

Thyroid disorders in type 2 diabetes mellitus

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Abstract

Background: The aim of the present study was to evaluate the clinical association of thyroid disorders in type 2 diabetes mellitus patients and to correlate the thyroid function tests with diabetic control, duration and its complications. **Materials and Methods:** A hospital based Case control study was conducted at Department of Medicine of a tertiary care hospital. The study population included diagnosed cases of type 2 DM and their non-diabetic family members of similar age and gender as control. A detailed history was taken and examination was done as per the pre-tested, structured interview schedule. All patients in addition to haematological and routine urine work up underwent target organ evaluation for diabetes. All patients were evaluated for thyroid status and assessment of T3, T4 and TSH levels was carried out at our institution. Diabetic state of the patients were estimated by analyzing HbA1c and blood sugar indices (FBS/ PPBS). Data was analyzed using SPSS software ver.21. **Results:** Mean age of diabetics (T2DM) and non-diabetics was 55.09±10.99 years and 51.11±8.78 years respectively while in each group 57 (50%) males and 57 (50%) females were included. Among cases, 33 (29%) patients were detected with thyroid disorders of which 25 (22%) were hypothyroid and 8 (7%) were hyperthyroid. Among controls, 15 (13%) patients were detected with thyroid disorders of which 11 (9.6%) were hypothyroid and 4 (3.5%) were hyperthyroid. A significant association was observed between prevalence of thyroid disorder and diabetes ($p < 0.05$). No association was observed between prevalence of thyroid disorder and control and duration of diabetes or presence of microvascular complications ($p > 0.05$) (Table 2-4). **Conclusion:** A high prevalence of Thyroid dysfunction was observed in type 2 Diabetes Mellitus patients as compared to non-diabetic population with Hypothyroidism and Clinical thyroid disorders being more common than hyperthyroidism and subclinical thyroid disease. Thus, one must have strong suspicion of thyroid dysfunction in patients with diabetes mellitus.


Key Words: Diabetes Mellitus, Hypothyroidism, Hyperthyroidism, Thyroid Function Tests.

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INTRODUCTION

Diabetes Mellitus (DM) and thyroid dysfunction (TD) are the two most common endocrine disorders in clinical practice¹. The association between DM and TD is widely known, with the first studies published in 1979². Diabetes Mellitus is the commonest endocrine disorder and the leading cause of death worldwide³. The WHO estimated diabetes prevalence was 2.8% in 2000 and 4.4% in 2030. The total no. of people with diabetes is projected to rise

from 171 million in 2000 to 366 million in 2030⁴. Thyroid dysfunction is a disorders of the thyroid gland which manifests either as hyper - or hypothyroidism and is reflected in the levels of thyroid stimulating hormone (TSH)⁵. Thyroid is the most common endocrine disorder in the general population after diabetes⁶. A number of studies estimated prevalence of thyroid dysfunction among diabetes patients ranging from 2.2-17%⁷⁻⁹. However, fewer studies have estimated higher prevalence of thyrodiabetics i.e. 31% and 46.5% respectively^{10,11}. These differences can be explained by different diagnostic criteria of TD, the degree of iodine intake among different regions, different sensitivities of the TSH assays and the large population diversity¹². Defective insulin secretion leads to various metabolic aberrations in T2DM, spanning from hyperglycemia due to defective insulin-stimulated glucose uptake and up regulated hepatic glucose production, along with dyslipidaemia, which includes impaired homeostasis of fatty acids, triglycerides, and lipoproteins¹³. DM appears to influence thyroid function in two sites; firstly at the level of

hypothalamic control of TSH release and secondly at peripheral tissue by converting T4 to T3. Hyperglycemia causes reduction in hepatic concentration of T4-5 deiodinase, low serum concentration of T3, raised levels of reverse T3 and low, normal, or high level of T4. Thyroid hormone regulate metabolism and diabetes can alter metabolism¹⁴. Thus the relationship between TD and DM is characterized by a complex interaction of interdependence. Screening of TD, especially the subclinical dysfunction, in patients with DM is justified because most patients can be asymptomatic. Determining the prevalence of clinical and subclinical thyroid disease in diabetic patients in our country and its implications in the course of diabetes and known factors for cardiovascular risk is necessary. The aim of this study is to establish the relationship between the diabetes and thyroid dysfunction and to observe whether detection of abnormal thyroid hormone levels in addition to other biochemical variables in the early stage of diabetes will help patients improve their health and reduce their morbidity rate.

MATERIAL AND METHODS

A hospital based Case control study was conducted at Department of Medicine of a tertiary care hospital for a duration of 2 years. The study population included diagnosed cases of type 2 DM with age > 30 years. Their non-diabetic family members of similar age and gender were selected as control.

Exclusion Criteria

- Age \leq 30 yrs.
- Non-Indian origin.
- Pregnant female.
- Critically ill patients.
- Known cases of thyroid disorders.
- Patients on Glucocorticoids, Valproate, Carbamazepine, Amiodarone.

Sample Size Calculation

In a study conducted by Saha *et al.*¹⁵, the occurrence of thyroid abnormalities in patients with type 2 DM was 25% and in non-diabetics is 9%. Taking the expected frequency of thyroid abnormalities to be 25% in diabetics and 9% in non-diabetics and the type 1 error to be 5% and power of the study to be 90%, the sample size at 95% confidence interval was 114 in each group (calculated by software G*Power ver. 3.1.7). So the final total sample size was 228.

Methodology

A detailed history was taken and examination was done as per the pre-tested, structured interview schedule. All patients in addition to haematological and routine urine work up underwent target organ evaluation for diabetes. All patients were evaluated for thyroid status and

assessment of T3, T4 and TSH levels was carried out at our institution. The laboratory evaluation of thyroid functions was done by estimation of serum T3, T4 and TSH levels by chemi-luminescence assay method. Two ml of blood was drawn and centrifuged and serum (500microml) collected from that and incubated with the reagent (separate for T3, T4 and TSH) for about 1 hour at room temperature. Later the readings were taken from the instrument COBAS 6000.

The normal readings are

- T3 – 0.7- 2.0 ng/ml
- T4 – 4.5- 11.0 microg/dl
- TSH- 0.4- 5.0 microIU/ml

Diabetic states of the patients were estimated by analyzing HbA1c and blood sugar indices (FBS/ PPBS) by glucose oxides wherein 1 ml of blood was drawn and centrifuged to collect the serum, 10 μ l of serum is incubated with 1 ml of reagent at room temperature for 15 min. Later the reading was taken from the instrument. Patients were diagnosed based on the ADA criteria for diabetes¹⁶:

- Symptoms of diabetes plus random blood glucose concentration of 11.1 mmol/L (200 mg/dL); or
- Fasting plasma glucose of 7.0 mmol/L (126 mg/dL); or
- Two-hour plasma glucose of 11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test; or
- HbA1C \geq 6.5%

Data Analysis

Data was analyzed using SPSS 21.0 (SPSS Inc., Chicago, IL, USA) using appropriate statistical tests.

RESULTS

The present study included a total of 228 subjects with 114 Cases (type 2 diabetics) and 114 controls (non-diabetics). Mean age of diabetics (T2DM) and non-diabetics was 55.09 \pm 10.99 years and 51.11 \pm 8.78 years respectively while in each group 57 (50%) males and 57 (50%) females were included. Both the groups were evenly matched with respect to age and gender distribution. Among cases, 33 (29%) patients were detected with thyroid disorders of which 25 (22%) were hypothyroid and 8 (7%) were hyperthyroid. Among controls, 15 (13%) patients were detected with thyroid disorders of which 11 (9.6%) were hypothyroid and 4 (3.5%) were hyperthyroid (Table 1). A significant association was observed between prevalence of thyroid disorder and diabetes ($p < 0.05$). Out of all the cases with thyroid disorders, about three fourth showed clinical features in both the groups while remaining were

subclinical (non-tabulated). No association was observed between prevalence of thyroid disorder and control and duration of diabetes or presence of microvascular complications ($p>0.05$) (Table 2-4).

Table 1: Comparison of Thyroid dysfunction among Cases and Controls

Thyroid Status	Group		Total
	Case	Controls	
Normal	81 71.1%	99 86.8%	180 78.9%
Hypothyroid	25 21.9%	11 9.6%	36 15.8%
Hyperthyroid	8 7.0%	4 3.5%	12 5.3%
Total	114	114	228
p- value	0.0137		

Table 2: Association of Thyroid Dysfunction with Duration of Diabetes

Thyroid Status	Duration of DM		Total
	<= 10 yrs	> 10 yrs	
Normal	69 69.0%	12 85.7%	81 71.1%
Hypothyroid	24 24.0%	1 7.1%	25 21.9%
Hyperthyroid	7 7.0%	1 7.1%	8 7.0%
Total	100	14	114
p- value	0.35		

Table 3: Association of Thyroid Dysfunction with Diabetic Microvascular Complications

Thyroid Status	Diabetic Complications		Total
	No	Yes	
Normal	41 69.5%	40 72.7%	81 71.1%
Hypothyroid	14 23.7%	11 20.0%	25 21.9%
Hyperthyroid	4 6.8%	4 7.3%	8 7.0%
Total	59	55	114
p- value	0.89		

Table 4: Association of Thyroid Dysfunction with Control of Diabetes

Thyroid Status	Diabetes Control (HbA1c)		Total
	<= 6.5%	> 6.5%	
Normal	10 76.9%	71 70.3%	81 71.1%
Hypothyroid	3 23.1%	22 21.8%	25 21.9%
Hyperthyroid	0 0.0%	8 7.9%	8 7.0%
Total	13	101	114
p- value	0.57		

Table 5: Comparison of results of present study with previous studies

Studies	Prevalence of Thyroid Disorder	Hypothyroidism	Hyperthyroidism
Pasupathi <i>et al</i>	45%	28%	17%
C. E. J. Udiog	46.5%	26.6%	19.9%
Radaideh <i>et al</i>	12.5%	-	-
Papazafiropoulou <i>et al</i>	12.3%	-	-
Present Study	29%	22%	7%

DISCUSSION

Diabetes mellitus is an important health problem affecting major populations worldwide. The influence of endocrine and non-endocrine organs other than the pancreas on diabetes mellitus is documented. Occasionally, other endocrine disorders such as abnormal thyroid hormone levels are found in diabetes. The major alterations in thyroid⁷ hormone system are a reduction in the TSH stimulation of the thyroid gland, probably caused by central hypothyroidism, and in the peripheral generation of T3 from T4. The present case control study was conducted with aim of studying the spectrum of thyroid dysfunction in diabetes mellitus patients. In present study, a significant association was observed between prevalence of thyroid disorder and diabetes ($p<0.05$). Among cases, 29% patients were detected with thyroid disorders (22% hypothyroid and 7% hyperthyroid) while among controls only 13% patients had thyroid disorders (9.6% hypothyroid and 3.5% hyperthyroid). Several reports documented a higher than normal prevalence of thyroid dysfunction in the diabetic population. Perros *et al.* demonstrated an overall prevalence of 13.4% of thyroid diseases in diabetics¹⁷. Recently, a prevalence of 12.3% was reported among Greek diabetic patients² and 16% of Saudi patients with type 2 diabetes were found to have thyroid dysfunction¹⁷. In Jordan, a study reported that thyroid dysfunction was present in 12.5% of type 2 diabetic patients¹⁸. Recently Pasupathi *et al.*¹⁹ in their study found that prevalence of thyroid disorder was 45% among type 2 diabetics. Hypothyroidism was present in 28% and 17% had hyperthyroidism. Udiog *et al.*²⁰ in his study from Nigeria found that prevalence of thyroid disorder was 46.5%. Hypothyroidism was present in 26.6% and 19.9% had hyperthyroidism. In a study by Ravishankar *et al.*, a total of 100 Type 2 DM patients were included. Thyroid disorders were present in 29%, Hypothyroidism in 1, hyperthyroid in 13 and subclinical hypothyroidism in 15 cases²¹. In present study we found that out of all the patients with thyroid disorders, about three fourth showed at least some kind of clinical features while remaining one fourth were subclinical. Shah *et al.* conducted study on 100 patients of diabetes mellitus in

which 38 were males and 62 were female. Out of 31 diabetics with thyroid dysfunction, 23 patients were already diagnosed, on treatment and well controlled. Remaining 8 patients (out of 31), clinical features of abnormal thyroid function such as weight gain (37%), facial puffiness (12.5%) were found in 4 patients while 4 patients did not show any clinical evidence²². Bazrafshan *et al.* observed a significant positive correlation between hemoglobin (HbA1c) concentration and TSH in their study²³. In another similar study by Ghafari *et al.*²⁴, a duration of diabetes of more than 10 years has a relative risk of 1.66 (95% CI, 1.06–2.61; p=0.02). They concluded that diabetes duration of more is an important risk factor for thyroid disorders. Similar association with control and duration of DM was observed in few other studies in different ethnic groups²⁵⁻²⁸. But in present study, no association was observed between the prevalence of thyroid disorder and control and duration of diabetes or presence of microvascular complications (p>0.05).

CONCLUSION

A high prevalence of Thyroid dysfunction was observed in type 2 Diabetes Mellitus patients as compared to non-diabetic population with Hypothyroidism and Clinical thyroid disorders being more common than hyperthyroidism and subclinical thyroid disease. Thus, one must have strong suspicion of thyroid dysfunction in patients with diabetes mellitus. An aggressive and early screening of type 2 diabetics may prevent thyroid and diabetes related complications in such patients. However more such studies on larger scale are needed to know the complete spectrum of thyroid dysfunction in diabetes.

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