Section: Biochemistry

Original Research Article

EVALUATION OF THYROID PROFILE IN PATIENTS OF TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Diabetes mellitus and thyroid disorders are two main endocrine disorders interrelated to each other and are encountered in clinical practice. Diabetes Mellitus is a leading cause of death in developing countries like India. Thyroid hormones and insulin both are involved in cellular metabolism antagonistically. Therefore, excess or deficit of any one of them may result in metabolic derangement of the other. The aim of our study is to determine the spectrum of thyroid dysfunction among type 2 diabetes mellitus.

Materials and Methods: The present study was undertaken to understand the associated trend of thyroid dysfunction with diabetic process by monitoring blood glucose, thyroid hormones -T3, T4, and TSH . A total of 80 cases, diagnosed as type 2 Diabetes and 100 non-diabetic healthy controls were included in the study.

Results: The study showed that thyroid dysfunction was more prevalent in diabetic subjects than in controls. In 80 patients of diabetic mellitus, subclinical hypothyroidism seen in 22 patients; 6 patients were hypothyroid. Subclinical hyperthyroidism seen in 4 cases; and hyperthyroid were 4.44 patients were found to be euthyroid. Among diabetics having hypothyroidism, subclinical hypothyroidism (27.5%), was more common than overt hypothyroidism (7.5%). The TSH mean in Diabetic Mellitus patients was 6.56 ± 10.3 more as compared to non-diabetic patients 5.3± 7.1& this difference is statistically significant('p' value 0.03). The mean T3 &T4 in Diabetic Mellitus patients as compared to non-diabetic patients their difference was found statistically significant ('p' value 0.04 & 0.03 respectively).

Conclusion: Although thyroid disorders are increasing among type 2 DM but it is frequently overlooked and not properly diagnosed in the early stage. Sub-clinical hypothyroidism in diabetics is more among females than males .Thus, the present study is conducted to find out the relationship between type 2 DM & thyroid dysfunction, as the benefits of identifying at an early stage is beneficial.

Keywords: Diabetes mellitus, Hypothyroidism, TSH, subclinical hypothyroidism.

INTRODUCTION

Diabetes Mellitus is a leading cause of death in developing countries like India. Diabetes Mellitus and thyroid disorders are two main endocrine disorders interrelated to each other and are encountered in the clinical practice,[1] Thyroid hormones and insulin both are involved in cellular metabolism antagonistically. Therefore, excess or deficit of any one of them may result in metabolic derangement.[2] Although thyroid disorders are increasing among T2DM but it is frequently overlooked and not properly diagnosed in the early stage. Present study was undertaken to find out the coexistence of thyroid Dysfunction with Diabetes Mellitus.

Hypothyroidism leads to reductions in hepatic glucose output, gluconeogenesis, and peripheral glucose utilization.[3] Hyperthyroidism impairs

glycemic control in diabetic subjects, while hypothyroidism predisposes to hypoglycemia thus complicating diabetes management.[4]

The prevalence of diabetes is increasing globally and the maximum increase is witnessed in developing countries like India. According to the International Diabetes Federation (IDF), in the year 2017, approximately 425 million adults worldwide were living with diabetes.[5] Total prevalence of diabetes is increasing and is expected to be 629 million by 2045. Various studies have reported different prevalence rates of thyroid hormone disorders in type 2 diabetes. Compared to normal population, diabetic patients have higher prevalence of thyroid disorder, with hypothyroidism being the most common disorder.

There is loss of vision in patients of Grave's disease who have superimposed diabetes and insulin resistance increases the nodularity of thyroid gland.[6] Unidentified thyroid dysfunction may alter the metabolic controls in patients with diabetes and may also exaggerate already existing cardiovascular risk.[7] Also thyroid hormone in excess decreases the insulin content of the pancreas, perhaps by decreasing levels at pro insulin mRNA stage. The co-existence of both diabetes and thyroid disorders has been associated with increased long-term morbidity and mortality.[8]

Hypothyroidism and diabetes show clinical signs and symptoms such as fatigue lethargy and wt gain, hyperthyroidism is typically associated with worse glycogenic control and increased insulin requirement, little attention is paid to the diagnosis of thyroid diseases in diabetics as they are diagnosed in only about half of the patients. Thus, Type 2 DM can mask thyroid disease and thyroid disease can mask early diabetic complications.[9] Thus, the present study is conducted to find out the relationship between type 2 DM & thyroid dysfunction, as the benefits of identifying at an early stage is beneficial.

Aim

To determine the spectrum of thyroid dysfunction among type 2 diabetes mellitus.

Objectives

1. To measure serum levels of T3, T4, TSH, FBS and PPBS in patients of type 2 DM and in non-diabetic healthy controls.
2. To evaluate thyroid dysfunction in patients of type 2 DM.

MATERIALS AND METHODS

This case control study was undertaken by Department of Biochemistry, Gandhi medical college and Hospital, Secunderabad. The study was conducted over a period of two years, from August 2017 to August 2019. A total of 80 cases, diagnosed as type 2 Diabetes from endocrinology departments, and 100 apparently healthy controls were included in the study.

Collection of blood samples for analysis

Blood samples of type 2 Diabetes mellitus patients and controls were collected for the estimation of Fasting blood Sugar (FBS), Postprandial blood sugar (PPBS), T3, T4, TSH at biochemistry laboratory, Gandhi Hospital, Secunderabad. Fasting blood samples after 10-12 hour of fasting were collected. The samples were centrifuged at 3000rpm for 10 minutes. Samples for PLBS were collected 2 hours post lunch.

Inclusion Criteria

1. All the known cases of type 2 NIDDM patients aged > 30 years. Gender- Male/Female.
2. All diabetics irrespective of glucose control and irrespective of treatment. (OHA/Insulin)

Exclusion Criteria

1. Type 1 Diabetes mellitus
2. Patients with GDM, Pancreatitis, steroid induced diabetes were excluded.
3. All those who have proven thyroid disorder and on treatment were also excluded.
4. The study excluded patients with complications of diabetes mellitus and those with known history of thyroid dysfunction.

Diabetic status was determined as per the American Diabetes Association criteria

We have measured Fasting blood sugar, postprandial blood sugars, T3, T4 and TSH in the present study in 80 cases of NIDDM (Type 2 DM) and 100 healthy controls by the following methods.

1. Fasting blood sugar: Hexokinase G-6-PDH method.
2. Postprandial blood sugar: Hexokinase G-6-PDH method
3. Thyroid profile assay (T3, T4 and TSH)-Chemiluminiscence method by Siemens centaur XPT system.

Our normal ranges were as follows

T3 : 0.6-1.8 ng/ml
T4 : 3.5-12.6 µg/dL
TSH : 0.35-5.5 µIU/ml
Fasting blood glucose : 70-110mg/dL
Postprandial blood glucose : 110-140mg/dL.

RESULTS

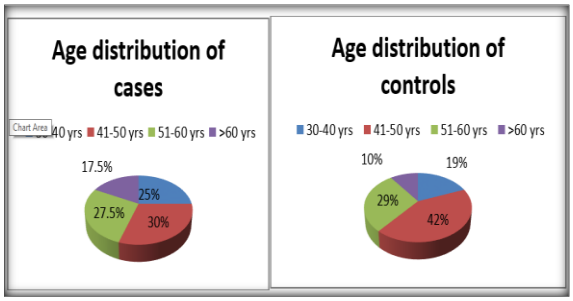
Participants were taken based on the inclusion criteria. The participants were then divided as hypothyroid, sub-clinical hypothyroid, hyperthyroid, sub-clinical hyperthyroid and euthyroid depending on thyroid profiles. A database was constructed on Microsoft Excel and results were tabulated in master chart.t test was done to analyse data. $p< 0.05$ was considered statistically significant.

• Highly significant (p value: $p <0.001$)
• Not significant (p value>0.05)

Age wise distribution of cases and controls

The distribution of the study samples according to the age is shown in Table 3 and graphically. The cases and controls were divided into 4 groups based on age (31-40, 41-50, 51-60, >60 yrs). Majority of the cases and controls were in the age group 41-50 yrs; (30%) in diabetic group (42%) non-diabetic group. There were 10 cases between 30-40years, 12 cases between

41- 50 years, 11 cases between 51-60 and 9 cases >60 years of age. The mean age in the present study was 49.3±11.7 in case group and 48.8±9.5 in the control group and this difference was found statistically not significant ('p' value 0.1).



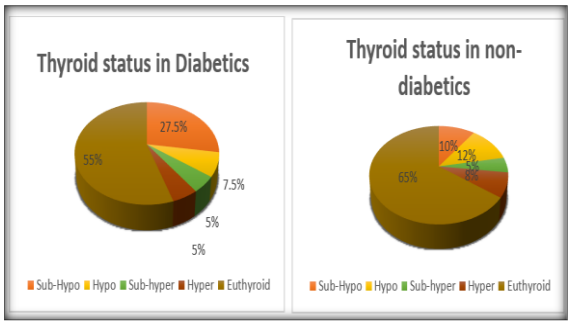


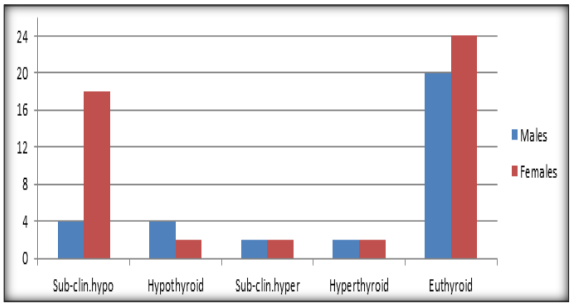
Table 1: Age wise distribution of cases and controls

S.NO	Age group (in yrs)	Cases n=80 No.	%	Controls n=100 No.	%
1.	30-40	20	25	19	19
2.	41-50	24	30	42	42
3.	51-60	22	27.5	29	29
4.	>60	14	17.5	10	10

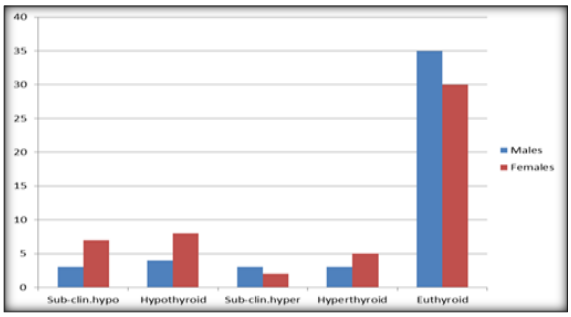
Table 2: Result of thyroid profile in cases and controls

THYROID DISORDER	CASES (n=80)		CONTROLS (n=100)	
	No.	%	No.	%
SUB-CLINICAL HYPOTHYROIDISM	22	27.5	10	10
HYPOTHYROIDISM	6	7.5	12	12
SUB-CLINICAL HYPERTHYROIDISM	4	5	5	5
HYPERTHYROIDISM	4	5	8	8
EUTHYROIDISM	44	55	65	65

Graph 4: Distribution of cases and controls with respect to thyroid status



Gender distribution of thyroid status among cases (diabetics)



Gender distribution of thyroid status among controls (non-diabetics)

Diabetic group [case group]

In 80 patients of diabetic mellitus, subclinical hypothyroidism seen in 22 patients; incidence {27.5%}, 6 patients were hypothyroid; incidence {7.5%},

Subclinical hyperthyroidism seen in 4 cases; incidence {5%}.and hyperthyroid were 4{5%}. 44 patients were found to be euthyroid; incidence being 55%.

Among diabetics having hypothyroidism, subclinical hypothyroidism (27.5%), was more common than overt hypothyroidism (5%).

Non-Diabetic [Control Group]:

Out of 100 Non- Diabetic [Control Group], subclinical hypothyroidism is seen in 10 {10%} ,12 were hypothyroid{12%}.Subclinical hyperthyroidism seen in 5 {5%} and 8 were hyperthyroid {8%}. Euthyroidism is seen in 65 controls {65%} in our study.

In type 2 diabetic patients incidence of sub-clinical hypothyroidism in males and females was found to be 4(5%) and 18(22.5%) respectively, while hypothyroidism was found to be 4(5%) and 2(2.5%) respectively. This shows sub-clinical hypothyroidism more common than overt hypothyroidism and is more common in females.

Sub-clinical hyperthyroidism and hyperthyroidism, showed incidence of 2.5% each in both males and females. The study showed euthyroidism in 20(25%) males and 24 females (30%).

In non- diabetic healthy subjects incidence of sub-clinical hypothyroidism in males and females was found to be 3(3%) and 7(7%) respectively, while hypothyroidism was found to be 4(4%) and 8(8%) respectively. Sub-clinical hyperthyroidism, in males and females is 3(3%) and 2(2%) respectively. Where as, hyperthyroidism seen in 3 (3%) males and 5(5%) females. Euthyroidism is seen in 35(35%) males and 30 (30 %) females.

Table 3: Comparison of Thyroid Dysfunction in Diabetic Mellitus & Control Group with gender distribution

THYROID DISORDER	CASES (n=80)			CONTROLS (n=100)		
	Male	Female	Total	Male	Female	Total
SUB-CLINICAL HYPOTHYROIDISM	4 5%	18 22.50%	22 27.50%	3 3%	7 7%	10 10%
HYPOTHYROIDISM	4 5%	2 2.50%	6 7.50%	4 4%	8 8%	12 12%
SUB-CLINICAL HYPERTHYROIDISM	2 2.50%	2 2.50%	4 5%	3 3%	2 2%	5 5%
HYPERTHYROIDISM	2 2.50%	2 2.50%	4 5%	3 3%	5 5%	8 8%
EUTHYROIDISM	20 25%	24 30%	44 55%	35 35%	30 30%	65 65%

Table 5: Comparison of Mean & SD in Diabetic Mellitus [case] & Non-Diabetic mellitus [control] group

S. No	PARAMETER	CASE GROUP [Mean±SD]	CONTROL GROUP [Mean± SD]	'p' Value
1.	FBS	138.6±33.6	91 ±12.8	<0.001
2.	PPBS	215 ±98.1	123.2± 8.7	<0.001
3.	T3 (ng/ml)	0.9 ±0.3	1.0±0.4	0.04
4.	T4 (µg/dL)	6.97±2.2	7.48± 3.0	0.03
5.	TSH (µIU/ml)	6.56± 10.3	5.3± 7.1	0.03

- The T3 mean in Diabetic Mellitus patients was 0.9 ±0.3 as compared to non-diabetic patients1.0±0.4& this difference was statistically significant ('p' value 0.04).
- The mean T4 in Diabetic Mellitus patients was less 6.97±2.2 as compared to non-diabetic patients 7.48± 3.0& this difference was also statistically significant ('p' value 0.03).
- The TSH mean in Diabetic Mellitus patients was 6.56 ± 10.3 more as compared to non-diabetic patients 5.3± 7.1& this difference is statistically significant('p' value 0.03).
- Both mean± SD for FBS and PLBS were statistically significant in Diabetic Mellitus & Non- Diabetic Mellitus groups. ('p' value<0.001).

DISCUSSIONS

Diabetic Mellitus is an important health problem affecting major population worldwide [9]. The fact that insulin and thyroid hormone influence each other's action assumes significance.

The present study is undertaken to find the functional status of the thyroid hormones on homeostasis of glucose. According to Patricia Wu2[10], diabetic patients have a higher prevalence of thyroid disorders compared with the normal population. Progression to overt thyroid dysfunction is associated with consequent morbidity including the adverse effects on lipid and bone metabolism.

In 2005, Den Hollander et al. reported that treating hypothyroidism improved renal function in diabetic patients.[11] As for retinopathy, Yang et al. demonstrated recently that diabetic patients with subclinical hypothyroidism have more severe retinopathy than euthyroid patients with diabetes [12].

The mean FBS is higher in diabetic group (138.6±33.6) than the control group (91 ±12.8). Also mean PLBS being higher (215 ±98.1) in cases than controls (123.2± 8.7). The 'p' value is highly significant p<0.001 for both FBS and PLBS in the present study.

In our study we have found that there is variation in the TSH levels and T3, T4 levels found in diabetics and non-diabetics with thyroid disorders. The TSH mean in Diabetic Mellitus patients was 6.56 ± 10.3 more as compared to non-diabetic patients 5.3± 7.1& this difference is statistically significant ('p' value 0.03).

In this study sub-clinical hypothyroidism in diabetics is more among females (22.5%) than males (5%). A prospective study on thyroid dysfunction in type DM conducted at MVJ medical college, by Ravishankar et.al showed similar findings of sub-clinical being more common in females (22%) than males (8%).[13] It also reports that elderly females had high incidence of sub- clinical hypothyroidism (18.2%).

Subclinical hypothyroidism (SCH), also called mild thyroid failure, is diagnosed when peripheral thyroid hormone levels are within normal reference laboratory range but serum thyroid-stimulating hormone (TSH) levels are mildly elevated. Of patients with SCH, 80% have a serum TSH of less than 10 mIU/L. The most important implication of

SCH is high likelihood of progression to clinical hypothyroidism. It is more common in women than men, and its prevalence increases with age.

Both clinical and subclinical hypothyroidisms are recognized as insulin resistant states.[14] In our study, sub-clinical hypothyroidism was more common in diabetic group (27.5%) compared to control group (10 %). Also it is more commonly seen in females (18 cases) {22.5%} than males (4 cases) {2.5%}.

Subclinical hypothyroidism can affect serum LDL, cholesterol levels; further increasing the risk of atherosclerosis. Since diabetic patient are at high risk for cardio-vascular disease, the diagnosis and treatment of subclinical thyroid diseases is necessary.[7] In subclinical hypothyroidism, diminished rate of insulin stimulated glucose transport rate caused by perturbed expression of glucose transporter type 2 gene (GLUT 2) translocation may lead to insulin resistance.[15]

Suzuki et al attributed the abnormal thyroid hormone levels found in diabetes to the presence of Thyroid Hormone Binding Inhibitor (THBI), an inhibitor of extra thyroidal conversion enzyme of T4 to T3, and dysfunction of the hypothalamus-hypophyseal-thyroid axis.[16]

The hallmark laboratory finding of subclinical hypothyroidism is an elevated TSH with a normal T4. However, non-thyroidal illness and some medications can cause an elevation of TSH, and they need to be ruled out before a diagnosis of subclinical hypothyroidism is established. In patients with TSH <10 mIU/L and normal free T4, thyroid profile should be repeated in 3 to 6 months before initiation of therapy as almost half of these patients have a resolution of the thyroid abnormalities.[17] TPO antibodies should be checked in patients. If positive for TPO antibodies, this may indicate an autoimmune etiology of hypothyroidism.[18]

Hyperthyroidism increases GLUT4 gene expression and glucose uptake in skeletal muscles.[19] Thyroid hormones also directly control insulin secretion by beta cells. Hypothyroidism reduces glucose-induced insulin secretion, whereas hyperthyroidism enhances the response of beta cells to glucose. Degradation of insulin is also increased by thyroid hormone, and thyrotoxicosis increases insulin clearance.[19] Thyroid hormone also increases glucagon secretion by pancreatic alpha cells.[19] Thyrotoxicosis may lead to ketoacidosis also due to elevated lipolytic actions and increased hepatic β oxidation.[20] Insulin resistance and hyperinsulinemia lead to proliferation of thyroid tissues, an increased incidence of nodular thyroid disease, and a larger goitre. One must have strong suspicion of thyroid dysfunction in patients with uncontrolled glycemic levels. Failure to recognize the presence of subclinical hypothyroidism in diabetes mellitus patients may be a primary cause of poor management often encountered in treated diabetics.

CONCLUSION

This study demonstrates the importance of recognition of the interdependent relationship between thyroid disease and type 2 DM. Although thyroid disorders are increasing among T2DM but it is frequently overlooked and not diagnosed properly in the early stage. Type 2 diabetes mellitus patients are at more risk of subclinical hypothyroidism and hence need to be followed regularly with serum thyroid profile to achieve good glycemic control and decrease the complications of type 2 DM.

Progression to overt thyroid dysfunction is associated with consequent morbidity including the adverse effects on lipid and bone metabolism. Therefore, routine assessment of thyroid hormone level in addition to other biochemical parameters in the early stage of diabetes mellitus will help in the management of diabetes mellitus particularly in those patients, whose conditions are difficult to manage.

Hyperthyroidism results in deterioration of diabetic control while hypothyroidism increases the susceptibility to hypoglycemia in diabetic patients thereby complicating the diabetic management in these individuals. A higher frequency of retinopathy and nephropathy was observed in diabetic patients with subclinical hypothyroidism.

Therefore, routine assessment of thyroid hormone level in addition to other biochemical parameters in the early stage of diabetes mellitus will help in the management of diabetes mellitus as well as to reduce the morbidity in them.

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