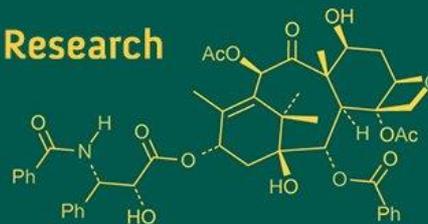
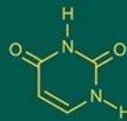
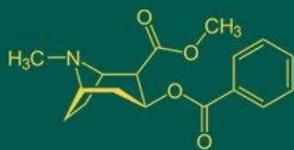


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To evaluate the presence of subclinical thyroid disorder in type 2 diabetes mellitus

Suresh KumarDOI: <https://doi.org/10.33545/26174693.2020.v4.i2a.52>**Abstract**

Objectives: Our objective is to determine the prevalence of subclinical thyroid disorders in patients with type 2 diabetes mellitus (T2DM) and to analyze the clinical and metabolic profile of patients with this dual endocrine disorder.

Methods and Results: Sixty consecutive type 2 diabetic patients without clinical manifestations of thyroid disorders were screened for SCH and subclinical hyperthyroidism using serum free T₃, free T₄ and thyroid stimulating hormone (TSH) levels. Individuals of subclinical thyroid disease were further screened for thyroperoxidase (TPO) antibodies. SCH was detected in 13% of type 2 diabetic patients and none had subclinical hyperthyroidism in our study. SCH was common among females with type 2 diabetes (84.6%). Elevated TPO antibody levels were present in 84.6% SCH patients. Diabetic retinopathy among SCH patients showed significant association with higher serum TSH levels. Left ventricular diastolic dysfunction was present in 30.8% of SCH patients.

Conclusion: SCH is common among type 2 diabetic patients, especially in females. It is most commonly secondary to autoimmune thyroid disease. Microvascular complications are commonly observed in this group of patients with dual endocrinal disorder and treating physician should be aware of the impact and should routinely screen SCH to prevent complications.

Keywords: Anti-thyroperoxidase antibody, subclinical hypothyroidism, subclinical hyperthyroidism, type 2 diabetes mellitus

Introduction

Diabetes mellitus is an important health problem affecting major populations in worldwide. It is characterized by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid, and protein metabolism [1]. Diabetic patients have higher prevalence of thyroid disorder when compared with the normal population, with hypothyroidism being the most common disorder [2]. Prevalence of thyroid dysfunction varied from 2.2%–17% in diabetics. Diabetic women are more frequently affected than men and hypothyroidism is more common than thyrotoxicosis [3]. DM often simply referred to as diabetes, is a group of common metabolic disorders that shares the phenotype of hyperglycemia, either because the body does not produce enough insulin or because the β -cells do not respond to insulin that is produced [4]. The metabolic deregulations associated with DM causes secondary pathophysiological changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. With an increasing incidence in worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future [5, 6].

Thyroid disorders are also very common in the general population and it is second only to DM as the most common condition to affect the endocrine system. As a result it is common for an individual to be affected by both thyroid diseases and diabetes. The first report showing the association between diabetes and thyroid dysfunction was published in 1979 [7, 8]. Since then a number of studies have estimated the prevalence of thyroid dysfunction among diabetes patients to be varying from 2.2 to 17 %, the most common disorder being subclinical hypothyroidism [9, 10]. According to National Health and Nutrition Examination and Survey III (NHANES III USA), in last 8 years duration, the prevalence of hypothyroidism was 4.6% (0.3% clinical and 4.3% subclinical) and of hyperthyroidism was 1.3% (0.5% clinical and 0.8% subclinical) in population aged at least 12, showing age and

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Sex dependence i.e. prevalence showing positive correlation with increasing age and female sex^[11].

Diabetic patients with sub-clinical hypothyroidism have been reported to be associated with an increased risk of nephropathy and cardiovascular disease^[12, 13]. Micro-angiopathic complications of diabetes like retinopathy and neuropathy can worsen in the presence of co-existing hypothyroidism due to dyslipidemia. Screening for thyroid abnormalities in diabetic patients will allow early treatment of sub-clinical and overt thyroid dysfunction.¹⁴ This study was done to determine the prevalence of subclinical thyroid disorders in patients with type 2 diabetes mellitus (T2DM) and to analyze the clinical and metabolic profile of patients with this dual endocrine disorder.

Materials and Methods

Study Area

The present study will be undertaken in the Department of Biochemistry in collaboration with Department of Medicine, M.M Institute of Medical Sciences and Research, Mullana, Ambala.

Ethical approval and Informed consent

The study protocol was reviewed by the Ethical Committee of the Hospital and granted ethical clearance. Prior informed consent for this study was obtained from subjects, in writing both in English and Vernacular.

Inclusion Criteria

1. Type 2 DM patient
2. Age Group: Between 35 -70 years.

Exclusion Criteria

1. Type 1 DM
2. Systemic hypertension
3. Symptomatic thyroid disease
4. Pre -existing renal disease
5. Pre -existing thrombocytopenia, hepatocellular damage

Patient selection

The present hospital based study is proposed to be undertaken with a total of 60 subjects in the age range of 35-70 years irrespective of sex from the OPD and wards of M.M Institute of Medical Sciences and Research, Mullana, Ambala. Detailed history of all the individuals was taken.

Collection and Processing of Blood Sample

5ml of venous blood sample was aseptically collected from ante-cubital vein and was poured in plain vacutainer. These samples were then carried to the Department of Biochemistry. In each case precautions were taken to prevent hemolysis of RBC's present in the samples. Samples were centrifuged at 3000 rpm for 10 minutes and clot was formed. Serum was separated, was pipette out from the top and stored in refrigerator at 2-8 °C for further investigations. The samples were analyzed within a week for estimation of serum T3, T4, and TSH hormone levels.

Statistical analysis

The recorded data was compiled entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations.

Results

Table 1: Age and Gender distribution of patients in the study population

Parameters	Frequency	Percentage
Age (Years)		
35 – 45	12	20.0
46 – 55	18	30.0
56 – 65	21	35.0
>65	9	15.0
Mean	54.47	
Gender		
Male	27	45.0
Female	33	55.0
Total	60	100

Maximum no. of patients in our study was age group 56-65 years (35%). Whereas (30%) of patients were in age group 46-55 years and 20% of patients were in age group 35-45 years. Mean age in study group was 54.47 years. Out of 60 patients 27(45%) were male patients and 33(55%) were female patients.

Table 2: Distribution of thyroid function in study population

Thyroid Function	Frequency	Percentage
Euthyroid	45	75.0
Subclinical Hypothyroidism	15	25.0
Total	60	100

The prevalence of thyroid dysfunction in our study was 25%. 75% of patients were euthyroid. Among the Type 2 diabetic had subclinical hypothyroidism, 25% (15/60) patients. None of the patients had subclinical hyperthyroidism.

Table 3: Age and Gender distribution of thyroid dysfunction in study population

Parameters	N	Euthyroid (N-45)	Thyroid Dysfunction (N-15)	p – value
Age				
35 - 45	12	11(24.5)	1(6.7)	0.096
46 – 55	18	14(31.1)	4(26.6)	
56 – 65	21	12(26.6)	9(60.0)	
>65	9	8(17.8)	1(6.7)	
Gender				
Male	27	21(46.7)	6(40.0)	0.653
Female	33	24(53.3)	9(60.0)	

Out of total 45 euthyroid patients 46.7% (21/45) were male and 53.3% (24/45) were females. Whereas out of total 15 patients with thyroid dysfunction 40% (6/15) were males and 60% (9/15) were females. So females had thyroid dysfunction more common than male patients in our study. However it was statistically non-significant (p = 0.653). Most of the patients (31.1%) with euthyroid were in age group 46 – 55 years. The second most common age group was 56 – 65 years which constituted 26.6% of patients. 24.5% of patients were in age group 35 – 45 years and 17.8% of patients were in age group > 65 years. But age distribution of patients according to thyroid dysfunction was statistically non-significantly (p=0.096)

Table 4: Comparison of mean distribution of fasting blood sugar in the study

Thyroid function	N	Mean	Std. deviation
Euthyroid	45	165.64	39.724
Subclinical hypothyroidism	15	174.27	14.129
t-value, p-value	0.820, 0.416		

Mean distribution of fasting blood sugar in our study in patients with thyroid dysfunction was 174.27% (+/-14.129). Mean distribution of fasting blood sugar in euthyroid patients in this study was 165.64(+/-39.724). But no statistical significance was found ($p=0.416$).

Table 5: Association between duration of diabetes and occurrence of thyroid dysfunction

Group	Duration (in years)	N	Euthyroid (N-45)	Subclinical Hypothyroidism (N-15)	p-value
A	1-3	27	22(48.9)	5(33.3)	0.171
B	4-6	24	15(33.3)	9(60.0)	
C	7-9	9	8(17.8)	1(6.7)	

Maximum no. of cases of thyroid dysfunction (60.0%) were in group B (4-6 years). 33.3% of cases were in group A (1-3 years) and 6.7% were in group C (7-9 years). In case of patients with euthyroid maximum no. of patients (48.9%) were in group A (1-3 years). 33.3% of patients were in group B (4-6 years) and 17.8% of patients were in group C (7-9 years). Correlation of duration of diabetes with thyroid dysfunction was statistically non-significant ($p=0.171$).

Discussion

Total 60 patients of Type 2 DM were studied for evaluation of thyroid dysfunction. Out of which 27 (45%) were male patients and 33 (55%) were female patients. Maximum number of patients in our study in age group 56 – 65 yrs (35%). Whereas minimum no. of patients (15%) were in study >65 yrs. Mean age in study group was 54.47 yrs. Mean age of association with thyroid dysfunction was 54.46(+/- 6.65) yrs.

The prevalence of thyroid dysfunction in our study was 25%. Results are similar to study done by Singh P *et al.* [15] in which prevalence of thyroid dysfunction was 29%. In study by Celani MF *et al.* [16] prevalence of thyroid dysfunction was 31.4%. Babu K *et al.* [17] in their study found 28% prevalence of thyroid dysfunction. Udiong C.E.J *et al.* [18] in their study found 46.5% prevalence of thyroid dysfunction in diabetic patients.

In this study 75% of patients were euthyroid. In a study by Singh P *et al.* [15] 71% of patients were euthyroid. Among the Type 2 diabetic patients with thyroid dysfunction 16% had subclinical hypothyroidism. Our study findings are similar to study done by Singh *et al.* [19] in which he found hypothyroidism in 23.75% (15% subclinical hypothyroidism and 8.75% primary hypothyroidism) and hyperthyroidism in 6.25% (all primary hyperthyroidism) of diabetic subjects. In this study 6% of patients had overt hypothyroidism similar to study by Saha *et al.* [20] Only 2% of patients had overt hyperthyroidism. None of the patient had subclinical hyperthyroidism.

Mean age of association with thyroid dysfunction was 58.46(+/-6.65) yrs. Mean age of euthyroid patient was 53.13 (+/- 10.29) yrs. The mean age of the diabetics with thyroid dysfunction was higher than euthyroids but was not significant ($p= 0.066$). In the study by Kim B *et al.*, [21] the mean age of euthyroid patients of Type 2 DM was 57.8 (SD \pm 11.8) years and the mean age of Type 2 diabetics with SCH was 61.7 (SD \pm 9.8) years.

Most of the patients (60%) with thyroid dysfunction were in age group 56 – 65 years. Whereas most of the patients (31.1%) with euthyroid were in age group 46 – 55 years. Thyroid dysfunction was seen to be more prevalent in

higher age group in comparison to euthyroid patients. But it was non-significant ($p=0.096$). In study done by Bhavthankar S *et al.* [22] maximum no. of patients (33.3%) were in age group 51- 60 yrs.

Out of total 45 euthyroid patients 46.7% (21/45) were males and 53.3% (24/45) were females. Whereas out of total 15 patients with thyroid dysfunction 40% (6/15) were males and 60% (9/15) were females. So females had thyroid dysfunction more common than male patients in our study. However it was statistically non-significant ($p=0.653$).

In our study 22.2% of female patients had subclinical hypothyroidism whereas 8.7% of male patients had subclinical hypothyroidism. Yang GR *et al.* [23] studied 371 diabetics, in which 83 subjects (22.4%) were diagnosed as SCH of whom 12.1% were males and 29.9% were females.

Most of the studies have shown that thyroid disorders are more common in females with Type 2 diabetes [15-17].

According to duration of diabetes the cases were divided into three groups. Maximum no. of patients were in group A (1- 3 yrs.) 45% and group B (4- 6 yrs.) 40%. Only 15% of cases were in group C (7- 9 yrs.). Maximum number of cases of thyroid dysfunction (60%) were in group B (4- 6 yrs.). Association of duration of diabetes with thyroid dysfunction was statistically non-significant ($p=0.171$). Which is similar to the study done by Diez JJ *et al.* [24] In study conducted by Kumar A *et al.*, [25] 29.5% of patients had duration of diabetes <5 years and significant correlation was found in duration of diabetes with thyroid dysfunction.

Conclusion

The prevalence of subclinical hypothyroidism disorder in our study was 25%. None of patient had subclinical hyperthyroidism. Subclinical hypothyroidism was most prevalent thyroid disorder in patients with Type 2 diabetes mellitus (15% in female patients and 10% in males). Thyroid disorder was more prevalent in females as compared to males. There was no correlation between age, gender, duration of diabetes between euthyroid patients and patients with thyroid disorder. Our study recommend the evaluation of TSH levels in all Type 2 diabetic patients, as subclinical hypothyroidism was most prevalent thyroid disorder in patients with Type 2 diabetes.

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