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Original Research Article

A Study to evaluate the relationship between glycemic control and occurrence of altered thyroid function in type 2 diabetes mellitus

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Abstract
Thyroid hormones affect glucose metabolism through several mechanisms. Hyperthyroidism has been recognized to promote hyperglycemia. During hyperthyroidism, the half-life of insulin is reduced most likely secondary to an increased rate of degradation and an enhanced release of biologically inactive insulin precursors. Randomly selected 100 patients, both male and female with type 2 diabetes mellitus above age of 40 years including newly diagnosed diabetics attending hospital were included in this study. Out of 12 patients 4 patients (33.3%) had systemic hypertension and 1 patient (8.33%) had ischemic heart disease, compared with normal thyroid profile group it is of no statistical significance with P value of 0.896. Comparing mean HbA1C of patients with abnormal thyroid profile with that of patients with normal thyroid profile it has no statistical significance with P value of 0.7944.
Keywords: Glycemic control, altered thyroid function, type 2 diabetes mellitus

Introduction
Diabetes mellitus and thyroid disease are the two common endocrine disorders in adult population since they influence each other. Poorly controlled diabetes results in loss of TSH response to TRH and a low T3 state. Regardless of glycemic control there is an absence of nocturnal TSH peak. In patients with Graves disease there is increased evidence of dysthyroid optic neuropathy with coexistent diabetes. After treatment prognosis is poor. 50% of thyrotoxic patients exhibit glucose intolerance who was previously euglycemic and exhibit frank diabetes in 2-3% cases. Presence of thyrotoxicosis deteriorates glycemic control in diabetics. Higher prevalence of thyroid dysfunction seen in type 1 diabetes mellitus patients nearly in third of all newly detected showing thyroid autoimmunity. Type 1 diabetes mellitus and hypothyroidism coexist with congenital rubella and in downs syndrome [1].
Thyroid hormones affect glucose metabolism through several mechanisms. Hyperthyroidism has been recognized to promote hyperglycemia. During hyperthyroidism, the half-life of insulin is reduced most likely secondary to an increased rate of degradation and an enhanced release of biologically inactive insulin precursors [2].
In untreated Graves' disease, increased proinsulin levels in response to a meal were observed in a study by Bech *et al*. In untreated hyperthyroidism there is an underlying defect in

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proinsulin processing as there is reduced C-peptide to proinsulin ratio. Another mechanism involved between hyperthyroidism and hyperglycemia is increase in glucose gut absorption mediated by excess thyroid hormones. Hyperthyroidism also enhances endogenous production of glucose. Thyroid hormones produce an increase in the hepatocyte plasma membrane concentrations of GLUT2 which is the main glucose transporter in the liver and consequently, the increased levels of GLUT-2 contribute to the increased hepatic glucose output and abnormal glucose metabolism [53]. Increase lipolysis seen in hyperthyroidism as a result increased production of free fatty acids which stimulates hepatic gluconeogenesis. Excessive thyroid hormones induces catecholamine stimulated lipolysis. The nonoxidative glucose disposal in hyperthyroidism results in overproduction of lactate that enters the cori cycle and promotes further hepatic gluconeogenesis. The increase in GH, glucagon and catecholamine levels associated with hyperthyroidism further contributes to the impaired glucose tolerance [3].

It is well known that diabetic patients with hyperthyroidism experience worsening of their glycemic control and thyrotoxicosis has been shown to precipitate diabetic ketoacidosis in subjects with diabetes.

In hypothyroidism, glucose metabolism is affected as well through several mechanisms. In hypothyroidism there is a reduced rate of liver glucose production as a result insulin requirement is decreased in hypothyroid diabetic patients. Recurrent hypoglycemic episodes are the presenting signs for the development of hypothyroidism in patients with type 1 diabetes and replacement with thyroid hormones reduced the fluctuations in blood glucose levels as demonstrated by Leong *et al*. In a case control study involving type 1 diabetics with subclinical hypothyroidism, 12 months prior to diagnosis of hypothyroidism experiences frequent episodes of hypoglycemia compared to euthyroid subjects [4].

On the other hand, both clinical and subclinical hypothyroidisms have been recognized as insulin resistant states. *In vivo* and *in vitro* studies have shown that this is due to impaired insulin stimulated glucose utilization in peripheral. One of the study showed higher TSH levels seen in patients with metabolic syndrome compared to that of non-metabolic syndrome suggesting subclinical hypothyroidism may be a risk factor for metabolic syndrome. study conducted among Chinese population. More recently, Erdogan *et al*. found an increased frequency of metabolic syndrome in subclinical and overt hypothyroidism compared to healthy controls [5]. Therefore, it seems prudent to consider hypothyroidism in newly diagnosed metabolic syndrome patients. Furthermore, an increased risk of nephropathy was shown in type 2 diabetic patients with subclinical hypothyroidism which could be explained by the decrease in cardiac output and increase in peripheral vascular resistance seen with hypothyroidism and the resulting decrease in renal flow and glomerular filtration rate. In 2005, Den Hollander *et al*. reported that treating hypothyroidism improved renal function in diabetic patients. As for retinopathy, Yang *et al*. demonstrated that diabetic patients with subclinical hypothyroidism have more severe retinopathy than euthyroid patients with diabetes [6].

The increased risk of retinopathy and nephropathy observed in diabetic patients with subclinical hypothyroidism provides evidence in favor of screening patients with type 2 diabetes for thyroid dysfunction and treating when present.

Methodology

Randomly selected 100 patients, both male and female with type 2 diabetes mellitus above age of 40 years including newly diagnosed diabetics attending hospital were included in this study.

- Informed consent was taken as per attached annexure.
- 100 type 2 diabetic patients, newly diagnosed was selected, as per inclusion and exclusion

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criteria.
- It is a cross sectional study.
- Detailed history was taken and examination performed as per attached annexure.
- Blood and other appropriate investigations were done as per attached annexure.
- Data compared and analysed as per chi-square test and student t test.

Inclusion criteria

Known type 2 diabetes mellitus and newly detected type 2 diabetes mellitus.

Exclusion criteria

Those who are not willing for the study
- Patient with known thyroid disease.
- Patient with chronic renal failure and diabetic nephropathy.
- Patient with acute illness like sepsis, acute MI, severe heart failure.
- Patient with hepatic dysfunction.
- Pregnancy.
- Patient on drugs like amiodarone, propranolol, corticosteroids and OCP.
- History of thyroidectomy.
- History of radioactive Iodine.

Thyroid profile

Reference values: Done in fasting serum sample
FT3:- 4-8.3pmol/L(ELFA method) (enzyme-linked immunosorbent assay).
FT4:- 9-24pmol/L(ELFA method).
TSH:- 0.25-5microIU/ml(ELFA method).

Subclinical Hypothyroidism is defined as TSH >5microIU/ml with normal FT3 and FT4levels.
Overt Hypothyroidism is defined as TSH >5microIU/ml with FT4 <9pmol/L.
Subclinical Hyperthyroidism is defined as TSH <5microIU/ml with normal FT3 and FT4 level Overt Hyperthyroidism is defined as TSH <5microIU/ml with FT4 >24pmol/L.

Results

Table 1: Relationship of Thyroid Profile and Gender

Gender	Normal thyroid profile	Abnormal thyroid profile	Chi square value	P value
Male	62	4	6.48	0.011*
Female	26	8		

Out of 12 patients with abnormal thyroid profile 4 patients (33.3%) were males and 8 patients (66.6%) were females, compared with normal thyroid profile group it has statistical significance with P value of 0.011.

Table 2: Relationship between Duration of Diabetes and Thyroid Profile

Thyroid Profile	Mean Duration	Standard Deviation	T Value	P Value
Normal	69.84	58.77	0.1781	0.8590
Abnormal	73	48.12		

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Comparing with mean duration of diabetes of patients with abnormal thyroid profile with that of patients with normal thyroid profile shows it has no statistical significance with P value of 0.8590.

Table 3: Relationship between Thyroid Profile and Type of Treatment for Diabetes

Type of treatment	Normal thyroid profile	Abnormal thyroid profile	Chi square value	P Value
OHA	63	9	3.11	0.211
Insulin	9	1		
Both OHA And Insulin	3	2		

Out of 12 patients with abnormal thyroid profile 9 patients (75%) were on oral hypoglycemic drugs, 1 patient (8.33%) on insulin and 2 patients (16.66%) on both. Compared with thyroid profile group it has no statistical significance with P value of 0.211.

Table 4: Relationship of Thyroid Profile with Adherence to Treatment in Diabetes

Adherence to Treatment	Normal Thyroid Profile	Abnormal Thyroid Profile	Chi Square Value	P Value
Adherent to Treatment	62	10	0.322	0.955
Not adherent to Treatment	13	2		

Out of 12 patients with abnormal thyroid profile 10 patients (83.33%) were adherent to treatment and 2 patients (16.66%) were not adherent to treatment, compared with normal thyroid profile group statistically not significant with P value of 0.955.

Table 5: Relationship of Thyroid Profile with Family History of Patient

Family history of diabetes	Normal thyroid profile	Abnormal thyroid profile	Chi square value	p value
Positive	41	7	0.583	0.445
Negative	47	5		

Out of 12 patients with abnormal thyroid profile 7 patients (58.33%) had family history of diabetes and 4 patients (33.3%) had no family history of diabetes, compared with normal thyroid profile group it is statistically not significant with P value of 0.445.

Table 6: Relationship of Thyroid Profile with Comorbid Conditions in the Patient

Comorbid Conditions	Normal Thyroid Profile	Abnormal Thyroid Profile	Chi Square Value	P Value
Hypertension	42	4	0.172	0.896
Ischaemic heart disease	9	1		

Out of 12 patients 4 patients (33.3%) had systemic hypertension and 1 patient (8.33%) had ischemic heart disease, compared with normal thyroid profile group it is of no statistical significance with P value of 0.896.

Table 7: Relationship of BMI with Thyroid Profile

BMI	Category	Patients with normal thyroid profile no. (%)	Patients with abnormal thyroid profile No. (%)	Chi-square Value	P Value
< 18.5	Underweight	0	0	4.26	0.039*
18.5-24.9	Healthy	34	1		
25-29.9	Overweight	46	7		

30-34.9	Obese I	5	4		
35-39.9	Obese II	1	0		
≥40	Obese III	2	0		

Out of 12 patients with abnormal thyroid profile none had below 18,5,1% between 18.5-24.9,7% were between 25-29.9,4% were between 30-34.99, compared with normal thyroid profile it is of statistical significant with P value of 0.039.

Table 8: Relationship of Mean Hba1c Levels with Thyroid Profile

Thyroid Profile	Mean HBA1C	Standard Deviation	T Value	P Value
Normal	7.87	1.49	0.2613	0.7944
Abnormal	7.75	1.51		

Comparing mean HbA1C of patients with abnormal thyroid profile with that of patients with normal thyroid profile it has no statistical significance with P value of 0.7944.

Discussion

Comparing mean T3 of patients with abnormal thyroid profile with that of patients with normal thyroid profile shows had no statistical significance with P value = 0.2429.
Comparing mean T4 of patients with abnormal thyroid profile with that of patients with normal thyroid profile shows it is statistically significant with P value = 0.0002.
Comparing mean TSH of patients with abnormal thyroid profile with that of patients with normal thyroid profile shows it is statistically significant with P value = <0.0001
Study conducted by Pankaj Kumar *et al*. shows that mean T3, T4 and TSH was 0.88±0.77, 80.51±40 and 9.69±2.5 respectively.
Among the study group of 100 patients age between 41 to 60 years 11 patients had abnormal thyroid profile and above age of 60 years 1 patient had abnormal thyroid profile. It is statistically significant with P value of 0.020.
Study conducted by Vondra *et al*. [7] observed that thyroid diseases in diabetic patients is 2-3 times higher than in non-diabetic subjects, it raises with age and is strongly influenced by female gender and autoimmune diabetes.
Study conducted by Papazafiropoulou *et al*. [8] found that age of patient is not statistically significant with altered thyroid profile.
Out of 12 patients with abnormal thyroid profile 4 patients (33.3%) were males and 8 patients (66.6%) were females, compared with normal thyroid profile group it has statistical significance with P value of 0.011.
Study conducted by Jimmy Anony *et al*. [9] observed that thyroid dysfunction is significantly more common in females than males.
Study conducted by Madavaran Sreelatha *et al*. [10] found significant correlation between female gender and altered thyroid profile.
Comparing with mean duration of diabetes of patients with abnormal thyroid profile with that of patients with normal thyroid profile shows it has no statistical significance with P value of 0.8590.
Study conducted by Madavaram Sreelatha *et al*. [10] observed there was no significant correlation between abnormal thyroid profile and duration of diabetes.
Out of 12 patients with abnormal thyroid profile 9 patients (75%) were on oral hypoglycemic drugs, 1 patient (8.33%) on insulin and 2 patients (16.66%) on both. Compared with thyroid profile group it has no statistical significance with P value of 0.211.
Study conducted by Celani MF *et al*. [11] observed prevalence abnormal thyroid function test results was significantly higher in insulin treated patients than in those receiving OHA. This

contradicts to our study.
Out of 12 patients with abnormal thyroid profile 10 patients (83.33%) were adherent to treatment and 2 patients (16.66%) were not adherent to treatment, compared with normal thyroid profile group statistically not significant with P value of 0.955.
Study conducted by Asha *et al*. [12] observed that 97% of type 2 diabetics were on antidiabetic agents and most were using them irregularly.
Study conducted by Madavaram Sreelatha *et al*. [10] observed that there was no statistically significant correlation between adherence of treatment in diabetics with abnormal thyroid profile.
Out of 12 patients with abnormal thyroid profile 7 patients (58.33%) had family history of diabetes and 4 patients (33.3%) had no family history of diabetes, compared with normal thyroid profile group it is statistically not significant with P value of 0.445.
Study conducted by Vishwanathan *et al*. [13] observed there was no significant correlation between family history of diabetics and abnormal thyroid profile.
Out of 12 patients 4 patients (33.3%) had systemic hypertension and 1 patient (8.33%) had ischemic heart disease, compared with normal thyroid profile group it is of no statistical significance with P value of 0.896.
Study conducted by Chubb *et al*. [14] found there was no significant correlation of ischemic heart disease and hypertension with abnormal thyroid profile.
Comparing mean BMI of patients with abnormal thyroid profile with that of patients with normal thyroid profile shows it is of statistical significance with P value of 0.039.
Study conducted by Papazafiropoulou *et al*. [8] found BMI was higher in diabetic patients with abnormal thyroid profile compared to diabetic patients with normal thyroid profile.
Study conducted by Madavaram Sreelatha *et al*. [10] found there was no significant correlation between BMI and abnormal thyroid profile.
Comparing mean HbA1C of patients with abnormal thyroid profile with that of patients with normal thyroid profile it has no statistical significance with P value of 0.7944.
Study conducted by Papazafiropoulou *et al*. [8] observed there was no correlation between HbA1C and abnormal thyroid profile.

Conclusion

In our study we found that there was significant correlation between abnormal thyroid profile and Age, Gender, BMI.

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