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ORIGINAL PAPER

A Study of Association of Thyroid Dysfunctions in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: *Type 2 diabetes mellitus is known to be associated with other endocrine dysfunctions and thyroid is one of them. In the current study we tried to evaluate the frequency of thyroid dysfunctions in patients with type 2 diabetes mellitus and compare them with a normal control population.*

Methods: *This cross-sectional study was carried out in the Department of Physiology and Department of General Medicine, Kakatiya Medical College, and MGM Hospital, Warangal, India. A total of 50 consecutive patients with diabetes mellitus type 2 were selected as cases, and an equal number of age- and sex-matched individuals with normoglycemia as controls. Laboratory investigations included measurements of fasting blood sugar [FBS] and HbA_{1c} values after overnight fasting for eight hours, serum triglycerides, along with serum TSH, FT3, and FT4, which were measured by chemiluminescence immunoassay.*

Results: *Among all cases of type 2 diabetes mellitus, eight (16%) presented thyroid disorders, with 10% in male patients and 6% in female patients. The overall frequency of thyroid disorders was found in four (8%) cases, of which two (4%) in males and two in females. The values of TSH μIU/ml and FBS mg/dl in type 2 diabetes mellitus cases were plotted and a Pearson correlation coefficient of +0.70 was calculated, indicating a positive correlation between the TSH and FBS. Along with TSH levels, the values of HbA_{1c} were plotted in patients with type 2 diabetes mellitus and a Pearson correlation coefficient of +0.76 was calculated.*

Conclusion: *Within the limitations of the present study, it can be concluded that the prevalence of thyroid dysfunctions is more common in patients with type 2 diabetes mellitus. Also, a continuous positive correlation of TSH with FBS and HbA_{1c} was found. Hence, a periodic screening for their coexistence in thyroid dysfunctions among diabetic patients is advisable.*

Keywords: thyroid dysfunctions, type 2 diabetes mellitus.

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INTRODUCTION

Thyroid dysfunctions and diabetes mellitus (DM) are the two most commonly prevalent endocrine disorders encountered in clinical practice. The link between thyroid dysfunction and DM has been a topic of interest in different clinical trials across the world. Diabetes mellitus is known to affect thyroid functions at various levels and thyroid hormones have to influence carbohydrate metabolism and pancreatic functions. It is believed that thyroid functions are significantly altered in patients with DM due to variations in thyrotropin-releasing hormone (TRH), which is released from the hypothalamus for the conversion of T4 (1). Several studies have pointed out biochemical, genetic, and hormonal malfunctions mirroring this pathophysiological association (2, 3). The 5'Adenosine monophosphate-activated protein kinase (APMK) is a central target for modulation of insulin sensitivity and feedback regulation of thyroid hormone associated with appetite and energy expenditure (3). A meta-analysis aimed to investigate the association between DM and thyroid dysfunctions has reported 11% thyroid dysfunctions in patients with DM (4). Autoimmunity has been also found to be an important cause of thyroid dysfunctions associated with DM (5-7). Hypothyroidism is associated with reduced glucose absorption from GIT and it is accompanied by prolonged peripheral glucose accumulation, diminished hepatic glucose output and reduced utilization of glucose, which were considered as hallmarks of hypothyroidism (8). In subclinical hypothyroidism, diminished rate of insulin-stimulated glucose transport rate is caused by disturbed expression of glucose transporter type 2 gene (GLUT 2) translocation, possibly leading to insulin resistance; also, given the reduced clearance of insulin in hypothyroid conditions, physiological requirements of insulin are diminished (9). In cases of hyperthyroidism, an increased glucose output from the liver is the central reason for the induction of hyperinsulinemia and glucose tolerance for the development of insulin resistance (10). Among all discussed facts, insulin resistance is the most important area connecting thyroid dysfunction and type 2 diabetes mellitus (T2DM) and insulin resistance is found both in hypo- and hyperthyroidism (11).

The main objective of the present study was to evaluate the association between thyroid dysfunction and diabetes mellitus in cases of known DM through comparison with normal age- and sex-matched controls. ❑

MATERIAL AND METHODS

This cross-sectional study was carried out in the Department of Physiology and Department of General Medicine, Kakatiya Medical College, and MGM Hospital, Warangal. Institutional Ethical Committee permission was obtained for the study. Written consent was given by all participants to the study. The inclusion criteria were new and old cases of T2DM recorded to the General Medicine OPD among both male and female patients. Exclusion criteria were history of malignancy, pregnancy, liver diseases, and renal failure, MI, on drugs such as OCP, amiodarone, and beta-blockers. A total of 50 consecutive patients with T2DM were selected from those visiting the Department of General Medicine, and an equal number of age and sex-matched individuals with normoglycemia were selected as controls. A detailed patient history, including the family history, T2DM, hypertension and thyroid dysfunctions, habits of smoking, medical history of microvascular and macrovascular complications in T2DM and medications were recorded. Anthropometric and physical examinations were performed by the same examiner. The BMI was calculated as weight in Kg divided by squared height in meters. Blood pressure was recorded as per standard protocol from the right arm, in sitting position, after 10 minutes of rest. The mean value of two successive SBP and DBP measurements was recorded. Hypertension was defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg [in hypertension cases 19 of dmso]. Laboratory investigations were done for all patients. Blood samples were collected in a vacutainer under aseptic conditions. Fasting blood sugar (FBS) and HbA_{1c} values were determined after overnight fasting for eight hours; serum triglycerides, serum HDL-C, LDL-C were estimated along with serum TSH, FT3, FT4, which were measured by chemiluminescence immunoassay. The reference values were TSH >5.5 mlU/ml, free T4 <0.8 ng/dl or free T3 <1.4 pg/ml for overt hypothyroidism; TSH <0.5 ml U/ml, free T4 >1.5 ng/dl or

free T3 >4.2 pg/ml for overt hyperthyroidism; TSH >5.5 mlU/ml with normal free T3 and free T4 for subclinical hypothyroidism; and TSH <0.5 mlU/ml with normal free T3 and free T4 for subclinical hyperthyroidism. Normoglycemia was defined as a fasting serum glucose of 110 mg/dl, prediabetes as a fasting serum glucose of 111 to 125 mg/dl, and type 2 diabetes mellitus as a fasting serum glucose ≥ 126 mg/dl and a HbA_{1c} value of 6.5% [in newly diagnosed T2DM cases [18 of dmso]. All data were recorded in a T2DM MS Excel spreadsheet and analyzed by SPSS version 19 on Windows format. ❑

RESULTS AND DISCUSSION

A total of 50 T2DM cases were included in the study, of which 36 were males and 14 females, with a male to female ratio 18:7. The frequency of thyroid disorders in all cases of T2DM was eight (16%), out of which 10% were male patients and 6% female patients. Among all cases, 42 (84%) were euthyroid, four (8%) had subclinical hypothyroidism, three (6%) overt hypothyroidism and one (2%) hyperthyroidism (Table 1). Jalal MJ *et al* (12) reported that the prevalence of thyroid dysfunctions was 16% in their subjects, which is in accordance with the results of the present study. In our study, four (8%) cases of subclinical hypothyroidism, three (6%) cases of overt hypothyroidism and one case (2%) of hyperthyroidism were found in the selected diabetic patients. In a study of Akbar *et al* (13), thyroid dysfunctions had an overall prevalence of 16% and latent autoimmune diabetes in adults a prevalence of 42%. Co-occurrence of hypothyroidism and diabetes mellitus is also frequent.

In the control group (50 subjects), thyroid disorders were found in four (8%) cases, of which two (4%) in males and two in females. Subclinical hypothyroidism was found in two (4%) cases, overt hypothyroidism in one (2%) case and hyperthyroidism in one (2%) case (see Table 2 for details). The prevalence of thyroid dysfunctions in the normal population was 8%, which was slightly higher than the percentage of 6.6% reported by Tunbridge *et al* (14), maybe owing to variations in the sample size, differences in the method of estimation, and other autoimmune factors in the studied population. The mean age of male patients was 49.5 years old in the study group and 46.3 years old in the control group, with p-values being not significant; also, the mean age difference of female subjects between the study and control groups was not significant. The mean weight of male patients in the study group was significantly higher than the control group. Similarly, the mean waist girth in centimeters was significantly greater in both males and

TABLE 1. The demographic profile of cases of type diabetes mellitus with thyroid disorders

Age group	Type II DM cases (N=50)							
	Male (N=3 6)				F emale (N=14)			
	Euthyroid	Subclinical hypothyroid	Overt hypothyroid	Hyper-thyroid	Euthyroid	Subclinical hypothyroid	Overt hypothyroid	Hyperthyroid
35- 40	6	·	·		1	·	·	1
41-50	9	2			3	1		
51-60	11	1	1	·	5	·	1	·
>60	5	·	1		2	·		·
Total	31	3	2	0	11	1	1	1

TABLE 2. The demographic profile of the control group about thyroid disorders

Age group	Control Group [Normoglycemic] (N=50)							
	Male (N=35)				Female (N=15)			
	Euthyroid	Subclinical hypothyroid	Overt hypothyroid	Hyper-thyroid	Euthyroid	Subclinical hypothyroid	Overt hypothyroid	Hyper-thyroid
35- 40	7	·	·		2	·	·	
41-50	12	1	·	·	3	·	·	1
51-60	10	·	·	·	7	1	·	·
>60	4	·	1		1	·		·
Total	33	1	1	0	13	1	0	1

females with T2DM than matched controls, indicating the presence of abdominal obesity in patients with T2DM.

In Figure 1, values of TSH μIU/ml and FBS mg/dl in T2DM cases were plotted and a Pearson correlation coefficient of +0.70 was calculated, which indicated a positive correlation between TSH and FBS. Consequently, the rise in TSH values correspondingly raised the FBS level in this group of patients. A common etiology of autoimmune destruction may explain myxedema with T2DM and few cases of autoimmune positive T2DM. The two diseases occur together more often than their frequencies. The sequel of Grave's diseases as hypothyroidism and pancreatic damage resulting from hyperthyroidism may develop some cases of diabetes. Drug-induced hypothyroidism, particularly from chlorpropamide, may lead to the simultaneous presence of both diseases. A high degree of thyroidal antibody is noted in type 1 DM (15). Diabetes mellitus with congenital cretinism has been also reported (16). Untreated or undetected hypothyroidism may reduce the severity of diabetes and drug dosage, but does not suppress the occurrence of severe uncontrolled diabetes or ketoacidosis. Of course, thyroid replacement may enhance the dosage of antidiabetic agents. The problem arises in differentiating myxedema and diabetic nephropathy with similar physical findings of facial puffiness, anemia, and edema.

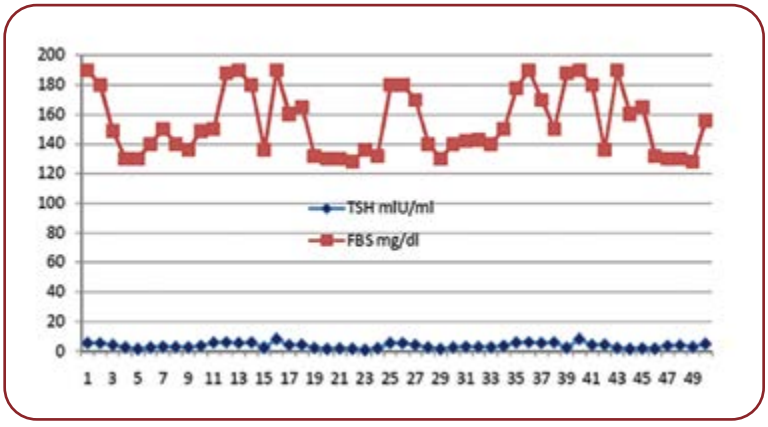

FIGURE 1. Correlation of TSH μIU/ml and FBS mg/dl in the diabetes mellitus type II cases

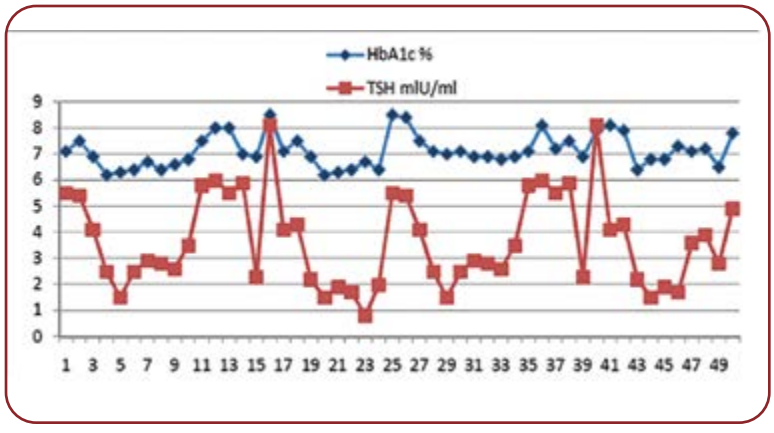

FIGURE 2. Correlation of TSH μIU/ml and HbA_{1c}% in the diabetes mellitus type II cases

The values of HbA_{1c} have been plotted along with the TSH levels in patients with T2DM and a Pearson correlation coefficient of +0.76 was calculated, as shown in Figure 2. Renal function alteration in chronic diabetes mellitus also distorts the thyroid function test due to urinary loss of TBG (thyroxine-binding globulin). Estimation of TSH and free FT4 solves the confusion rather than conventional T4 values. Given that both disorders require lifelong therapy early recognition, diagnosis will help in the prevention and postponement of chronic complications, thereby reducing related morbidity and mortality. The majority of male patients in the study group had overweight and obesity, and p values were found to be significant when compared to the control group. Similarly, the mean SBP and DBP values were found to be significantly higher in the study group than the control group. However, there were no significant differences in pulse rates and respiratory rates between males in the study and control groups. In female subjects with T2DM, only SBP values were significantly higher than those measured in matched controls.

The mean values of TSH in males with T2DM were found to be significantly higher than matched controls, which was similar for female subjects. In males, the values of FT3 were significantly lower in the study group as compared to controls (Table 3). Increased levels of TSH in type 1 DM, both under basal condition and TRH stimulation, were reported by Raptis *et al* (17). However, other studies could not prove any effect of TSH on the diabetic process until now (18). Joslin *et al* (19) detected clinical diabetes in 2.5% of cases with primary hyperthyroidism and 4.3% of cases with adenomatous goiter with hyperthyroidism. Kreines *et al* (20) found that glucose intolerance was consistent with diabetes in 57% of cases before antithyroid treatment and 30% of cases after antithyroid treatment. Diabetes is

TABLE 3. The mean values of TSH, FT4, and FT3 between both groups

	Male [Type 2 DM cases] N=36	Male [Control group] N=35	P value	Female [Type 2 DM cases] N=14	Female [Control group] N=15	P value
TSH (µlU/ml)	4.155 ±0.68	2.13 ±0.51	<0.03*	3.99 ±0.589	1.92 ±0.23	<0.05*
FT4 (ng/dl)	1.01 =0.04	1.55 ±0.035	2.368	0.987 ± 0.0221	1.31 ±0.41	1.998
FT3 (pg/ml)	1.69 ±0.03	3.2 ±0.022	0.0412*	1.235 ±0.02	2.94 ± 0.036	0.254

* **Significant** [µlU/ml: micro International Units *per* milliliter, ng/dl: nanograms *per* deciliter, pg/dl: picograms *per* deciliter]

more common in older patients with toxic nodular goiter than young persons with Grave's disease. Regarding the overall prevalence found in our study, thyroid dysfunctions were seen in eight (16%) cases of patients with T2DM. ❑

CONCLUSION

Within the limitations of the present study, the prevalence of thyroid dysfunctions was found to be more common in patients with T2DM and a continuous positive correlation of TSH with FBS and HbA_{1c} was also detected. Hence, periodic screening for their coexistence in thyroid dysfunctions among diabetic patients is advisable. ❑

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