Association of Thyroid Dysfunction in Patients withType-2 Diabetes Mellitus

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Abstract

Background: Diabetes Mellitus is the most common endocrine disorder worldwide. The role of insulin and thyroid hormones appears to be vital in regulating cellular metabolism. Co-existence of thyroid abnormality and diabetes may influence each other in disease process. The aim of the present study is to correlate thyroid disorders among diabetic case group.

Materials and Methods: The present study was done on 350 subjects, which include 175 healthy subjects and 175 type 2 diabetic cases. Thyroid hormones, Blood glucose levels and Glycosylated haemoglobin (HbA_{1c}) were analyzed and results were compared with healthy individuals.

Results: In this study, the thyroid dysfunction was observed in 17.71% of case group. Out of 175 cases the frequency of hypothyroidism and hyperthyroidism is 16% and 1.71% respectively and euthyroid state was 82.29%.

Conclusion: The interrelationship between type 2 diabetes and thyroid disease is found to be significant in this study. By considering this association, regular screening for thyroid function test along with the diabetic profile in diabetics may help in better management of these patients.

Keywords: Hyperthyroidism, Hyperglycaemia, Subclinical Hypothyroidism, Diabetes Mellitus, Thyroid Dysfunction

Access this article online	
Quick Response Code:	**Website:** www.innovativepublication.com
	DOI: 10.5958/2394-6377.2016.00034.4

Introduction

Diabetes Mellitus (DM), a common endocrine metabolic disorder, is one of the leading causes of death worldwide.[(1)] Most individuals with diabetes are between the ages of 40 to 59 years. Wild s et al and Whiting et al predicted that by 2030, DM may afflict up to 79.4 million individuals in India. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual and on health care system.[(2, 3, 4)]

Thyroid hormones, tri-iodothyronine (T_3) and thyroxine (T_4) are secreted by the thyroid gland under the influence of its physiological regulator, thyroid stimulating hormone (TSH). [(5)]

DM and thyroid dysfunction are the two most common endocrine disorders in clinical practice and these appear to be closely linked. Epidemiological evidence suggests a common genetic background for both thyroid disease and DM. However, presently most attention on genetic study is on type 1 diabetic autoimmune causes.[(6,7)]

Thyroid hormones have profound effects in the regulation of glucose homeostasis. These include modifications of circulating insulin levels and counter regulatory hormones, intestinal absorption, hepatic production and peripheral tissues uptake of insulin as well as stimulation of gluconeogenesis and glycogenolysis.[(8)] Marked hyperglycaemia decreases the activity and concentration of hepatic T_4 – 5' deiodinase. The characteristic findings include low serum concentrations of T_3, elevated levels of reverse T_3 (rT_3) and low, normal or high levels of T_4.[(9,10)]

Keeping the above view, the present study is planned to examine the association of thyroid dysfunction in patients with type 2 DM. Additional to the diabetic profile it should be aimed for routine screening of thyroid profile in Type 2 diabetic patients of all age groups.

Materials and Methods

Study was carried out on total 350 subjects, which is divided equally into case and control groups. Analysis of thyroid status was done in patients with high blood glucose and HbA1c levels. Number of subjects visiting to clinical OPD and those admitted in wards between age group of 30 to 60 years were included. The ethical committee of the institution has approved the study. Inclusion criteria for study involve individuals with type 2 DM irrespective of glucose control and treatment. The exclusion criteria are patients with type-1 diabetes, already proven thyroid disorders on treatment and pregnant women. Patients on exposure to radiation and surgeries like thyroidectomy, consumption of alcohol and drugs like steroids, lithium etc are also excluded.

After obtaining informed consent from the patient, under aseptic condition venous blood samples were collected in plain tube and subjected for centrifugation after proper clotting. The serum obtained is used for assessing thyroid function tests like Free T_3 (FT_3), Free

T_4 (FT_4) and Thyroid Stimulating Hormone (TSH) by chemilumenescence immunoassay (CLIA) methods on fully automated hormone analyzer (Siemens Advia centaur cp). Analysis of biochemical parameters is including serum glucose like fasting and postprandial blood sugar (FBS and PPBS) done on fully automated chemistry analyser (Siemens dimension RXL Max) by Hexokinase method. Glycosylated Haemoglobin (HbA_{1C}) by High Performance Liquid Chromatography (HPLC) method (Bio-Rad D10).

Statistical analysis was done by student `t' test using SPSS version 20.0.

Results:

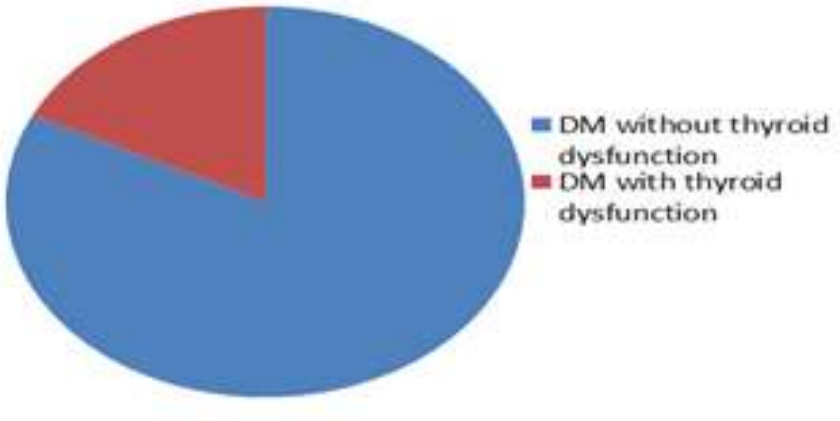

Fig. 1

Table 1: Demographic representation of Control and Diabetic Group

Subjects	Age Mean±SD	Thyroid status		Sex	
				Male	Female
Control Group (n=175)	44.67±8.58	Euthyroid	170	71	99
		Thyroid Disorder	5	1	4
Diabetic Group (n=175)	48.87±7.93	DM without Thyroid Disorder	144	65	79
		DM with Thyroid Disorder	31	11	20

Table 2: Thyroid Status in Diabetes Mellitus (DM) (total n= 175)

Thyroid Status in Diabetes Mellitus (DM) (total n=175)							
Parametres	DM with Euthyroid state (n=144)	Clinical Hypothyroidism		Subclinical Hypothyroidism (n=22)	Clinical Hyperthyroidism (n=2)	Subclinical Hyperthyroidism (n=1)	Reference Values
		Primary Hypothyroidism (n=3)	Secondary Hypothyroidism (n=3)				
FT3 (pg/ml)	3.17±0.40	1.98±0.271	2.04±0.034	3.05±0.409	4.94±2.015	3.47	2.3 - 4.2
FT4 (ng/dl)	1.32±0.18	0.54±0.230	0.91±0.211	1.26±0.088	2.44±0.106	1.09	0.89 - 1.8
TSH (µIU/ml)	2.59±1.26	28.206±5.392	0.40±0.10	8.6±2.534	0.035±0.035	0.02	0.35 - 5.5

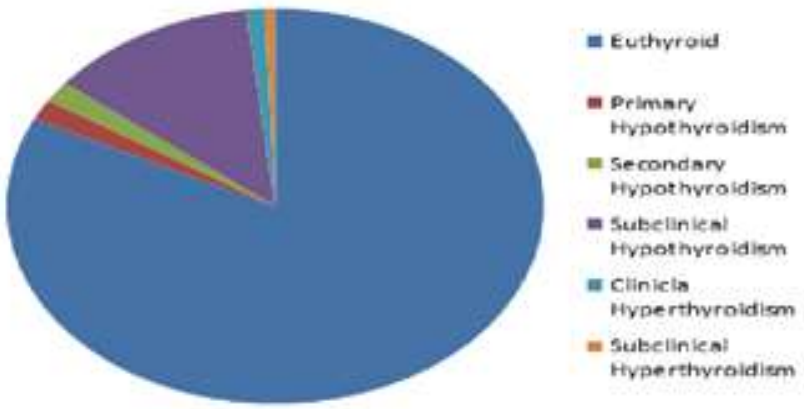

Fig. 2

Table 3: Comparison of Biochemical Parameters in Control and Case Groups

Parameter	Control Group (n=175)	Case Group (n=175)	p value
FBS (mg/dl)	89.14 ± 10.36	156.37 ± 68.51	<0.001
PPBS (mg/dl)	99.5 ± 18.05	226.23 ± 96.82	<0.001
HbA1c (%)	5.11 ± 0.62	7.82 ± 1.94	<0.001

Analysis of thyroid profile in 175 cases of type 2 diabetic patients showed thyroid dysfunction in 17.71% (n=31) of individuals, remaining 82.29% (n=144) presented without any thyroid abnormalities (Fig.1). Out of 175 normal healthy controls 2.85% (n=5) subjects exhibited thyroid diseases.

Table 1 shows demographic distribution of thyroid disorders. Among 175 diabetics 6.28% (n=11) of males and 11.43% (n=20) of females exhibited thyroid disorders. This shows females are more prone for thyroid dysfunction.

In this study mean age ± SD of cases were 48.87±7.93 years and controls were 44.67±8.58 years.

Frequency of thyroid dysfunction in diabetics is represented in Table 2. Among 31 cases of thyroid diseases, clinical hypothyroid state was found in 6 (3.43%) individuals. 22 (12.57%) out of 31 cases had subclinical hypothyroidism and clinical hyperthyroidism is observed in 2 (1.14%) diabetic persons, but subclinical hyperthyroidism is observed only in 1 (0.57%) case and remaining 144 subjects exhibited euthyroid state.

In our study biochemical parameters like FBS, PPBS and HbA_{1C} (Table 3) levels were significantly ($p<0.001$) elevated, in diabetes group when compared with control group.

Discussion

In our study total 175 type 2 diabetic patients were investigated. Majority of subjects fall into euthyroid state (82.29%), remaining 16% had low levels of thyroid hormones and 1.71% showed raised levels. Nearly $1/5^{th}$ of diabetic individuals have presented with thyroid disorder which makes a major impact on health status of people in more populous country like India.

As role of insulin on physiological, biochemical functions and their interrelationship are well known. Also impact of insulin and thyroid hormones together in the metabolism of carbohydrate, protein and lipid are well documented.[11,12] Thyroid hormones have well described effects on glucose and lipid metabolism, both by short term and long term interaction with the regulatory network for energy homeostasis and via direct interaction with insulin regulation and glucose disposal in peripheral tissues.[13]

In our study mean age group of diabetic cases were 48.87±7.93 years. This study reflects the significance of sex related proportion of thyroid disorder in females which is almost double than that of males. This report is in agreement with Ghazali SM et al and Tajinder singh et al.[11,14] The finding may be associated with the higher prevalence of obesity recorded in diabetic females.[15]

Inappropriate secretion of thyroid hormones may occur in many thyroid diseases. Both hypothyroidism and hyperthyroidism are known to have adverse effects on glycaemic control in diabetics.[8] The present study reflects proportion of subclinical hypothyroidism of 12.57% and clinical hypothyroidism of 3.43% in diabetics; which shows females are at more risk of hypothyroidism than males. These observations are in accordance with Unnikrishnan AG et al, Gurjeet Singh et al and who had also reported high prevalence rate of hypothyroidism in females in India.[16,17] Hypothyroidism is characterised by impaired glucose absorption from the gastro intestinal tract, delayed peripheral glucose assimilation, gluconeogenesis, decreased or normal hepatic glucose output and decreased peripheral tissue glucose disposal.[18]

Insulin which is used in treating type 1 diabetes mellitus and is produced in normal quantities or in excess

in type 2 diabetics has been associated with increased anabolic activity.[19] Most of the diabetic subjects of this study were on oral hypoglycaemic drugs and few were receiving both oral hypoglycaemic drugs as well as insulin injections. According to some studies conducted states that, abnormal levels of thyroid hormones occurred due to intake of medications in diabetics like phenylthiourea which suppress the level of FT_4 and T_4, while causing raised levels of TSH.[20] Insulin enhances the level of FT_4 while it suppresses the level of T_3 by inhibiting hepatic conversion of T_4 to T_3 and decreased TRH synthesis in diabetics.[21]

The proportion of hyperthyroidism was found to be more in females than males contributing only 1.71% of total abnormal thyroid diseases. This was in contrast to studies done by Vikram BV et al[22] and Udiong et al[23] showed prevalence rate of hyperthyroidism is more in males than females. This may be due to difference in the time of sample collection. Excess thyroid hormones leads to hyperglycaemia via increased glucose absorption by gastro intestinal tract, increased hepatic glucose output, hyperproinsulinaemia, hyperinsulinaemia, high free fatty acid levels, increased peripheral glucose transport.[24]

Among the thyroid disorders of this study group, it clearly indicates proportion of subclinical hypothyroidism is more than clinical hypothyroidism/ hyperthyroidism and that to gender distribution is higher in females. These are in accordance with Pranav Kumar et al.[25]

Conclusion

In our study, we found 17.71% thyroid disorders in type 2 diabetes patients as compared to 2.85% in healthy group. High frequency of subclinical hypothyroid cases associated with type 2 diabetes mellitus may cause severe health complications like cardiovascular diseases, neuropathy, retinopathy etc. as the disease progresses.

Therefore, routine screening of thyroid profile in such clinical scenario which will help to reduce mortality and morbidity as a consequence of complication of diabetes mellitus. To generalize the above finding and to support for inclusion of routine thyroid profile screening in diabetic patient requires analysis of thyroid status on large diabetic population.

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