



A Study of Prevalence of Thyroid Dysfunction in Diabetic Population and its Clinical Correlation: A Cross Sectional Study

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ABSTRACT

Introduction: Diabetes mellitus and thyroid dysfunction are two common endocrine disorders in clinical practice. The co-existence of two disorders in same individual will obviously add to the worsening of cardiovascular and other co-morbidities and their outcome. Hence there is greater need for diagnosing them and institution of therapy as early as possible. So aim of our study is to assess the prevalence of thyroid dysfunction in diabetic population and its clinical correlation.

Materials and Methods: Study enrolled 132 outdoor patients attending medicine OPD and who were admitted in Medicine ward in Maharaja Yashwantrao Hospital, Indore, Madhya Pradesh, India. Patients were assessed by questionnaire, clinical examination followed by Immunoassay testing for TSH, T₃, T₄ Free T₃ and Free T₄ and measurement of fasting and post prandial blood sugar.

Results: A total 16.66% (2/12) T1DM patients and 19.16% (25/120) T2DM were found to have altered thyroid test due to primary thyroid disorder. In T1DM, hyperthyroidism and, in T2DM patients, hypothyroidism was most prevalent disorder. Hypothyroid patients were having higher mean total cholesterol level and hyperthyroid patients were having lower level as compared to euthyroid patients. Female patients were found to have a higher proportion of altered thyroid function (15/75=20%) than the male population (10/57=17.54%); with primary thyroid disease occurring in 20% of females and 15.79% of male population.

Conclusions: Prevalence of thyroid dysfunction was higher in T2DM compare to T1DM patients. In T1DM hyperthyroidism and in T2DM primary hypothyroidism followed by subclinical hypothyroidism was most prevalent disorder. We should not delay the thyroid function test in diabetic patient till clinical sign become overt because they were less sensitive.

Keywords: Diabetes mellitus, Thyroid dysfunction, Subclinical hypothyroidism.

INTRODUCTION

Diabetes Mellitus and Thyroid dysfunction are two common endocrine disorders in clinical practice. The co-existence of two disorders in same individual will obviously add to the worsening of cardiovascular and other co-morbidities outcome. It has been estimated that about 42 million people in India suffer from thyroid disease^[1]. Later in their life these patients would have associated with thyroid dysfunction^[2-4,7]. However prevalence of the thyroid dysfunction and its clinical correlation in diabetes has not been investigated. Many reports have shown that only clinical assessment might not be able to detect all the cases of thyroid dysfunction as a large percentage of

them are subclinical which can be diagnosed by biochemical assessment only^[4-6]. Hence there is greater need for diagnosing them and institution of therapy as early. So, aim of our study is to assess the prevalence of thyroid dysfunction in diabetic population.

MATERIALS AND METHODS: A cross sectional observation study was carried in Department of Medicine M.G.M. Medical College, Indore, Madhya Pradesh, India. The study was performed on 132 patients attending medicine OPD and who were admitted in medicine ward under Department of Medicine.

Eligibility criteria

Patients attending medicine OPD and admitted in medical ward at Maharaja Yashwantrao Hospital with history of diabetes or were found to be diabetic on assessment at presentation.

Exclusion criteria

1. Patients who were on drugs that are known to modify the thyroid functions e.g. Lithium, Amiodarone.
2. Patients who had undergone surgery on thyroid gland.
3. Patients who had undergone exposure to radiation of the thyroid gland.
4. Patients of drug-induced hyperglycemia e.g. high dose steroids, pentamidine, diazoxide etc.

Criteria for diagnosis of DM^[8]

FBS ≥ 126 mg/dl and/or

PPBS ≥ 200 mg/dl and/or

HbA1C $\geq 6.5\%$

Known diabetic patients taking treatment

Assessment of Thyroid Function Test

Immunoassay testing for TSH, T3, T4, fT3 and fT4.

Definition of Thyroid Dysfunction^[9]

Euthyroid status - Normal TSH, T3, T4 or fT4

Primary hypothyroidism - Elevated TSH with subnormal T3, T4 or fT4

Primary hypothyroidism -Elevated T3, T4 or fT4 with subnormal TSH

Subclinical hypothyroidism - Elevated TSH with normal fT4

Subclinical hypothyroidism - Subnormal TSH with normal fT4

T3 toxicosis syndrome -Elevated T3 or fT3, normal fT4 and normal TSH

Statistical analysis

The discrete data were assessed in numbers and in percentages.

Following data were analyzed

- To find out the proportion of diabetic population suffering from any form of thyroid dysfunction.
- To find out whether there is any difference in the age and sex wise distribution of the patients and type of diabetes mellitus.
- To find out if there is any correlation between clinical signs and symptoms with the biochemical evidence of thyroid dysfunction in diabetic patients.

Statistical significance was assessed by SPSS version 16.

RESULTS

As shown in table 1, out of 132 diabetic patients, prevalence of euthyroid, hypothyroid, hyperthyroid, subclinical hypothyroid, subclinical hyperthyroid and non thyroid illness were 81.06%, 6.82%, 1.5%, 5.30%, 3.79%, and 0.76% respectively.

Table 1: Age wise distribution of thyroid profile in the entire study population

Age Group	Euthyroid	Hypothyroid	Hyperthyroid	Subclinical Hypothyroid	Subclinical Hyperthyroid	T3 Toxicosis	NTI	Total
<20	2	0	1	0	0	0	0	3
20-29	2	0	0	0	0	0	0	2
30-39	7	1	0	0	0	1	0	9
40-49	23	4	0	1	0	0	0	28

50-59	34	3	0	3	2	0	0	42
60-69	27	1	1	3	0	0	1	33
70-79	9	0	0	0	2	0	0	11
≥80	3	0	0	0	1	0	0	4
Total	107	9	2	7	5	1	1	132

As shown in table 2, out of 132 diabetic patients, 9.09%(12/132) were suffering from T1DM and 90.9%(120/132) from T2DM. 8.33 % (1/12) were having primary hyperthyroidism, 8.33% (1/12) were having T3 toxicosis in T1DM patients. In T2DM patients, primary hypothyroidism was the most prevalent disorder occurring in up to 7.5% of total diabetic population followed by subclinical hypothyroidism in 5.83%, subclinical hyperthyroidism in 4.16%, hyperthyroidism in 0.83%, and non thyroid dysfunction in 0.83%. Out of these, the prevalence of hypothyroidism in males and females was 3.33% and 4.16% respectively. Prevalence of subclinical hypothyroidism in males and females was 1.66% and 4.16% respectively. Prevalence of subclinical hyperthyroidism in male and females was 1.66% and 2.5% respectively and non thyroid illness was 0.83% in males.

Table 2: Distribution of thyroid profile in the types of diabetes mellitus

Type of DM	Euthyroid		Hypothyroid		Hyperthyroid		Subclinical Hypothyroid		Subclinical Hyperthyroid		T3 Toxicosis		NTI		Total	
T1DM	9(81.82 %)		0		1(9.09 %)		0		0		1(9.09 %)				11(8.33%)	
T2DM	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
	41	57	4	5	1	0	2	5	2	3	0	0	1	0	51	70
Total	98		9		1		7		5		0		1		121	

NTI- Non Thyroid Illness

As shown in table 3, in 21.5% euthyroid, 22.22% hypothyroid, 14.29% subclinical hypothyroid and 20% of subclinical hyperthyroid had blood sugar below the normal level. In 12.15% euthyroid and 14.29% subclinical hypothyroid patients had deranged FBS. In 10.28% euthyroid and 11.11% hypothyroid patients had deranged PPBS. In 56% euthyroid, 66.67% hypothyroid, 100% hyperthyroid, 71.42% subclinical hypothyroid and 80% subclinical hyperthyroid patients had both deranged FBS and PPBS.

Table 3: Correlation of thyroid profile with the blood sugar level

Thyroid profile	FBS<7 PPBS<11.1	FBS>7 PPBS<11.1	FBS<7 PPBS >11.1	FBS>7 PPBS>11.1	Total
Euthyroid	23	13	11	60	107
Hypothyroid	2	0	1	6	9

Hyperthyroid	0	0	0	2	2
Subclinical hypothyroid	1	1	0	5	7
Subclinical hyperthyroid	1	0	0	4	5
T3 toxicosis	0	0	0	1	1
Non thyroid illness	0	0	0	1	1
Total	27	14	12	79	132

FBS and PPBS values expressed in mmol/L

As shown in table 4, most common diabetic complication was CAD (n=26) followed by diabetic nephropathy (n=20), diabetic neuropathy, diabetic retinopathy (n=15), Diabetic keto acidosis (n=6), CVA (n=4) and least NKHC (n=1) and diabetic foot (n=1). These complications were more prevalent in primary and subclinical hypothyroidism than in hyperthyroidism.

Table 4: Correlation of thyroid profile with various diabetic complications

Age Group	Euthyroid	Hypothyroid	Hyperthyroid	Subclinical Hypothyroid	Subclinical Hyperthyroid	T3 Toxicosis	NTI	Total
Diabetic ketoacidosis	6	0	0	0	1	1	0	9
Non ketotic hyperosmolar coma	1	0	0	0	0	0	0	1
Retinopathy	15	0	0	0	0	0	0	15
Nephropathy	20	1	0	0	0	0	0	21
Neuropathy	16	2	0	1	1	1	0	21
Coronary ARTERY Disease	26	2	1	1	0	0	0	30
Cerebrovascular Accident	4	0	0	1	2	0	0	7
Diabetic Foot	1	0	0	0	0	0	1	2

NTI- Non Thyroid Illness

As shown in table 5, in hypothyroidism, most common symptoms were tiredness (75%) followed by constipation (68.75%), high BMI (56.25%) and shortness of breath(50%).

Table 5: Predictive value of sign and symptoms in hypothyroidism

Clinical sign and symptom	sensitivity	specificity	Positive predictive value	Negative predictive value	Odds ratio
Weight gain	37.50 %	88.10 %	28.57 %	91.74 %	4.44
Cold intolerance	12.50 %	100 %	100 %	89.23 %	0
Constipation	68.75 %	56.03 %	17.74 %	92.86 %	2.80
Tiredness	75.00 %	25.00 %	12.12 %	87.88 %	1
Hoarseness	6.25 %	98.27 %	33.33 %	88.37 %	3.8
Menstrual problem	6.25 %	99.13 %	50.00 %	88.46 %	7.67
Shortness of breath	50.00 %	59.48 %	14.55 %	89.61 %	1.47
Decreased sweating	25.00 %	96.55 %	50.00 %	90.32 %	9.33
Decreased appetite	25.00 %	59.48 %	7.84 %	85.19 %	0.49
Dryness of mouth	43.75 %	81.89 %	25.00 %	91.35 %	3.52
Dryness of skin	12.50 %	96.55 %	33.33 %	88.89 %	4.0
Depression	43.75 %	72.41 %	17.90 %	90.30 %	2.04
Facial puffiness	6.25 %	94.83 %	14.29 %	88.00 %	1.22
Pedal edema and facial puffiness both	12.50 %	94.83 %	25.00 %	88.71 %	2.61
High BMI	56.25 %	56.52 %	15.00 %	90.28 %	0.64
Delayed Deep tendon reflex	37.50 %	98.28 %	75.00 %	91.94 %	34.20
Palpable thyroid	18.75 %	98.28 %	60.00 %	89.76 %	13.15

As shown in table 6, in hyperthyroidism most common symptoms were tiredness (100%) followed by shortness of breath (87.5%) and rest sign and symptoms were less sensitive (less than 50 %).

Table 6: Predictive value of signs and symptoms in hyperthyroidism

Clinical sign and symptom	sensitivity	specificity	Positive predictive value	Negative predictive value	Odds ratio
Weight Loss	37.50 %	79.84 %	10.71 %	95.19 %	2.38

Warm intolerance	37.50 %	85.84 %	14.29 %	95.50 %	3.53
Diarrhea	25.00 %	96.77 %	33.33 %	95.24 %	10
Tiredness	100 %	26.61 %	8.08 %	100 %	0
Palpitation	37.50 %	88.70 %	17.65 %	95.65 %	4.71
Increased sweating	37.50 %	95.97 %	37.50 %	95.97 %	14.28
Increased appetite	12.50 %	83.60 %	4.54 %	93.64 %	0.70
Shortness of breath	87.50 %	60.48 %	12.50 %	98.68 %	10.71
Restlessness	12.50 %	98.39 %	33.33 %	94.57 %	8.71
Tachycardia	37.50 %	86.29 %	15.00 %	95.54 %	3.78
Low BMI	25.00 %	91.12 %	15.38 %	94.96 %	3.42
Exaggerated Deep tendon reflex	25.00 %	99.19 %	66.67 %	95.35 %	41
Palpable thyroid	12.50 %	96.67 %	20.00 %	94.49 %	4.29

DISCUSSION:

In our study, primary hypothyroidism was the most prevalent disorder in diabetic patients in 6.8%, followed by subclinical hypothyroidism in 5.3%, subclinical hyperthyroidism in 3.7%, hyperthyroidism in 1.5%, and non thyroid dysfunction in 0.75% of total diabetic patients and all forms of thyroid disease were found more frequently in females than males. In study done by laloo Demistrost et al in Manipur India showed prevalence of thyroid dysfunction in T2DM was 31.2% but excluded the patients with previous history of hypothyroidism^[2]. Similarly a study done in Spain by Deiz et al who found an overall prevalence of thyroid dysfunction in 32.4% of T2DM patients^[10]. Another study in Jordan by Radiaheh et al also found prevalence of thyroid disease in T2DM to be 12.5 % and 6.6 % in the control group^[11]. In study done in Greece, the prevalence of thyroid dysfunction in T2DM was found to be 12.3 % with higher prevalence in female^[12]. Above three studies done only in T2DM but we also found prevalence of thyroid dysfunction in T1DM.

In our study, prevalence of thyroid dysfunction was higher in T2DM compare to T1DM patients. Hyperthyroidism (16.66% of total T1DM patients) was the most prevalent disorder in T1DM patients, of which males and females were equally affected whereas in T2DM patients primary hypothyroidism in 7.5% was the most prevalent disorder followed by subclinical hypothyroidism in 5.83%, subclinical hyperthyroidism in 4.16%, hyperthyroidism in 0.83% and nonthyroid dysfunction in 0.83% patients. A study by Perros et al also found a prevalence of 13.4% in diabetics but more in T1DM female patients^[4].

Another aspect of our study is that most of the clinical findings of thyroid dysfunction were not very sensitive of the disease for which they were being utilized. This corroborates with a study done by Safeeq A where the researchers also found that the clinical manifestation of thyroid disease were not at all sensitive (with most findings below 50 %) but were quite specific^[11].

All the cases of subclinical hypothyroidism were found in patients above the age of 40 years. Although

subclinical hyperthyroidism was found to be more evenly distributed, maximum number of them was found above the age of 50 years. This supports Perros observation that all elderly diabetics should undergo annual screening for thyroid disease^[4].

Another similarity that was noted by us was that to the result published in Colorado study that investigators confirm that modest elevation of TSH correspond to changes in lipids (mainly total cholesterol and LDL cholesterol)^[14]. In our study it was the total cholesterol level. Although serum lipids might be deranged in both Diabetes mellitus as well as hypothyroidism, due to effect of insulin and thyroxine on the total cholesterol and triglycerides etc. We found average serum cholesterol level were higher in patients suffering from concurrent hypothyroidism as well as subclinical hypothyroidism than those who were euthyroid, which was in turn higher than those who had subclinical hyperthyroidism, with the lowest values obtained in those suffering from hyperthyroidism.

As has already been discussed, male patients were found to suffer lesser from thyroid disease than female patients. Another notable difference is fact that males tend to have hypothyroidism at younger age {1 patient being younger than 40 years (25%)} but subclinical hypothyroidism tend to occur at an older age with all cases occurring in males above the age of 40 years and the same pattern was noticed in female patients as well.

CONCLUSIONS:

1. Prevalence of thyroid dysfunction is higher in T2DM patients compare to T1DM patients.
2. Prevalence of thyroid dysfunction increases with age.
3. In T1DM patients, hyperthyroidism and in T2DM patients, primary hypothyroidism followed by subclinical hypothyroidism was most prevalent disorder.
4. We should not delay the thyroid function test in diabetic patient for clinical signs become overt because they are less sensitive and thyroid dysfunction can be raised.
5. Prevalence was higher in females than males.
6. Patients with BMI higher than 25 were having more prevalence of thyroid dysfunctions.

7. Higher mean cholesterol level in hypothyroid patients and lower mean cholesterol level in hyperthyroid patients as compared to euthyroid patients was also found in our study.

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Disclosure

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Conflict of interest: Not declared

Ethical approval: The study was approved by the institutional ethics committee.

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