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Evaluation of Thyroid Function Tests in Patients with Type 2 diabetes at Mansoura Specialized Medical Hospital and Its Relation to Cardiovascular Risk Factors

Mohamed Gweeq[*1], Nagy Shaaban[1], Osama Saad Salama[2], Ahmed Albehairy[1]
Departments of [1]Endocrinology and Diabetes, Internal Medicine and
[2]Clinical Pathology Faculty of Medicine, Mansoura University, Egypt
***Corresponding author:** Mohamed Gweeq, **Mobile:** (+20)1270302257, **E-Mail:** mgweeq@gmail.com

ABSTRACT

Background: The two most common endocrinopathies are diabetes mellitus (DM) and thyroid diseases (TD), which frequently coexist and influence each other. Thyroid dysfunction in type 2 diabetic patients can help clinicians to provide the best treatment for metabolic disorders, as thyroid abnormalities like hypothyroidism can make achieving glucose targets and other comorbidities difficult.

Objective: The aim of the current work was to detect prevalence of thyroid dysfunction in patients with type 2 diabetes attending diabetes outpatient clinic at Mansoura Medical Specialized Hospital and their association with cardiovascular risk factors.

Patients and methods: This cross-sectional study included a total of 100 type 2 diabetic patients aged 35-55years, attending at Mansoura Specialized Medical Hospital (SMH) and 50 normal healthy controls. The included subjects were divided into two groups; **Group 1 (diabetics)** consisted of 100 patients, and **Group 2 (control)** consisted of 50 normal healthy individuals matched in age, sex with group 1.

Results: There was a statistically significant increase in the mean BMI, SBP and W/H ratio in (Group 1) compared to (Group 2). The median duration of diabetes mellitus in the group 1 was 9 years (1-25). There was a statistically significant increase in the mean serum triacylglycerols (TG), serum LDL and serum cholesterol levels in (Group 1) compared to (Group 2). There was a significant difference between studied groups with higher percentage of normal thyroid among group 2 (90% versus 71%) ($P < 0.05$) .and significant higher percentage of subclinical hypothyroidism in (Group 1) as compared to (Group 2).

Conclusion: It could be concluded that thyroid dysfunction is frequently developed among patients with type 2 diabetes mellitus. Screening for the thyroid functions among diabetic patients is needed to prevent cardiovascular risks.

Keywords: Type 2 Diabetes, Thyroid dysfunction, TSH, Dyslipidemia.

INTRODUCTION

Diabetes mellitus (DM) and thyroid disorders (TD) are the two foremost common endocrinopathies, which often co-exist and mutually influence each other. Numerous research studies have reported the alliance among diabetes and thyroid disorders [(1)].

Confirmed associations involving abnormal biochemical pathways, aberrant genetic expressions, and hormonal malfunctions, explaining their pathophysiological association [(2)].

The association between thyroid dysfunction and type 2 diabetes mellitus (T2DM) has also been recommended, but the potential causative mechanisms are intricate [(3)].

The most accepted mechanism for advancement of T2DM in patients with thyroid dysfunction could be due to disturbed genetic expression of several genes in conjunction with physiological aberrations leading to impaired glucose consumption by the muscles, augmented hepatic glucose output and higher glucose absorption from intestine [(4)].

These endocrine disorders impact each other in a variety of ways. Thyroid hormones (TH) contribute to the regulation of carbohydrate metabolism and pancreatic function, and on the contrary, diabetes affects thyroid function tests to variable extents [(5)].

To clarify the link between DM and TD, the association of Hashimoto's thyroiditis (Hypothyroidism) and Graves' disease (thyroid over activity) has been explored in reference to DM. The consequence of hyperinsulinemia/insulin resistance, in thyroid cell proliferation, which manifested as increased thyroid volume and nodule have been also observed [(6)].

Detecting thyroid dysfunction in type 2 diabetes patients will inform clinicians to give optimal treatment for metabolic conditions since thyroid condition such as hypothyroidism will delicate achievement of glycemic target and other comorbidities [(7)].

The aim of the present study was to detect prevalence of thyroid dysfunction in patients with type 2 diabetes attending diabetes outpatient clinic at Mansoura Medical Specialized Hospital and their association with cardiovascular risk factors.

PATIENTS AND METHODS

This cross-sectional study included a total of 100 patients with type 2 diabetes aged 35-55years, attending at Mansoura Specialized Medical Hospital (SMH) and 50 normal healthy controls. This study was conducted between March 2021 to December 2021.

The included subjects were divided into two groups; **Group 1 (diabetics)** consisted of 100 patients, and **Group 2 (control)** consisted of 50 normal healthy individuals matched in age, sex with group 1.

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Inclusion criteria: Entire cases with diabetes mellitus type 2 who were diagnosed according American Diabetes Association (ADA) criteria [8].

- A fasting plasma glucose (FPG) level ≥ 126 mg/dL (7.0 mmol/L)
- A 2-hour plasma glucose level ≥ 200 mg/dL (11.1 mmol/L) during a 75-g oral glucose tolerance test (OGTT).
- A random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis.
- A hemoglobin A1c (HbA1c) level ≥ 6.5% (48 mmol/mol).

Exclusion criteria: Age less than 35 or more than 55, and patients refused to participate in the study.

Both groups were subjected to the following:

I) Complete history taking including age, sex, residency, and previous history of medical or surgical problems.

II) Physical examination was done for patients and control with emphasis on family history of thyroid disease, duration of diabetes, use of insulin as well as oral hypoglycemic agents (OHA).

III) Investigations: The following investigations were performed:

- Fasting and 2 hour post prandial plasma glucose.
- HbA1c.
- Free T3 and Free T4.
- Thyroid stimulating hormone (TSH).
- Lipid profile.
- Blood pressure.
- Weight (kg), Waist/Hip (W/H), ratio and Body Mass Index (BMI), (kg/m^2)
- Homeostasis Model of Insulin Resistance (HOMA-IR).

Ethical consideration:

An approval of the study was obtained from Mansoura University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. 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

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

This study included 100 patients with diabetes (Group 1) in addition to 50 age and sex matched individuals (Group 2) as a control group. The mean age of (Group 1) was 43.14 ± 8.46 and 45.58± 7.95 years in the (Group 2) with no statistically significant difference between the two groups. females represented the higher percentage in the two groups (54% and 58%) respectively with no statistically significant difference between the two groups. the higher percentage in the two study groups was rural residence that was 64% in (Group 1) vs 62% in (Group 2 with no statistically significant difference between the two groups (Table 1).

Table (1): Comparison of the demographic data between cases and control groups:

		Groups				Test of significance	P value
		Cases (N=100)		Control (N=50)			
Age (years)		43.14 ± 8.46		45.58± 7.95		t= -1.846	0.236
Gender	Male	46	46%	21	42%	□2= 1.427	0.324
	Female	54	54%	29	58%		
Residence	Urban	36	36%	19	38%	□2= 1.114	0.461
	Rural	64	64%	31	62%		

P: probability. Continuous data are expressed as (mean ± SD) Categorical data expressed as Number (%), X^2= Chi-square test T: independent samples t-test. *: statistically significant (p< 0.05)

There was a statistically significant increase in the mean BMI, mean SBP and mean W/H ratio in the (Group 1) as compared to the controls (p= 0.015, 0.001 and 0.021) respectively. There is no statistically significant difference of mean diastolic blood pressure between (Group 1) & the control group (p=0.229) (Table 2).

Table (2): Comparison of the vital signs and anthropometric measures between cases and control groups:

	Groups		Test of significance	P value
	Cases (N=100)	Control (N=50)		
BMI (kg/m^2)	30.94 ± 3.35	24.42 ± 1.87	t= 4.316	0.015*
SBP (mmHg)	122.17 ± 13.04	108.33 ± 11.40	t= 7.008	0.001*
DBP (mmHg)	74.65 ± 3.87	72.94 ± 3.35	t= 2.114	0.229
W/H ratio	1.26 ± 0.19	0.74 ± 0.12	t= 3.914	0.021*

P: probability. Continuous data are expressed as (mean ± SD) T: independent samples t-test. *: statistically significant (p< 0.05)

The mean duration of diabetes mellitus in the

(Group 1) was 9.58 ± 6.88 years, the median duration was 9 years with range between 1 and 25 years. Regarding the regimen of treatment, 2 cases required lifestyle modification, oral antidiabetic drugs were used in 70 cases, insulin in 4 cases while combined regimen of insulin and oral antidiabetics in 24 cases (Table 3).

Table (3): Analysis of the criteria for DM in the cases group (n=100).

	No. (%)
Duration of DM	
Mean ± SD	9.58 ± 6.88
Median (Min. – Max.)	9 (1 – 25)
Medication	
Lifestyle modification	2 (2 %)
Oral	70 (70 %)
Insulin	4 (4%)
Both	24 (24%)

There was a statistically significant increase in the mean TGs level, serum LDL and serum cholesterol levels in (Group 1) as compared to the controls (p= 0.007, <0.001 and 0.011) respectively. There was no statistically significant difference between studied groups regarding ALT (p=0.193), AST (p=0.360), INR (p=0.337), HGB (p=0.228), WBCs (p=0.475) platelets count (p=0.119), HDL (p=0.219) and serum creatinine (0.809) (Table 4).

Table (4): Comparison of the laboratory parameters in the cases and control groups:

	Groups		Test of significance	P value
	Cases (N=100)	Control (N=50)		
ALT (IU/L)	27.7±4.3	24.7±4.5	**t=1.336**	0.193
AST (IU/L)	23.62±2.1	21.73±3.4	**t=0.913**	0.360
INR	1.07±0.1	1.06±0.1	**t= 0.975**	0.337
Hemoglobin (g/dl)	12.18± 2.08	11.36± 2.65	**t=1.458**	0.228
Platelet ($x10^3$/ul)	267.6±6.3	287.68±7.9	**t= -2.412**	0.119
WBCs ($x10^3$/ul)	7.39±1.6	6.95±1.8	**t=0.738**	0.475
Serum creatinine (mg/dl)	1.06±0.26	1.05±0.23	**t=0.227**	0.809
TGs (mg/dl)	219.93±36.7	193.64±5.4	**t=2.951**	0.007*
LDL (mg/dl)	138.41±20.1	115.94±23.3	**t=4.063**	<0.001*
Cholesterol (mg/dl)	202.64 ±37.5	165.21 ± 33.19	**t= 3.146**	0.011*
HDL (mg/dl)	55.34± 6.52	61.47± 2.03	t= - 1.229	0.219

P probability. Continuous: data are expressed as (mean ± SD) T: independent samples t-test. *: statistically significant (p< 0.05).

There was statistically significant difference between studied groups with higher percentage of normal thyroid among (Group 2) as compared to (Group 1) (90% versus 71%). A statistically significant higher percentage of subclinical hypothyroidism among Diabetic as compared to control group (23% versus 4%, respectively) (Table 5).

Table (5): Comparison of thyroid state between studied groups:

Thyroid state	Cases (n=100)	Control (n=50)	test of significance
Normal thyroid functions	71 (71%)	45 (90.0%)	χ^2=6.85, P=0.008*
Subclinical hypothyroidism	23 (23%)	2(4.0%)	χ^2=8.66, P=0.003*
Overt hypothyroidism	3 (3%)	2(4.0%)	FET, P=1.0
Subclinical hyperthyroidism	1 (1%)	1(2.0%)	FET, P=1.0
Overt hyperthyroidism	2 (2%)	0(0.0)	FET, P=0.443

On sub-analysis of laboratory parameters in (Group 1) There was statistically significant difference in the mean total cholesterol level, TGs level and LDL level between the diabetic cases with normal thyroid functions and Diabetic cases with hypothyroidism, the mean total cholesterol level, TGs level and LDL was statistically significantly higher in the diabetic cases with hypothyroid functions as compared with diabetic patients with normal thyroid function (Table 6).

Table (6): Comparison of laboratory profile according to the state of thyroid affection in the diabetic group:

Parameters	Diabetic (n=72)	Diabetic with hypothyroidism (n=25)	Diabetic with hyperthyroidism (n=3)	Significance test
Total Cholesterol (mg/dL)				KW =6.55 P =0.002*
Mean ± SD	182.50 ± 21.75	220 ± 9.50	186.50± 6.75	
Triglycerides (mg/dL)				KW =6.38 P= 0.0025*
Mean ± SD	148± 4.25	187.5± 5.25	163 ± 7.25	
HDL (mg/dL)				KW = 11.28 P =0.004*
Mean ± SD	51.50± 10.50	44.01 ± 3	41 ± 6.73	
LDL (mg/dL)				KW =5.14 P =0.007*
Mean ± SD	114.50± 28.50	137.25 ±5.84	120 ± 3.25	
Urea (mg/dL)				KW =2.34 P= 0.184
Mean ± SD	33.14 ± 5.06	31.24 ± 3.75	35 ±13.75	
Creatinine (mg/dL)				KW =1.78 P= 0.146
Mean ± SD	0.87 ± 0.16	0.90± 0.20	0.94 ± 0.2	

There was a statistically significant positive

correlation between TSH and the following: diastolic blood pressure (r=0.645), Cholesterol (r=0.840) and TGS (r=0.745). Free T3 shows statistically significant positive correlation with systolic blood pressure (r=0.601) and negative correlation with the following: Cholesterol (r=-0.745) and TGS (r=-0.658). Free T4 illustrates statistically significant positive correlation with systolic blood pressure (r=0.215) and show negative correlation with cholesterol level (r=-0.584) (Table 7).

Table (7): Correlation between thyroid hormones and cardiovascular factors among studied cases:

	TSH	FT3	FT4
HOMA IR	r=0.57 p=0.08	r=-0.547 p=0.17	r=-0.417 p=0.28
SBP (mmHg)	r=0.447 p=0.21	r=+0.601 p=0.02*	r=+0.215 p=0.714
DBP (mmHg)	r=0.645 p=0.003*	r=-0.528 p=0.07	r=-0.481 p=0.21
BMI (kg/m^2)	r=0.254 p=0.35	r=-0.325 p=0.54	r=-0.248 p=0.584
Waist /hip ratio	r=0.154 p=0.41	r=-0.241 p=0.38	r=-0.124 p=0.58
Cholesterol (mg/dl)	r=0.84 p<0.001*	r=-0.745 p=0.002*	r=-0.584 p=0.03*
HDL (mg/dl)	r=0.521 p=0.12	r=-0.258 p=0.49	r=-0.415 p=0.09
TGs (ng/mL)	r=0.745 p=0.002*	r=-0.658 p=0.02*	r=-0.459 p=0.09

DISCUSSION

Hyperglycemia is the hallmark of the metabolic abnormalities in diabetes mellitus (DM) due to dysfunction of the pancreatic β cells. The second most common endocrinal pathology, after DM, is thyroid dysfunction [9].

Insulin resistance, increased glucagon secretion, increased hepatic glucose synthesis, and elevated catecholamines are thought to have a role in hyperthyroidism etiology [10, 11, 12].

The aim of the current study was to detect prevalence of thyroid dysfunction in patients with type 2 diabetes attending diabetes outpatient clinic at Mansoura Medical Specialized Hospital and their association with some cardiovascular risk factors.

This was a cross sectional study conducted on a total of 100 patients with type 2 diabetes aged 35-55years attending diabetes outpatient clinic at Mansoura Medical Specialized Hospital (Group 1) in comparison to 50 normal healthy controls matched in age, sex with the patients (Group 2). Regarding sociodemographic factors, both groups demonstrated insignificant differences in terms of age, sex, and residency.

Such fact indicated that both groups were comparable and sociodemographic features were not interfering with net result of the study.

In terms of comparison of thyroid state between study groups, the current study demonstrated that, there was statistically significant difference between both groups with higher percentage of normal thyroid among control group as compared to cases (90% versus 71%). A statistically significant higher percentage of subclinical hypothyroidism among cases as compared to control group (23 versus 4%, respectively).

This came in accordance with **Elgazar and his colleagues** [9] who have demonstrated that, the prevalence of thyroid dysfunction in patients with type 2 DM was 29% compared to only 5% in a sample of apparently healthy non-diabetic population.

Similarly, **Elmenshawi and his colleagues** [13] have demonstrated that, prevalence of thyroid dysfunction among diabetic patients was 31%. Among the diabetic patients studied, 69% had normal thyroid profile (euthyroid) and 31% showed thyroid dysfunction (25% had subclinical hypothyroidism, 3.5% had clinical hypothyroidism, and 2.5% had clinical hyperthyroidism) while no cases of subclinical hyperthyroidism were found.

This was in line with **Hollowell and his colleagues** [14] who have reported that, the overall prevalence of thyroid dysfunction among diabetic patients was 35%.

In north India, **Ozair and his colleagues** [15] have demonstrated that, a high prevalence of thyroid dysfunction (28%) was observed in type 2 diabetic patients with subclinical hypothyroidism (18.8%) as the commonest thyroid disorder followed by overt hypothyroidism (8%) and overt hyperthyroidism (1.2%). There was no subject suffering from subclinical hyperthyroidism.

In addition, **Mehalingam and his colleagues** [16] have conducted a cross-sectional study at on a total of 331 patients with type 2 diabetes mellitus. They have demonstrated that, the prevalence of thyroid dysfunction is 17.5% in patients with type 2 diabetes mellitus. In addition, thyroid dysfunction did not have any correlation with diabetic complications. Patients with type 2 diabetes mellitus are more prone to develop thyroid disorders. Hypothyroidism was more common among the study subjects.

The actual mechanisms of thyroid dysfunction mediated by diabetes mellitus not well understood. However, insulin resistance as well as autoimmunity may have a role in the development of thyroid dysfunction in patients with type 2 diabetes mellitus [9].

This could be confirmed by a study conducted by **Radaideh and his colleagues** [17] who have showed that 12.5% of diabetic patients were found to have thyroid disease. Among the diabetic patients with thyroid dysfunction, thyroid peroxidase antibody was found to be positive in 8.3% of cases. This study showed that screening for asymptomatic thyroid dysfunction may be helpful in diagnosing thyroid disease among diabetic patients.

Additionally, DM affects hypothalamic control of TSH release and diminishes the conversion of T4 to T3 in peripheral tissues. Severe hyperglycemia leads to decreased levels of T3 and increased T4. Moreover, high insulin levels associated with DM enhance TSH turnover, increase the levels of FT4 and suppress the levels of T3 by inhibiting hepatic conversion of T4 to T3 [18, 19, 20].

The current study demonstrated that there was a statistically significant increase in the mean BMI, mean SBP and mean W/H ratio in the patients' group (Group 1) as compared to the control (Group 2) (p= 0.015, 0.001 and 0.021) respectively. There was no statistically significant difference of mean diastolic blood pressure between cases & control groups (p=0.229).

Similarly, **Ozair and his colleagues** [15] were in accordance with the current study regarding BMI which demonstrated significant difference among both groups (thyroid dysfunction and euthyroid), while they were in disagreement with current study in terms of SBP (non-significant) and DBP (significant).

The current study demonstrated that, there was no statistically significant correlation between HBA1C with thyroid hormones (TSH, FT3&FT4).

This came in accordance with, **Aljabri and his colleagues** [21] who have demonstrate that, there was no significant difference in HbA1c levels between diabetic patients with and without hypothyroidism (P = 0.2).

In addition, **Ozair and his colleagues** [15] have demonstrated that, there was no statistically significant difference among thyroid dysfunction cases and euthyroid cases in terms of HbA1c (8.14±1.8 versus 7.8±1.8) FBS and PPG.

In the contrary, **Elgazar and his colleagues** [9] have demonstrated that, thyroid dysfunction was substantially more common in patients with a HbA1c of less than 8% (P = 0.0001) and those who had had diabetes for longer (P 0.001), indicating that poor glycemic control may have a role in thyroid dysfunction in diabetic patients.

Moreover, **Sreelatha and his colleagues** [22] stated that the prevalence of patients with thyroid dysfunction was more when HbA1c was ≥7% (78.57%) when compared to HbA1c <7% (21.4%).

In terms of comparison of laboratory profile according to the state of thyroid affection in the diabetic group, there was statistically significant difference in the mean total cholesterol level, TGs level, LDL level between the diabetic cases with abnormal thyroid functions, Diabetic with hypothyroidism showed significant rise in the mean total cholesterol level, TGs level, LDL level However, the mean HDL was statistically significantly higher in the diabetic cases with normal thyroid functions as compared with diabetic patients with hypothyroidism and diabetic patients with hyperthyroidism

This came in agreement with **Ravishankar and his colleagues** [23] who have demonstrate that diabetic patients have an increased risk of high serum lipids due to increased mobilization of free fatty acids from the peripheral stores.

In the same line, **Pasupathi and his colleagues** have reported that Diabetic individuals were shown to have a considerable rise in blood lipids when compared to healthy controls. Serum cholesterol and triglycerides were found to be considerably greater in diabetic patients with thyroid failure than in diabetics with normal thyroid function [24].

In addition, **Ozair and his colleagues**[15] have demonstrated that, thyroid dysfunction was more prevalent in diabetic cases with dyslipidemia, retinopathy, poor glycemic state (HbA1c ≥7) and cases with longer duration of diabetes as compared to euthyroid diabetics.

Concerning predictors of TSH, FT3 & FT4 level among diabetic cases, DBP, Cholesterol & TGs were considered as significant predictors of Serum TSH among studied cases with 74.1% of TSH level is predicted by their combination (the highest is for cholesterol followed by TGS & diastolic blood pressure). Cholesterol & TGs are significant predictors of Serum FT3 among studied cases with 62.2% of FT3 level is predicted by their combination (the highest is for cholesterol followed by TGS & DBP). Cholesterol is statistically significant predictor of FT4 with 51.4% of FT4 is predicted by serum cholesterol level.

In the same line, **Ozair and his colleagues** [15] have demonstrated that, increased body mass index (BMI), raised diastolic blood pressure, increased serum total cholesterol level were found in diabetic subjects with thyroid disorder than subjects in euthyroid group.

CONCLUSION

It could be concluded that thyroid dysfunction was frequently developed among patients with type 2 diabetes mellitus. Screening for the thyroid function among diabetic patients is needed to prevent cardiovascular risks.

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