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Prevalence of Thyroid Dysfunction in Patients with Diabetes Mellitus

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ABSTRACT

Background: Diabetes mellitus (DM) and thyroid dysfunction (TD) are common endocrine diseases experienced clinically. The thyroid gland releases hormones that play a considerable role in terms of carbohydrate (CHO) metabolism. As a result, CHO metabolism was significantly affected among type 2 diabetes mellitus (T2DM) cases with TD compared to the non-diabetic (NDM) subjects.

Objective: To assess the prevalence of TD in diabetic cases.

Patients and Methods: This cross-sectional study investigated 193 diabetic patients. Venous samples (5 ml) were obtained from each patient via venipuncture under aseptic conditions. Body mass index (BMI), glycosylated hemoglobin (HbAlc), free tri-iodothyronine (fT3), free thyroxine (fT4) and thyroid-stimulating hormone (TSH) were evaluated.

Results: Prevalence of thyroid dysfunctions in diabetic patients was found to be (9.3%). There was a significant negative relationship between fT4 and the duration of DM, and statistically significant negative relationship between HbA1c and fT3 level. There was negative correlation between the BMI and fT3 and fT4 levels but this correlation was not statistically significant.

Conclusion: Thyroid dysfunctions were found to be more common in older females. Among the studied cases HbA1c was found to be significantly higher in hypothyroidism than cases of normal thyroid function.

Keywords: Diabetes Mellitus, Thyroid Dysfunction, Hyperglycemia, Hyperthyroidism.

INTRODUCTION

Diabetes mellitus (DM) and TD are common endocrine diseases experienced clinically. Much research has shown that DM and TD could interfere with each other's, and both conditions frequently co-occur [1]. DM is a complicated metabolic disease characterized by chronic hyperglycemia. The main two causes of DM are inadequate insulin release or insulin resistance [2].

It has been demonstrated that thyroid gland hormones could play a considerable role in terms of CHO metabolism. As a result, CHO metabolism was significantly affected among T2DM cases with TD compared to the NDM individuals [3].

The relation between DM and TD has been broadly evaluated in several studies globally since 1979. Of note, the frequency of TF in the general population varies widely [4]. Hyperglycemia has been demonstrated to be accompanied by reversible reduction in the hepatic concentration and activities of T4-5-deiodinase enzyme, reduction in T3 concentration, elevation in the level of reverse T3 and normal, low, or high level of T4 [5].

The thyroid function could be assessed by serum TSH, FT4, and FT3 values. TSH has been considered the most helpful tool for thyroid function assessment. TD could be diagnosed when there is an alteration in the serum TSH level even with normal T4 and T3 levels [6].

Hypothyroidism is the most frequent form of TD in adults; it is the case of inadequate formation of thyroid hormones. Hyperthyroidism is the rarest type of TD, characterized by abrupt weight loss, tachycardia, diaphoresis, irritability, and increased body metabolic rate [7].

AIM OF THE WORK

To evaluate the prevalence of TD in diabetic patients and to correlate the relationship between the thyroid function and the level of HBA1c in these patients.

PATIENTS AND METHODS

This cross-sectional study investigated 193 diabetic patients of both sexes who were followed up at diabetes outpatient clinic of Specialized Medical Hospital, Mansoura University, Egypt, started in July 2022. The cases were diagnosed by the clinician as diabetics according to preceding fasting plasma sugar >126 mg/dl, postprandial blood glucose >200 mg/dl, and who were receiving oral hypoglycemic medications and/or insulin, and also the patients being diagnosed as T1DM and receive insulin therapy. This study excluded pregnant females, cases with recent interventions, patients used pulse corticosteroids and/or radioiodine, and patients used amiodarone.

Clinical and anthropometric measurements:

Every patient was subjected to detailed medical history and anthropometric measurements including gender, age, residence, BMI, duration of diabetes, associated comorbidities such as hypertension, liver diseases, and rheumatoid arthritis, lines of treatment, HbAlc, fT3, fT4 and TSH.

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Blood sampling and biochemical measures:

Venous samples were obtained from the patients via venipuncture under aseptic conditions. HbA1c underwent measurement by ion exchange chromatography technique (Biosystem co. Spain). Measurement of serum levels of TSH, fT3 and fT4 was conducted by (Cobas e411, Roche Diagnostics, Germany), which worked by electrochemiluminescence immunoassay technology approach. TSH normal level is (**0.27-4.2 µIU/ml**), fT3 normal level (**0.8-2.2ng/ml**) while fT4 level range is **(5.1-14.2 µg/dl)**.

Diabetic cases with elevated TSH levels and normal fT3 and fT4 levels were diagnosed as subclinical hypothyroidism (SCH). Diabetic cases with increased TSH levels and diminished fT3 and fT4 levels were diagnosed as clinical hypothyroidism. Diabetic cases with reduced TSH levels and normal fT3 and fT4 levels were diagnosed as subclinical hyperthyroidism. Diabetic cases with reduced TSH levels and elevated fT3 and fT4 levels were diagnosed as clinical hyperthyroidism.

Ethical approval:

The study was approved by the Institutional Review Board (IRB), Faculty of Medicine, Mansoura University with code number: (MS.22.06.2048). The researcher explained the aim of the study to all participants who were free to participate in the study and had the right to withdraw at any time. Ethics, values, culture and beliefs of participants were respected. The agreement of participation was based on informed written consent. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

SPSS software, version 26, was used to analyse the data. Numbers and percentages were utilized to define the qualitative data, which were compared by chi-square test. The range and median were used to express non-normally distributed quantitative data, which were compared by Mann-Whitney test. Mean± SD was utilized for quantitative data with a normal distribution following the Kolmogrov-Smirnov test to verify normality. T-test was used to compare two independent groups with properly distributed data. The (0.05) level was used to assess the results' significance.

RESULTS

Table (1) illustrates that the studied 193 diabetic cases have mean age (51.89) years. Female patients were 69.9%. Rural residences were 50.3%. Mean body mass index was (33.71±6.77). According to the duration of DM, the median duration was **7** years and according to the methods of treatment **101** patients **(52.3%)** were using oral hypoglycemic medications.

Table (1): Characteristics, anthropometric measurements and diabetes duration and lines of treatment of the studied cases

	Total number =193	**%**
Age/years Mean ± SD (Min-Max)	51.89±10.17 (21-75)	
Sex		
Male	58	30.1
Female	135	69.9
Residence		
Urban	96	49.7
Rural	97	50.3
Height /cm	165.69±5.57	
Weight /kg	91.69±15.09	
Body mass index (kg/m^2)	33.71±6.77	
Diabetes duration /years Median (Min-Max)	7(0.02-30)	
Treatment Lines		
Oral	101	52.3
Insulin	5	2.6
Combined	87	45.1

Data expressed as percentage and Mean± SD.

Table (2) shows the distribution of the studied cases according to associated comorbidities with 46.6% of the diabetic cases studied were hypertensive.

Cardiac patients were 6.2%. Hepatic patients were 2.1% while rheumatoid and asthma patients were 1%. 48.7% of the patients had no comorbidities.

Table (2): Associated comorbidities in the studied cases

	n=193	**%**
Comorbidities	94	48.7
No	1	0.5
Acromegaly	2	1.0
Rheumatoid hypertensive	90	46.6
Hepatic	4	2.1
Cardiac	12	6.2
Asthma	2	1.0

Table (3) shows mean HBA1c value of 8.52±2.36, median value of TSH was 1.77, while median value of fT3 value was 1.2 and fT4 median value was 7.8.

According to the laboratory findings, 18 cases (9.3%) show (TD) while 175 (90.7%) show normal thyroid function. 14 patients (7.3%) of the studied patients showed SCH. Of all thyroid dysfunction patients (18 cases), SCH was the commonest type of TD (77.8%), subclinical hyperthyroidism represented (16.7%) of thyroid dysfunction cases and clinical hypothyroidism represented (5.6%) of thyroid dysfunctions.

Table (3): Lab findings and prevalence of thyroid abnormalities in the studied cases

	Total number=193	
HBA1c Mean ± SD (Min-max)	8.52±2.36 (4.3-15)	
TSH median (Min-max)	1.77 (0.18-40)	
fT3 median (Min-max)	1.2 (0.8-11.3)	
fT4 median (Min-max)	7.8 (0.8-13.5)	
Thyroid profile		
Normal	175	90.7 %
Subclinical hypothyroidism	14	7.3 %
Clinical hypothyroidism	1	0.5 %
Subclinical hyperthyroidism	3	1.6 %

Table **(4)** shows a significant negative correlation between HbA1c and fT3 level, also it shows a significant negative correlation between the duration of DM and fT4 level.

Table (4): Correlation between thyroid hormone and diabetes duration, body mass index and HbA1c among studied cases

		TSH	fT3	fT4
BMI	r	0.061	-0.110	-0.035
	P	0.396	0.126	0.625
Duration of DM	r	-0.134	-0.118	**-0.179***
	P	0.063	0.102	**0.013**
HBA1C	r	-0.007	**-0.161***	-0.085
	P	0.918	**0.025**	0.240

r: Spearman correlation coefficient, *statistically significant.

Table **(5)** shows the relation between thyroid dysfunctions and sociodemographic, diabetes and clinical characters of the studied cases, showing no statistically significant difference in both of age and sex among cases of abnormal thyroid profile versus cases of normal thyroid profile.

Table (5): Thyroid dysfunctions and sociodemographic, diabetes and clinical characteristics of the studied cases

	Total number =193	**Normal thyroid function n=175**	**Abnormal thyroid function n=18**	**test of sig.**
Age/years	193	52.05±9.94	50.28±12.38	t=0.704 p=0.483
Sex				
Male	58	55(31.4)	3(16.7)	χ^2=1.69
Female	135	120(68.6)	15(83.3)	p=0.193
Residence				
Urban	96	85(48.6)	11(61.1)	χ^2=1.03
Rural	97	90(51.4)	7(38.9)	p=0.311
Height /cm	193	165.77±5.52	164.94±6.08	t=0.595 p=0.553
Weight/kg	193	91.78±14.97	90.78±16.67	t=0.268 p=0.789
Body mass index (kg/m^2)	193	33.74±6.86	33.38±5.86	t=0.213 p=0.831
Comorbidities				
Absent	101	91(52)	10(55.6)	χ^2=0.083
Present	92	84(48)	8(44.4)	p=0.774
Diabetes duration /years	193	7(0.02-30)	7.0(0.42-30)	z=0.991 p=0.322
Treatment lines				
Oral	101	95(54.3)	6(33.3)	χ^2=3.18
Insulin-injection	5	4(2.3)	1(5.6)	p=0.204
Combined	87	76(43.4)	11(61.1)	
HBA1c	193	8.48±2.37	8.84±2.44	t=0.605 p=0.546

χ^2: Chi-Square test, t: Student t test, Z: Mann Whitney U test

DISCUSSION

T1DM and T2DM are heterogeneous diseases in which clinical presentation and disease progression could differ significantly. The thyroid hormones have a significant role in body metabolism such as CHO metabolism and pancreatic insulin secretion regulation [3,8]. Furthermore, different studies found a high incidence of diabetic adverse events in TD cases. Therefore, it is important to evaluate TD prevalence among T2DM individuals to help with good glycemic control and few complications [9].

The present study was a cross-sectional study that was conducted on 193 diabetic cases who were recruited from the outpatient endocrinology and diabetes clinic of Specialized Medical Hospital of Mansoura University.

During the conduction of this study, the incidence of TD in the studied DM cases was **9.3%**, This is in agreement with previous researches such as the study done by **Ahmed *et al***. [10] in which TD prevalence in diabetic cases has been detected (9.5%), **Subekti *et al***. [11] found that the prevalence of TD was 9.9%. Also, **Akbar *et al***. [12] showed that TD prevalence in diabetic cases was 9.5%. In contrast, **Asuti *et al***. [13] found that the prevalence of TD was 23.4%. **Elgazar *et al***. [9] displayed that TD prevalence in T2DM cases was 29%.

The most frequent TD in this study was hypothyroidism (15 cases) representing **(7.8%)** of the studied cases and **(83.3%)** of all thyroid dysfunction patients. SCH was the most frequent TD with (**7.3%)** of all studied cases and (**77.8%)** of thyroid dysfunction patients. This agrees with **Asuti *et al***. [13] who displayed that SCH (67.79%) was the most frequent among TD in diabetic cases. **Ozair *et al***. [14] had the same agreement that SCH is the most common subtype of TD with prevalence of 18.8%. Also, **Bukhari *et al***. [15] found SCH (17.4%) to be the commonest TD accompanied by T2DM, followed by hypothyroidism (8.5%), hyperthyroidism (5.0%), and subclinical hyperthyroidism (6.0%).

A review and meta-analysis revealed an increase in the risk of SCH in T2DM patients compared to that in NDM cases. In addition, the authors recorded that DM adverse events were more predominant in cases with T2DM and SCH compared to cases with T2DM and normal thyroid function [16]. This outcome was in agreement with **Han *et al.***[17] who conducted another systematic review and meta-analysis and reported the same conclusion. It was advocated that chronic hyperglycemic state of T2DM initiates the onset of SCH [18]. The prolonged decrease in assimilation of peripheral glucose results in increased TSH release in spite of having normal values of thyroid hormones [7].

In this study, female represented the majority of cases of TD, 83.3%, although results showes no statistically significant difference in sex among cases of abnormal thyroid profile versus cases of normal thyroid profile. **Hadgu *et al***. [16] found that there was a significant relationship between sex and TD, which reveals a greater incidence of TD with being female. Another study conducted on a total of 411 cases with T2DM in Saudi Arabia revealed that being female has 1.95 greater odds of having TD compared to matched-age males. TD prevalence in diabetic cases is affected by female sex, where T2DM cases that are female are more susceptible to TD development [19]. This is maybe due to the fact that sex hormones and the skewed suppression of the X chromosome are believed to be triggers for the development of hypo- or hyperthyroidism [20]. Another factor participating in the increased TD prevalence among females is the interactions between thyroid hormones and hormones that differ throughout the menstrual cycle [21].

Our study showed insignificant difference in mean age between the TD patients (50.28±12.38) compared to cases with normal thyroid profile (52.05±9.94). On other hand **Bukhari *et al***. [15] found a significant relationship of hyperthyroidism with age (57.9%) between 56 and 65 age group In addition, a significant relationship of subclinical hyperthyroidism with age was revealed with (50%) in each age group (46–55) and (56–65) years. They revealed a significant relationship between age and clinical hypothyroidism, with the condition being more prevalent (59.3%) in those aged 56 to 65.

Also, **Khassawneh *et al***. [22] said that TD prevalence was demonstrated to be considerably greater as age increased, with the greatest prevalence occurring in subjects older than sixty years old (49.8%) and the lowermost prevalence (6.4%) in the younger age group.

Although we demonstrated a negative relationship between the BMI and fT3 and fT4 levels, but this correlation wasn't statistically significant, the same result obtained by **Khassawneh *et al***. [22]. On the other side, **Elgazar *et al***. [9] and **Ogbonna *et al***. [23] found TD was found to be more common in obese diabetics in comparison with non-obese.

Leptin is an essential neuroendocrine hormone that regulates controlling TRH gene expression in the paraventricular nucleus. The correlation between increasing TSH, overweight, and SCH in certain subjects could be clarified by several theories such as iodine deficiency, autoimmune thyroiditis, and TSH receptor gene mutation [23].

According to the duration of DM we found statistically significant (–ve) correlation between the duration of DM and fT4 level. **Al-Geffari *et al***. [19] stated that DM >10 years was a risk factor for hypothyroidism. On the contrary **Asuti *et al***. [13] found insignificant correlation between TD and the duration of DM.

Our study displayed that a statistically significant (–ve) relationship was detected between HbA1c and fT3 level. Another Indian study displayed that basal HbA1c values were significantly greater in cases with hypothyroidism, in comparison with those in control subjects in spite of comparable glucose levels [13]. This also goes with the results obtained by **Ogbonna *et al***. [23] who displayed that T2DM cases with ≥ 7% HbA1c were 4.3 times more likely to acquire TD than their

counterparts with good glycemic control (HbA1c < 7%). In agreement, **Khassawneh *et al***. [22] revealed that when compared to those with HBA1c ≤ 7%, those with HBA1c ≥ 7% had a 2.55-fold increased risk of developing TD.

CONCLUSION

The prevalence of TD in DM subjects was found to be **(9.3%)** with SCH is the most common TD. Thyroid dysfunctions were found to be more common in older females. Among the studied cases HbA1c was found to be significantly higher in hypothyroidism than cases of normal thyroid function.

RECOMMENDATIONS

Measurement of thyroid function tests has to be conducted regularly as a routine clinical practice for all diabetic cases, which could permit rapid detection of SCH with subsequent reduction in morbimortality accompanied by the coexistence of TD in diabetic cases.

LIMITATIONS

The main limitations were the relatively small number of studied cases and being a single-centered study (one hospital), which cannot be generalized to the overall population. In addition, lack of studying correlation of diabetic complications with thyroid disorders is another limitation.

Conflict of interest: None.
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