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Original article

Evaluation of Thyroid Dysfunction among Libyan Patients with Type-2 Diabetes Mellitus

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ABSTRACT

Thyroid disorders are more common in people with diabetes compared to the general population. This study aimed to evaluate the prevalence of thyroid disorders in Libyan patients with type 2 diabetes mellitus (T2DM) and the association between thyroid dysfunction and T2DM parameters. The current study included a total of 50 participants: 40 with T2DM, and 10 healthy volunteers. They were divided into three groups: G1 (10 healthy controls), G2 (30 patients with T2DM [DM]), and group 3 [10 patients with T2DM and thyroid dysfunction (DM+TD)]. The average age of control and patients was 33.1±10.9 years and 55.3±12.8 years, respectively. The diabetes profile (FBS, RBS, and HbA1c), and thyroid profile (TSH, FT3, and FT4) of each participant were assessed. The levels of FBG, RBS, and HbA1c showed a highly significant (P=0.000) increase in the DM and DM+TD groups compared to the healthy control group. Additionally, the findings indicated that the majority of the participants with diabetes (75%) had normal thyroid function, while 25% had thyroid disorders., Among the patients with thyroid disorders, 10% had subclinical hypothyroidism, 7.5% nonthyroidal illness syndrome (NITS), and 7.5% exhibited high levels of TSH, FT4, and FT3.,. The prevalence of thyroid disorders was higher in women (22.5%) than in men (2.5%). None of the diabetic patients showed hyperthyroidism in this study. The study concluded that 25% of patients with type 2 diabetes mellitus had a thyroid disorder, and subclinical hypothyroidism was more prevalent. Also, the current study showed that female gender and family history of thyroid disorders are important risk factors.

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INTRODUCTION

The status of diabetes has altered over the past 30 years from being seen as a minor disease affecting the elderly to one of the leading causes of morbidity and mortality affecting young and middle-aged adults [1]. According to the International Diabetes Federation, there are over 463 million individuals with diabetes mellitus worldwide, and this number is likely to rise to 578 million by 2030 [2].

Type 2 diabetes mellitus (T2DM) is a complex disorder characterized by insulin resistance and varying degrees of insulin secretory defects, leading to reduced insulin secretion from the pancreatic beta cells. It is a metabolic disease associated with high blood sugar levels and changes in carbohydrate, protein, and fat metabolism [3]. Obesity, lack of

exercise, unhealthy food, insulin resistance, a family history of diabetes, and genetic factors are risk factors for T2DM [4].

Thyroid hormones play an important role in the body's metabolism, including regulating carbohydrate metabolism and insulin secreted by the pancreas [5]. Studies have revealed a reciprocal relationship between thyroid problems and diabetes [6]. Patients with T2DM are more likely to experience thyroid disorders than people without diabetes, and this can have a negative impact on metabolic management [7]. People with hypothyroidism and those with lower free thyroxine (FT4) levels in the reference range have an increased risk of developing T2DM [8]. Thyroid hormones may directly impact insulin secretion. Conversely, diabetes can disrupt the conversion of thyroxine (T4) to triiodothyronine (T3) in peripheral tissues and alter levels of thyroid stimulating hormone (TSH) at the level of the hypothalamus, both of which can affect thyroid function [7]. This study aimed to evaluate the prevalence of thyroid disorders in Libyan patients with type 2 diabetes mellitus (T2DM) and the association between thyroid dysfunction and T2DM parameters.

METHODS

Study population

The population of the current study consists of 10 healthy individuals in group 1, comprising 6 males and 4 females. The patient group includes 40 individuals of both sexes who attended the outpatient Department of Diabetes and Endocrinology Hospital Salah El-din and Polyclinic Abusalim, with 31 females and 9 males. The patients were classified into two groups: 30 patients (75%) in group 2 have T2DM, and 10 patients (25%) in group 3 have both T2DM and thyroid dysfunction (TD). Demographic data, including age, gender, weight, height, family history of diabetes, family history of TD, and duration of diabetes, was collected via a questionnaire given to each participant. Pregnant women, patients with Type 1 diabetes mellitus, and individuals with a history of thyroid surgery were excluded from this study.

Blood collections

The study samples were obtained from May to July 2023. Venous blood samples of 5 milliliters were collected from the patients and healthy subjects after an overnight fast. The blood sample was separated into two aliquots, the first of which (1 ml) was immediately transferred into a tube containing ethylene diamine tetra acetic acid (EDTA) to estimate glycated hemoglobin (HbA1c). The second one was transferred into a plain tube and left for clotting at room temperature for 30–60 minutes. The serum was then separated by centrifugation at 3000 rpm for 10 minutes. Serum was used to estimate fasting blood glucose (FBS), random blood glucose (RBS), and thyroid function tests (FT3, FT4, and TSH).

Biochemical assays

Serum TSH, FT3, and FT4 levels were estimated using a Roche electrochemiluminescence immunoassay (Roche Cobas E411 automated analyzer). HbA1c, FBS, and RBS were assessed using the Roche Cobas Integra 400 Plus analyzer.

Statistical analysis

One one-way ANOVA test was used to compare more than 2 independent groups, followed by the Post Hoc Tukey test. A student t-test was used to compare two independent groups. Categorical variables were expressed as a percentage and analyzed by the chi-square test. Pearson correlation was used to assess the relationship between thyroid and diabetes profiles. P-values below 0.05 were considered statistically significant.

RESULTS

The average age of the control group and patients was 33.1±10.95 years and 55.3±12.8 years respectively (P=0.000). In the control group (n=10), 40% were female and 60% were male, while the majority of patients were female (77.5%) and male (22.5%) (Figure 1).

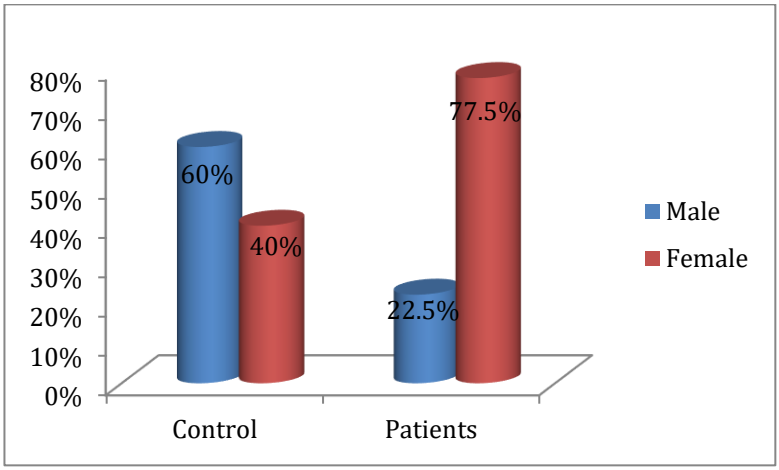

***Figure 1. Distribution of gender among control and patients'* group**

There was a significant (P=0.000) difference in the age of the DM (56.1±12.1 years) and DM+TD (53.6±12.2 years) groups compared to the control (33.1±10.95 years), while there was no significant difference between the DM and DM+TD groups (P=0.585). Regarding the mean weight of healthy individuals (75.5±17.15 kg) and patients with DM (78.1±15.2 kg) and DM+TD (85.1±14.6 kg), there was no statistically significant difference between the control and two groups of patients (P=0.374) as shown in Table 1.

The level of FBS showed a highly significant (p=0.000) increase in the DM (209.1±79.7 mg/dl) and DM+TD (184.8±41.1 mg/dl) groups compared to the healthy control group (74.4±7.4 mg/dl), as shown in Table (1); however, the difference between the DM and DM+TD groups was insignificant (P = 0.061) Table 2. Similarly, the RBS levels in the DM and DM+TD groups, respectively, 294.8±130.4 mg/dl and 263.9±100.6 mg/dl, were found to be significantly different (P=0.000) when compared with the control group (100±±10.47 mg/dl) (Table 1).

Table 1. Comparison between control (G 1), DM (G 2) and DM+TD (G 3)

Variable	Control (G 1)	DM (G 2)	DM+TD (G 3)	P-value
Age (years)	33.1±10.95	56.1±12.1	53.6±12.2	0.000
Weight (kg)	75.5±17.15	78.1±15.2	85.1±14.6	0.374
Hb1AC (mmol)	5.6±0.38	10.6±2.7	10.1±2.7	0.000
FBS (mg/dl)	74.4±7.44	209.1±79.7	184.8±41.1	0.000
RBS (mg/dl)	100±10.47	294.8±130.4	263.9±100.6	0.000
TSH (µIU/ml)	2.8±2.12	2.7±0.89	13.99±9.75	0.000
FT3 (pmol/l)	4.4±0.98	3.99±1.44	5.2±2.95	0.171
FT4 (pmol/l)	17.79±1.45	17.02±2.49	23.27±6.78	0.049

P-value<0.05 was considered statistically significant. Data are presented as mean ± SD. Abbreviations: DM, Diabetes Mellitus; TD, Thyroid Dysfunction; G, group; Hb1AC, Glycated hemoglobin; FBG, Fasting Blood Glucose; RBS, Random Blood Sugar; TSH, Thyroid Stimulating Hormone; FT3, Free Triiodothyronine; FT4, Free Thyroxin.

In addition, there was also a highly significant difference (P=0.000) between the control, DM and DM+TD groups regarding HbA1c: 5.6±0.38 mmol, 10.6±2.7 mmol, and 10.1±2.7 mmol, respectively, as presented in Table 1. In contrast, there was no substantial difference between the DM and DM+TD groups in RBS and HbA1c (Table 2).

The mean values of TSH in non-diabetic individuals and the DM group were 2.8 ± 1.12 (µIU/ml) and 2. 7 ± 0.89 (µIU/ml), respectively, compared to the DM+TD group 13.99± 9.75, and this difference was highly significant (P=0.000). The FT3 mean values in the control, DM, and DM+TD groups were 4.4±0.98 (pmol/l), 3.99±1.44, and 5.2±2.95 (pmol/l, respectively), but this difference was not statistically significant (P = 0.171) (Table 1). The level of FT4 was statistically substantially higher (0.049) among the DM+TD group than in other groups.

Additionally, a non-significant difference was observed in the mean period of diabetes (15.63 ± 6.68 vs. 11.88 ± 9.1, respectively) between patients with thyroid dysfunction and diabetic patients without thyroid disorder (P= 0.221). Also, there was no statistical difference in the percentage of patients with a family history of diabetes between the two groups (P=0.225). However, patients with thyroid dysfunction had a considerably greater proportion of patients with a positive family history of thyroid disease (90%) compared to diabetic patients with normal thyroid function (3.3%) (P=0.011) as shown in table 2.

Table 2. Comparison between DM (G 2) and DM+TD (G 3)

Variables	DM (G2)	DM+TD (G3)	P-value
Age (years)	56.1±12.1	53.6±12.2	0.585
Weight (kg)	78.1±15.2	85.1±14.6	0.226
Duration of diabetes (years)	11.88±9.1	15.63±5.36	0.226
Family history of diabetes†	63.6%	88.8%	0.221
Family history of thyroid disease	3.3%	90%	0.011
Hb1AC (mmol)	10.6±2.7	10.1±2.7	0.404
FBS (mg/dl)	209.1±79.7	184.8±41.1	0.061
RBS (mg/dl)	294.8±130.4	263.9±100.6	0.244
TSH (µIU/ml)	2.7±0.89	13.99±9.75	0.000
FT3 (pmol/l)	3.99±1.44	5.2±2.95	0.085
FT4 (pmol/l)	17.02±2.49	23.27±6.78	0.027

P-value<0.05 was considered statistically significant. Data are presented as mean ± SD, Data presented as (%). Abbreviations: DM, Diabetes Mellitus; TD, Thyroid Dysfunction; G, group; Hb1AC, Glycated hemoglobin; FBG, Fasting Blood Sugar; RBS, Random Blood Sugar; TSH, Thyroid Stimulating Hormone; FT3, Free Triiodothyronine; FT4, Free Thyroxin.

Table 3 shows a considerable correlation (r=0.049, P<0.05) between HbA1c and FT3, while there was no significant association between other diabetic parameters and thyroid profile.

In this investigation, out of 40 diabetic subjects studied, 75% were euthyroid, 25% had thyroid dysfunction, 10% exhibited subclinical hypothyroidism, 7.5% had nonthyroidal illness syndrome (NITS), and 7.5% showed high levels of TSH, FT4, and FT3. The prevalence of thyroid disorders was higher in women (22.5%) than in men (2.5%). None of the diabetic patients showed hyperthyroidism in this study.

Table 3. Correlation of diabetic markers in all participants with thyroid profile

Variables	TSH	FT3	FT4
Hb1AC	0.900	0.049*	0.356
FBG	0.154	0.775	0.878
RBS	0.261	0.523	0.610

**Significant P value <0.05. Abbreviations: Hb1AC, Glycated hemoglobin; FBG, Fasting Blood Glucose; RBS, Random Blood Sugar; TSH, Thyroid Stimulating Hormone; FT3, Free Triiodothyronine; FT4, Free Thyroxin.*

DISCUSSION

There have been many studies conducted globally on thyroid dysfunction in the diabetic population; however, until recently, few studies were done on thyroid dysfunction in Libyan patients with T2DM. Therefore, this study sought to evaluate the prevalence and features of thyroid dysfunction among Libyan individuals with T2DM who attended the outpatient Department of Diabetes and Endocrinology Hospital Salah El-din and Polyclinic Abusalim.

The findings indicated that among the three groups, there were highly significant differences in age, FBS, RBS, HbA1c, TSH, and FT4 while regarding FT3 and weight, no statistically significant result was detected, this is consistent with the findings of earlier research [9, 10] which revealed that a substantial difference was found between control and diabetic subjects in HbA1c, TSH and FT4. Moreover, levels of TSH, FT3, and FT4 between 340 patients with T2DM and 120 healthy individuals ages 18–90 were found to be significantly lower in diabetic patients compared to the healthy group [11]. On the contrary, it has been reported that there is no significant difference in the thyroid profile (TSH, FT3, and FT4) between healthy and diabetic groups [12].

The current study showed that the two groups of diabetic patients with and without thyroid dysfunction [G2 (DM), G3 (DM+TD)] differed insignificantly in age, weight, duration of diabetes, family history of diabetes, FBS, RBS, Hb1Ac, and FT3, but significant differences were found in TSH, FT4, and family history of thyroid disease, as presented in Table 2. These results are in accordance with a study by Al-Geffari et al. [13] conducted in Saudi Arabia, which found insignificant differences between diabetic subjects with or without thyroid disease in age, weight, family history of diabetes, FBS, Hb1Ac, and FT3, and substantial differences in TSH and FT4 and family history of thyroid disease.

According to the results of this study, 25% of the diabetes patients exhibited thyroid dysfunction; of these, 10% had subclinical hypothyroidism, 7% had NITS, and 7% had high levels of TSH, FT3, and FT4; the remaining 75% showed euthyroid. These findings agree with the study of Abidi *et al*. [12], who investigated the association between diabetes

and thyroid hormone disorders in 100 diabetic patients and 50 non-diabetic subjects of both sexes. The results of the diabetic group showed that 78% were euthyroid and 22% had thyroid abnormalities.

Moreover, this result is consistent with the results obtained by other studies, which reported that the prevalence of thyroid dysfunction was 21.9% in Bangladesh (Kamrul-Hasan et al., 2018) [14] and 22% in India (Abidi *et al*., 2020) [12]. The slightly different rates observed among various studies may be a result of changes in sample size, variations in the estimate technique, as well as additional autoimmune elements in the population under study (Vamshidhar et al., 2020) [15], or could be due to variations in ethnicity and local food habits (Bukhari et al., 2022) [10]. However, the results of the current study differ from the previous study reported by Ahmed et al. [16] who found that thyroid dysfunction was 9.5% in diabetic patients in western Libya (Surman).

The most frequent explanations for this unusual pattern of thyroid function tests (excessively high levels of TSH, FT3, and FT4) that were observed in 3 cases of this study are assay interference, medication side effects (such as amiodarone or heparin), or thyroxine replacement therapy (Gurnell et al., 2011) [17]. Another reason for this unusual pattern might be pituitary adenoma, which secretes TSH, or resistance to thyroid hormone [18].

The current study found that 10% of diabetic patients had subclinical hypothyroidism. These results are in line with previous studies that showed that subclinical hypothyroidism is the most prevalent thyroid disorder in diabetic patients. [10, 13, 19-22]. Furthermore, similar results were reported by Ghimire et al. [23], who found that 14.7% of patients with T2DM in India had subclinical hypothyroidism. On the contrary, a previous study revealed that overt hypothyroidism is more prevalent (85.7%) among Egyptian females than subclinical hypothyroidism [9].

Subclinical hypothyroidism can cause episodes of critical functions, such as left ventricular diastolic disorder, anovulation, and low-density lipoprotein receptor expression, leading to increased low-density lipoprotein and reduced high-density lipoprotein cholesterol [21]. Also, Chen et al. [24] reported that there is a higher risk of cardiovascular disease and nephropathy in diabetic patients with subclinical hypothyroidism. The results of this study indicated that the prevalence of thyroid dysfunction was higher in women (22.5%) compared to men (2.5%). Numerous studies have revealed that thyroid disorders are more prevalent in females with T2DM than in male individuals [13, 20, 25]. The results obtained are also consistent with studies by Jugati and Birader [21] and Bukhari et al. [10], whose findings indicate that thyroid disorders are more common in female diabetics than in male diabetics. The direct impact of estrogen hormone on thyroid follicular cells and its influence on thyroxine-binding globulin may account for the increased frequency of thyroid dysfunction in females with T2DM [16]. Other studies also reported that thyroid disorders are more common in women than in men [10, 22, 23].

Many studies on patients with T2DM have revealed a positive correlation between increased age, female gender, obesity, thyroid peroxidase antibody and the risk of developing hypothyroidism [13, 26]. Furthermore, the results showed no apparent association between the thyroid and diabetic parameters, as no significant association was observed between them in this study, except that a significant positive correlation was found between Hb1Ac and FT3. This is harmonized with the findings of Nobre et al. (27), in contrast to those of Billic-Komarica et al. [20], who reported a significant positive correlation between HbA1c and TSH.

CONCLUSION

In this study, 25% of patients with T2DM were found to have thyroid disorders, with subclinical hypothyroidism being more prevalent. Additionally, the study showed that female gender and family history of thyroid disorders are important risk factors.

Conflicts of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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تقييم مدى انتشار اضطرابات الغدة الدرقية لدى المرضى الليبيين المصابين بداء السكري من النوع الثاني

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المستخلص

تعد اضطرابات الغدة الدرقية أكثر شيوعا لدى مرضى السكري مقارنة بعامة الناس. تهدف هذه الدراسة الى تقييم مدى انتشار اضطرابات الغدة الدرقية لدى المرضى الليبيين المصابين بداء السكري من النوع الثاني (T2DM) وكذلك العلاقة بين خلل الغدة الدرقية ومؤشرات T2DM. شملت الدراسة الحالية 50 مشارك: 40 مصابا بـ T2DM و 10 متطوعين أصحاء. تم تقسيمهم الى ثلاث مجموعات: المجموعة الاولى (10 أصحاء) ، المجموعة الثانية (30 مريضاً يعانون من مرض السكري فقط DM) والمجموعة الثالثة (10 مرضى يعانون من مرض السكري وخلل في الغدة الدرقية DM+TD). كان متوسط عمر الاصحاء والمرضى 33.1 ± 10.9 و 55.3 ± 12.8 سنة على التوالي. تم تقييم مؤشرات مرض السكري (HbA1c, RBS, FBS) ومؤشرات الغدة الدرقية (TSH, FT3, FT4) لكل مشارك. أظهرت نتائج الدراسة ان مستويات HbA1c, RBS, FBS كان مرتفعا (P=0.000) في مجموعتي DM و DM+TD مقارنة بمجموعة الأصحاء. بالإضافة إلى ذلك، أشارت النتائج الى أن غالبية المشاركين المصابين بداء السكري (75%) لديهم وظائف الغدة الدرقية طبيعية، بينما كان 25% يعانون من اضطرابات الغدة الدرقية. المرضى الذين لديهم خلل في الغدة الدرقية كان منهم 10% يعانون من قصور الغدة الدرقية تحت السريري ، و 7.5% يعانون من متلازمة NITS ، و 7.5% لديهم مستويات عالية من هرمونات TSH, FT3, FT4. وكان معدل انتشار اضطرابات الغدة الدرقية أعلى لدى النساء (22.5%) مقارنة بالرجال (2.5%) . لم يظهر أي من مرضى السكري فرط نشاط الغدة الدرقية في هذه الدراسة. خلصت الدراسة الى أن 25% من من مرضى السكري من النوع الثاني يعانون من اضطراب الغدة الدرقية، وأن قصور الغدة الدرقية تحت السريري كان أكثر انتشارا. كما أظهرت أن الإناث والتاريخ العائلي لاضطرابات الغدة الدرقية من عوامل الخطر المهمة.

الكلمات الدالة. مرض السكري من النوع الثاني، إضطراب الغدة الدرقية، هرمون TSH