

The Relation of Glycemic Control and Primary Hypothyroidism in Saudi Patients with Type 2 Diabetes Mellitus

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Abstract

Background and objective: The associations between diabetes and hypothyroidism have long been reported. Thus, we conducted a cross sectional study to find out the relationship between Type 2 Diabetes Mellitus (T2DM) and hypothyroidism in Saudi patients with T2DM.

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 1168 patients with T2DM were included in this study. Average age of the study population was 55.1 ± 16.2 . Hypothyroidism was present in 92 (7.9%) with males were non-statistically significant more prevalent than females in patients with HbA1c <7 and $\geq 7\%$. There was a trend up as age advanced with females were statistically significant more prevalent than males in the fifth decade ($p=0.01$).

Patients with HbA1c ≥ 7 were statistically significant older compared to patients with HbA1c <7 ($p=0.005$) with females were statistically significant more prevalent in patients with HbA1c <7 and ≥ 7 , (61.6 vs 38.4% and 75 vs 25%) respectively, $p<0.0001$. TSH was statistically significant higher in patients with HbA1c ≥ 7 compared to patients with HbA1c <7 ($p=0.02$). FT4 was statistically significant lower in patients with HbA1c ≥ 7 compared to patients with HbA1c <7 ($p=0.01$). HbA1c was found to be an independent predictor of TSH level ($P=0.02$).

A statistically significant positive correlation was observed between TSH and HbA1c ($r=0.06$, $P=0.04$). Also, a significant negative correlation was observed between FT4 and HbA1c ($r=-0.068$, $P=0.03$).

Conclusion: The frequency of primary hypothyroidism was high with poor glycemic control in patients with T2DM.

Keywords: Hypothyroidism; Glycemic control; Type 2 Diabetes

Introduction

Diabetes mellitus and thyroid diseases are common endocrine disorders. Diabetes and thyroid disorders have been shown to influence each other and associations between both conditions have long been reported [1,2]. On one hand, diabetes affects thyroid function tests to variable extents [3].

Thyroid disorders are common with variable prevalence. The most common type of thyroid dysfunction in patients with type 2 diabetes mellitus (T2DM) is hypothyroidism. It results in reduced hepatic glucose production. Moreover, impaired insulin stimulated glucose utilization in peripheral tissues has been reported in primary hypothyroidism which accounts for insulin resistance [4].

In the NHANES III study, a survey representing the US population, hypothyroidism was found in 4.6% [5]. Perros P, et al. [6] demonstrated an overall prevalence of 13.4% of thyroid diseases in diabetics where

hypothyroidism was found in 0.9%. Recently, a prevalence of 12.3% was reported among Greek diabetic patients and 16-30.7% of Saudi patients with T2DM were found to have thyroid dysfunction [7-9]. In Jordan, a study reported that thyroid dysfunction was present in 12.5% of patients with T2DM where the prevalence of hypothyroidism was 6.6% [10].

Several studies have been conducted to find out the prevalence of hypothyroidism in patients with T2DM but only few studies have compared the levels of glycemic status with hypothyroidism in patients with T2DM. The present study was carried out to find out the interrelation between hypothyroidism and glycemic status in Saudi patients with T2DM.

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 1168 patients who were diagnosed as T2DM on the basis of ADA criteria [11]. Patients who are pregnant were excluded. Thyroid stimulating hormone (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 [12]. High performance liquid chromatography was used. HbA1c was expressed as percentage. Primary hypothyroidism was defined as an elevated TSH >4.2 mIU/l and decreased serum levels of FT4 below the reference range [13]. The total number of cohort was separated on basis of age values into six groups: 20-29, 30-39, 40-49, 50-59, 60-69 and ≥ 70 years.

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. Logistic regression analysis was carried out to identify the independent predictors of primary hypothyroidism considering age, gender and HbA1c as risk factors and to estimate Odds Ratio (OR) and 95% CI. 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 1168 subjects with T2DM were included in this study. Average age of the study population was 55.1 ± 16.2 (Table1). 31.7% was male and 68.3% was female. Mean HbA1c (%), TSH and FT4 were 7.4 ± 2.0, 3.3 ± 4.8 mIU/l and 13.7 ± 3.2 pmol/L respectively. Primary Hypothyroidism was present in 92 (7.9 %) with males were non-statistically significant more prevalent than females in patients with HbA1c <7 and ≥ 7% (Figure 1). There was a trend up as age advanced with females were statistically significant more prevalent than males in the fifth decade (p=0.01) (Figure 2).

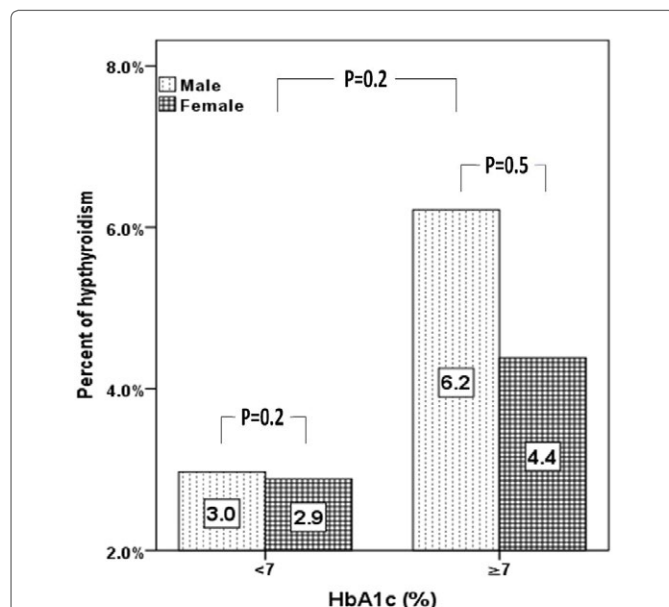


Figure 1: Prevalence of hypothyroidism between gender in relation to HbA1c categories.

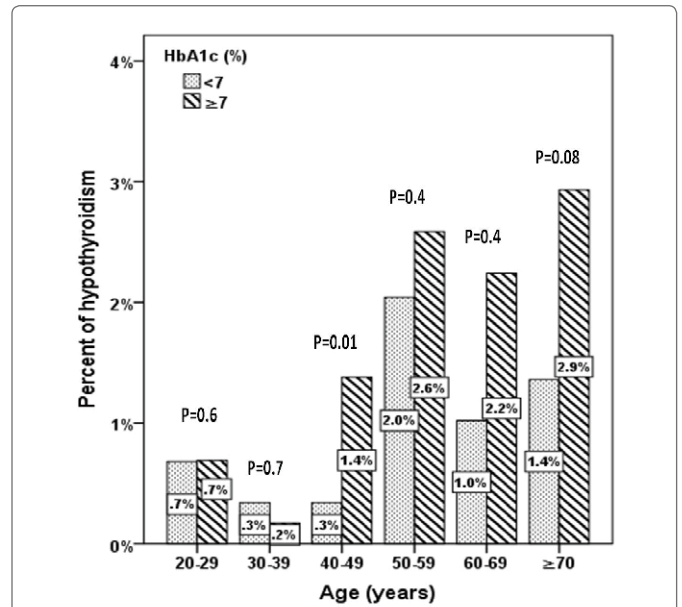


Figure 2: Prevalence of hypothyroidism between HbA1c categories in relation to age distribution.

Table 1: Baseline characteristic of total population.

Parameters		Total (1168)
Age (years)		55.1 ± 16.2
Gender	Male	370 (31.7)
	Female	798 (68.3)
HbA1c (%)		7.4 ± 2.0
TSH (mIU/l)		3.3 ± 4.8
FT4 (pmol/l)		13.7 ± 3.2

Patients with HbA1c ≥ 7 were statistically significant older compared to patients with HbA1c < 7 (p=0.005) with females were statistically significant more prevalent in patients with HbA1c < 7 and ≥ 7, (61.6 vs 38.4% and 75 vs 25%) respectively, p<0.0001 (Table 2). TSH was statistically significant higher in patients with HbA1c ≥ 7 compared to patients with HbA1c < 7 (p=0.02). FT4 was statistically significant lower in patients with HbA1c ≥ 7 compared to patients with HbA1c < 7 (p=0.01).

In order to identify the independent factors affecting primary hypothyroidism, a multivariate regression model was constructed using hypothyroidism as the dependent factor. The constructed model is shown in table 3. Age, gender and HbA1c were the independent predictors of primary hypothyroidism. In the constructed model, HbA1c was found to be an independent predictor of TSH level (P=0.02).

A statistically significant positive correlation was observed between TSH and HbA1c (r=0.06, P=0.04) (Figure 3). Also, a significant negative correlation was observed between FT4 and HbA1c (r=-0.068, P=0.03) (Figure 4).

Discussion and Conclusion

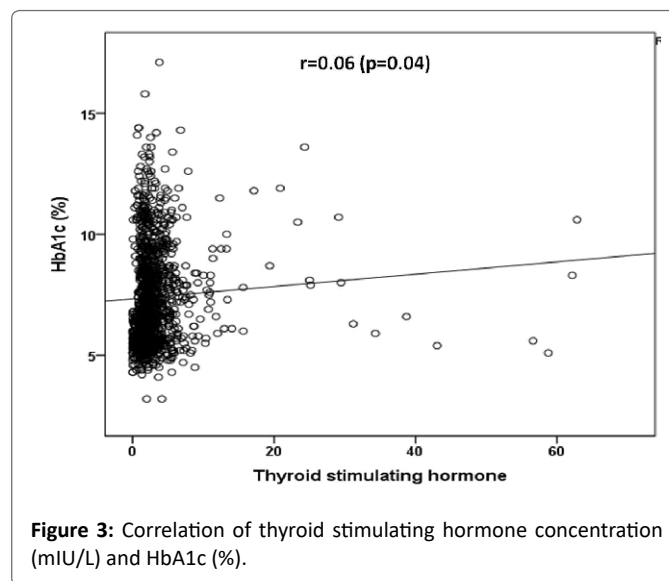
Among the endocrinal metabolic diseases diabetes occupies the major share. There is a complex interaction between thyroid

Table 2: Characteristic of patients according to HbA1c (%).

Variable	HbA1c (%)		P values
	<7	≥ 7	
Numbers	588 (50.3)	580 (47.7)	
Age (years)	53.8 ± 16.0	56.4 ± 16.2	0.005
Gender	Male	223 (38.4)	<0.0001
	Female	347 (61.6)	
HbA1c (%)	5.8 ± 0.6	9.1 ± 1.7	<0.0001
TSH (mIU/l)	2.9 ± 4.8	3.6 ± 4.9	0.02
FT4 (pmol/l)	14.0 ± 3.8	13.4 ± 2.5	0.01
Hypothyroidism	34 (5.8)	58 (10.0)	0.009

Table 3: Regression analysis using hypothyroidism as the dependent variable.

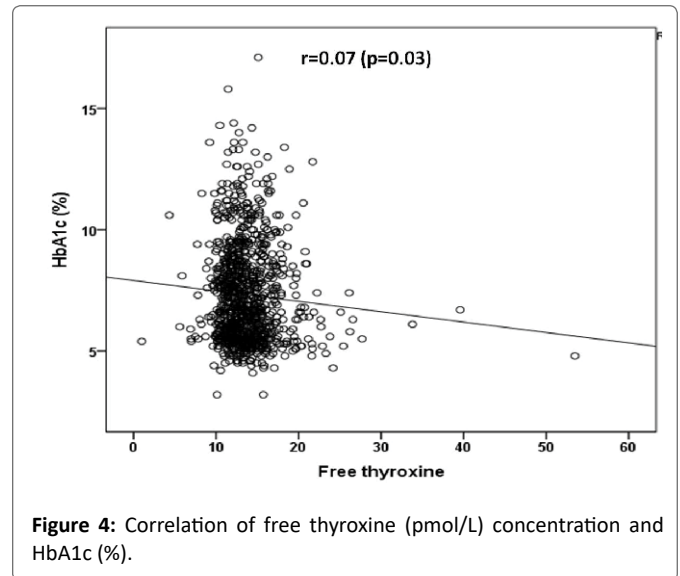
Parameters	Coefficients	95% Confidence Interval	P value
Age (years)	1.013	0.999-1.027	0.07
Gender	1.207	0.770-1.892	0.4
HbA1c ≥ 7 (%)	1.709	1.094-2.671	0.02



dysfunction and diabetes mellitus [1-3,10,14-18]. We found primary hypothyroid was present in 7.9% among the 1168 subjects with T2DM. Poor glycaemic control was associated with more prevalent of primary hypothyroidism.

In our study we found that diabetic patients with uncontrolled diabetes HbA1c ≥ 7 when compared to patients with HbA1c < 7 have statistically significant higher prevalence of primary hypothyroidism (5.8 vs 10.0%) respectively, p=0.009. These findings are supported by various studies [19-21]. Hypothyroidism falsely raises HbA1c due to decreased erythropoiesis [14].

In our study, we found that 7.9% of patients with T2DM were suffering from primary hypothyroidism. Patients with HbA1c ≥ 7 have low levels of FT4 when compared to patients with HbA1c < 7 in discordance with Uppal V, et al. [22] and Makandar DA, et al. [23]. The presence of both raised and low levels of thyroid hormones in diabetic might be due to modified Thyrotropin Releasing Hormone (TRH)



synthesis and release [14]. The hyperglycaemia seen in type-2 diabetics is known to have a negative effect on thyroid function precisely blunting the pituitary TSH response to stimulation by hypothalamic TRH. This might be due to possible alteration of post translational glycosylation of TRH hence affecting its biological activity [24]. 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 [25,26].

Our results showed a non-statistically significant difference in both males and females in relation primary hypothyroidism in diabetics with HbA1c ≥ 7 as compared to < 7. Still, sex hormones can regulate the thyroid function [27]. The difference in sex hormones may partly explain the sex-difference in the relationship between thyroid hormone levels. 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 (31.7%) than in females (68.3%), the precision and statistical power of the analysis may be lower for males.

Our result of positive correlation between HbA1c and TSH is consistent with the results by Uppal V, et al. [22] and Velija-Asimi Z, et al. [28]. Uppal V, et al. [22] correlated the levels of insulin and HbA1c with thyroid hormones and reported that the levels of HbA1c have a positive and significant correlation with TSH level. In addition, we found a negative correlation between FT4 and HbA1c and these findings are supported by various studies who stated that derangement in glycaemic control influences the thyroid hormone levels [14,19,20].

We aimed to identify the relation of glycaemic control and primary hypothyroidism in Saudi patients in hospital-based health care setting. In our 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 relation of glycaemic control and primary hypothyroidism in patients with T2DM.

We conclude that despite the limitations of this hospital-based retrospective study, the frequency of primary hypothyroidism was high with poor glycaemic control in patients with T2DM. 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 relation nationally.

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Funds for Study

Nil

Conflict of Interest

None

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