding globulin (TBG) [16], explain higher level of TSH and FT3 in T2DM females [25,37].

It is reported that DM appears to influence thyroid function in at least two sites, one at the level of hypothalamic control of TSH release and the other at the conversion of thyroxine to triiodothyronine in the peripheral tissues [38]. Perros et al. [11] reported that "the thyroid hormones, triiodothyronine and tetraiodothyronine are insulin antagonists that also potentiate the action of insulin indirectly." TRH synthesis decreases in diabetes, and this could be responsible for the occurrence of low thyroid hormone levels in diabetics. In the literature, it is well known that thyroid hormones directly control insulin secretion, thus affecting the control of diabetes. In hypothyroidism, there is a reduction in glucose induced insulin secretion by beta cells, and the response of beta cells to glucose or catecholamine is increased in hyperthyroidism due to increased beta cell mass. Moreover, insulin clearance is increased in thyrotoxicosis. [39,40] However, in our study, we failed to establish the association between T2DM with hypothyroidism and T2DM without hypothyroidism represented by HbA1c,  $7.9\pm2.3$  and  $8.1\pm2.1$  respectively, p value 0.2. This can be explained by the other various factors that can play role in the control of diabetes including patients lifestyle, compliance to treatment, other used medications, and the duration of diabetes and thyroid disease.

Primary hypothyroidism occurs in all ages, but it is usually more prevalent, in both community- and hospital-based populations, in older people in their sixth and seventh decades. [28,32] Out of 1521 diabetic patients who had hypothyroidism, 31.5% of patients had age 50-59 years. Thus, the prevalence of thyroid disorder was found to be lower in patients with more age. The results of present study are in disconcordance with the previous studies of Feely, et al. [8], Michalek, et al. [34], Whitehead, et al. [40], Vondra, et al. [41], Moulik, et al. [42] and Johnson et al, who also found high prevalence of thyroid disorders in diabetic patients with advancing age [43].

We aimed to identify the frequency of hypothyroidism in patients with T2DM in primary health care setting. Furthermore, due to the retrospective nature of this study, the observed population reflects a selected yet comprehensive group of patients rather than the general population. Our study could be limited by the question of clustering of cases within the study region and the effect that might have on our estimates, in addition, the current study population may appear limited in size and therefore may underestimate the true frequency of hypothyroidism in patients with T2DM. In addition, the study shares the limitations of all retrospective studies.

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 females. 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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