

Thyroid Dysfunction in Diabetes Mellitus: A Cross-Sectional Study from a Western State in India

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Abstract: Thyroid Dysfunction (TD) and Diabetes Mellitus (DM) are often found associated in the same patient and TD may affect the metabolic control of DM. TD is more prevalent in diabetics than in general population. The current study investigates the prevalence of TD in patients with DM, and explores its correlation with age, sex, type and duration of DM, and glycemic control (HbA1c levels). This was an observational, cross-sectional study of 212 patients with DM. All patients had undergone routine clinical and laboratory evaluations as per the standard clinical care. Medical data was collected and analyzed using Epi Info V3.5.4. Among the 212 DM patients evaluated, the overall prevalence of TD was 24.52%. The overall prevalence of TD was less in type-2 DM (T2DM; 24.46%) as compared to type-1 DM (T1DM; 37.5%); and slightly more in females (31.94%) as compared to males (28.65%). The prevalence of TD was high in the middle age (41-60 years) group (52.17%) as compared to other age groups. Subclinical hypothyroidism (SCH) was the most common type of TD (11.79%) with maximum prevalence (50%) in T2DM. Patients with DM reported a high prevalence rate of 24.52% for TD. Patients between 41-60 years of age had higher prevalence of TD. Prevalence was slightly more in more in females as compared to males. Our data suggests for screening of DM patients for risk of TD that might be helpful in secondary and primary prevention and possible better metabolic control.

Keywords: Diabetes Mellitus, Thyroid Dysfunction, Prevalence, Subclinical hypothyroidism, Hyperthyroidism.

INTRODUCTION

Thyroid Dysfunction (TD) and Diabetes Mellitus (DM) are endocrinopathies often found associated in the same patient and reported to have an interdependent relationship at the genetic, biochemical and hormonal level [1, 2]. In 1927, *Coller and Huggins* first reported the role of hyperthyroidism in worsening of diabetes; primarily characterized by a composite interaction of interdependence between the two pathologies [3].

Thyroid dysfunction is known to have a higher prevalence (10-24%) in diabetics as compared to non-diabetics (6-13%) [1, 2]; in women as compared to men; and an increased prevalence rate with age [6]. Subclinical hypothyroidism (SCH) has been reported in 4 to 8.5% of middle-aged women, while in 20% of women above 60 years [7]. Literature suggests a high prevalence of TD amongst Type-2 Diabetes Mellitus (T2DM) patients. *Akbar et al.* investigated the association between TD, thyroid autoimmunity and T2DM in a random sample of 100 Saudi T2DM patients

and 100 age and sex-matched controls, and reported 6% prevalence for TD in T2DM patients [3]. A study from Greece in 1,092 patients with T2DM reported a high prevalence rate of 12.3% for TD amongst female T2DM patients attending an outpatient clinic [2]. A retrospective study in 202 T2DM patients from India reported 139 (68.8%) patients with euthyroidism, 33 (16.3%) with SCH, 23 (11.4%) with hypothyroidism, 4 (2%) with SCH and 3 (1.5%) with hyperthyroidism. Maximum cases of subclinical and clinical hypothyroidism were seen in the age group of 45-64 years, and in females [1].

Globally, India is one of the countries where highest number of new DM cases is reported. The public burden of the disease in India is very high and a significant proportion of the age group it affects is the economically productive age group. There is a thrust to understand factors that may influence the course or severity of the disease or its treatment as the increasing number of new DM cases every year with its associated morbidities and mortality. Considering the dearth of

data it would be of scientific value to study the prevalence of TD in Indian patients with DM.

MATERIALS AND METHODS

This was a single-centre, observational, cross-sectional study conducted at the SSG Hospital, a government hospital and medical college, Vadodara, Gujarat, India during the period of January 2015 to September 2015. The study planned to enrol 212 patients, for a 80% power and allowable error of 20% (relative error). The aim of the study was to investigate the prevalence of TD in DM patients and explore its correlation with age, gender, type of diabetes.

Adult patients ≥ 18 years of age with newly diagnosed or existing Type-1 Diabetes Mellitus (T1DM) or T2DM, who regularly attended both in-patient and out-patient clinics of the diabetes unit at the hospital were considered. The study protocol, patient informed consent documents and study conduct were approved by the Institutional Ethics Committee (IEC) for Human Research, Medical College, Vadodara prior to the study initiation. Written informed consent was obtained from each patient prior to entry into the study, in compliance with regulatory requirements.

Patients were either receiving regular diabetes treatment (insulin and/or oral hypoglycemic); or were treatment naive or on diet therapy alone. Patients with a history of thyroid disorder or being treated with drugs like amiodarone, antithyroid medications, lithium etc. that may alter the thyroid function; patients having

diabetic ketoacidosis and DM secondary to pancreatitis; and on steroid therapies were excluded. Old debilitated patients who were comatose or had an altered sensorium, those who could not communicate for any reason and patients who were not willing to give informed consent were also excluded.

Demographic and clinical data were recorded for all the patients. Clinical laboratory investigations including hematological tests - Hb%, total count and platelet counts and biochemical parameters - serum creatinine; random blood sugar (RBS); fasting blood sugar (FBS); post-prandial blood sugar (PP2BS); HbA1C and thyroid profile (fasting) - Serum Thyroid Stimulating Hormone (S.TSH), Free T3, Free T4 were also performed for all the patients.

Patients were diagnosed for DM based on the American Diabetes Association (ADA), 2013 criteria for diabetes as follows: Symptoms of diabetes plus glucose of more than 200 mg/dl or fasting glucose more than 126 mg/dl or 2-hour post-prandial glucose more than 200 mg/dl or HbA1C value of more than 6.5 g/ml. Patients having onset of diabetes at an age of < 35 years and with dependence on insulin therapy alone for complete control, were considered as T1DM patients and rest as T2DM.

The TD status of patients was analyzed by thyroid function tests taken in a fasting state and was categorized as:

Table-1: Categorization of thyroid dysfunction status among diabetic patients

Category	Reference value
Euthyroid	<ul style="list-style-type: none"> • Free T4 was 0.93-1.70 ng/ml, • Free T3 was 2.00-4.43 ng/ml, and • S.TSH was 0.27-4.2 μIU/ml
Subclinical Hypothyroidism (SCH)	<ul style="list-style-type: none"> • T3 was 2.00-4.43 ng/ml, • T4 was 0.93-1.70 ng/ml, and • S.TSH was >4.2 μIU/ml
Hypothyroidism	<ul style="list-style-type: none"> • T3 was <2 ng/ml, • T4 was <0.93 ng/ml, • and S.TSH was >4.2 μIU/ml
Hyperthyroidism	<ul style="list-style-type: none"> • T3 was >4.34 ng/ml, • T4 was >1.70 ng/ml, and • and S.TSH was <0.27 μIU/ml

STATISTICAL ANALYSIS

Patient data were processed using Epi-info software V3.5.4; and presented as frequency, proportions and percentages. The difference between groups were compared using the Chi-square test at 95% confidence limits. The probability (p) level of <0.05 was considered statistically significant.

RESULTS

A total of 212 DM patients - 16 patients with T1DM and 196 patients with T2DM - were included in the study.

Patient Demographics

Of the 212 patients enrolled, 103 (48.58%) were males and 109 (51.42%) were females. The demographic details of study population are given in Table-2.

Table-2: Demographic details of study population (n=212)

Age (years)	Male N (%)	Female N (%)	Total No. of Patents N (%)
18-40	24 (23.3%)	15 (13.76%)	39 (18.4%)
41-60	52 (50.48%)	60 (55.04%)	112 (52.83%)
61-80	24 (23.30%)	32 (29.35%)	56 (26.41%)
>80	3 (2.91%)	2 (1.83%)	5 (2.35%)
TOTAL	103 (48.58%)	109 (51.42%)	212 (100%)

Prevalence of Thyroid Dysfunction in Type 1 and Type 2 Diabetics

TD was reported in 52 (24.52%) of 212 patients. Of these, (11.79%) patients had SCH, 19 (8.96%) patients were hypothyroid and 8 (3.77%) patients were hyperthyroid (Figure 1). SCH was the most common type of TD, reported in 25 patients (11.79%) with amongst T2DM patients [23 (50%)] as

compared to T1DM patients [2 (33.33%)]. Hypothyroidism and hyperthyroidism were seen in 16 (8.96%) and 8 (3.77%) patients in the study, with a higher prevalence of 50% and 16.66%, respectively, amongst T1DM patients as compared to T2DM patients (Table 3). The overall prevalence of TD was more in patients with T1DM (37.5%) as compared to patients with T2DM (23.46%).

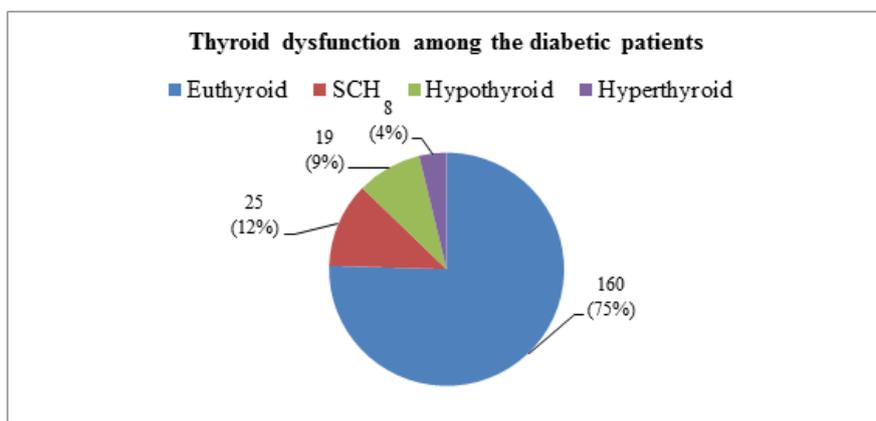


Fig-1: Thyroid dysfunction among the diabetic patients

Table-3: Prevalence of thyroid dysfunction in type of diabetes mellitus

Thyroid Dysfunction	T1DM N (%)	T2DM N (%)	Total N (%)
SCH	2 (33.33)	23 (50)	25 (11.79)
Hypothyroid	3 (50)	16 (34.78)	19 (8.96)
Hyperthyroid	1 (16.66)	7 (15.21)	8 (3.77)
Total	6 (100)	46 (100)	52 (100)

Total number of TD patients = 52.

Prevalence of Thyroid Dysfunction in Gender

Among the 52 diabetic patients with TD, 31 were females (Table 4). The prevalence of types of TD - euthyroid, hypothyroid and hyperthyroid varied and

were comparable amongst males vs. females (Figure 2), except for SCH which was more prevalent in females (17; 15.6%) as compared to males (8; 7.76%).

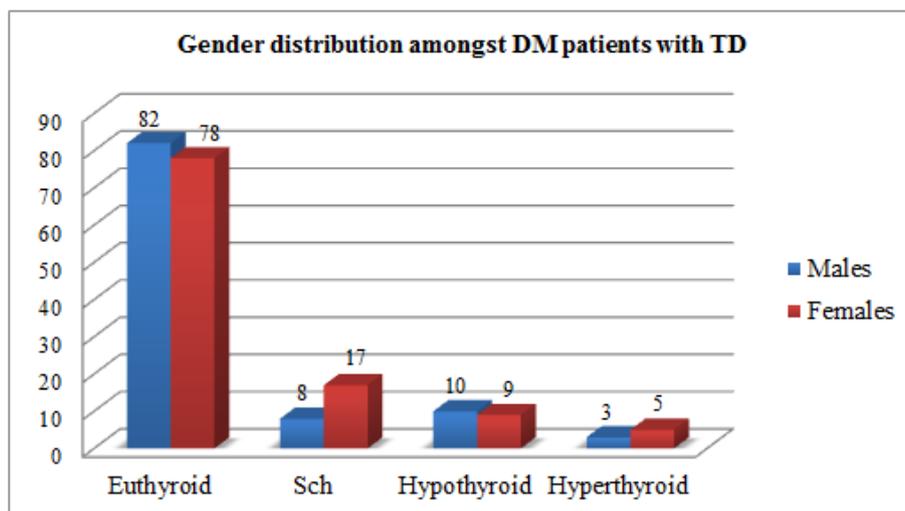


Fig-2: Gender distribution amongst diabetic patients with thyroid dysfunction

Prevalence of Thyroid Dysfunction and Age

In our study, the prevalence of TD increased with increase in age; maximum prevalence was observed in the age group of 41-60 years (52.17%), and declined thereafter. SCH was the most common type of TD across all age groups with a female predominance. Hypothyroidism was almost equally distributed (10 males and 9 females) albeit with more male diabetic

patients in the age group of 18-40 years (20.83%). SCH had more prevalence among the male diabetic patients of middle age group (5.76%). SCH and hypothyroidism had a comparable and maximum prevalence among male patients with elderly age group of 61-80 years and >80 years (8.33% and 33.33%, respectively). Eight patients were hyperthyroid with 3 males and 5 females being

diagnosed (See Table-4).

Table-4: Thyroid dysfunction across age and gender distribution

Age Group (N)/ Type of TD	Euthyroid		SCH		Hypothyroidism		Hyperthyroidism		Total no. of patients with TD	
	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N	Female N
18-40 years (N=39)	16(66.66%)	11(73.33%)	2(8.33%)	2(13.33%)	5(20.88%)	2(13.33%)	1(4.16%)	0 (0)	8	4
41-60 years (N=112)	46(88.74%)	45 (75%)	3(5.76%)	7(11.67%)	2 (3.85%)	6 (10%)	1(1.92%)	2(3.34%)	6	15
61-80 years (N=56)	19(79.17%)	21(65.63%)	2(8.33%)	7 (21.9%)	2 (8.33%)	1 (3.13%)	1(4.16%)	3(9.38%)	5	11
>80 years (N=5)	1(33.34%)	1 (50%)	1(33.33%)	1 (50%)	1(33.33%)	0 (0%)	0 (0)	0 (0)	2	1
Total no. of patients with thyroid dysfunction across all age groups									21	31
									52	

DISCUSSION

Thyroid dysfunction is reported at a higher prevalence in DM population when compared with normal population [4,5]. Our study suggests similar pattern with 24.52% patient’s frequency of prevalence of TD (24.52%) amongst patients with DM. The larger population of DM, SCH being the most common type

of TD among T2DM. Both hypothyroidism and hyperthyroidism were more common in T1DM. The prevalence of TD was high in T1DM (37.5%) compared to T2DM patients (23.46%).

A study conducted by *Palma CC et al.* [10] on 386 diabetic patients reported a higher prevalence of

TD in T1DM (13.3%) as compared to T2DM (13%). Our findings are consistent with this study and we found 37.5% of TD prevalence in T1DM as compared to 23.46% in T2DM patients. However, another systematic review of several similar clinical trials reported an overall high prevalence of TD in T2DM patients rather than T1DM patients, and this was attributed to a greater duration of exposure to diabetes in T2DM and younger age group of patients falling under T1DM.

In our study, SCH was most prevalent in female diabetic patients followed by hypothyroidism in the age group 18-40 and 41-60 years and hyperthyroidism in the age group of 61-80 years. The overall prevalence of TD was more in female diabetic patients (31.94%) compared to males (28.65%). These results are in concordance with multiple literature reports [11, 2, 11] that showed similar results demonstrating overall female predominance.

There was an age wise increase observed in prevalence of TD with maximum prevalence being in the middle age group and thereafter decline in the elderly age group. The prevalence of TD was 18.4 % in 18-40 years age group and 52.83%, 26.41%, 2.35 % in 41-60, 61-80, >80 years age group, respectively. These results are consistent with similar descriptive study conducted by *Sriram Shanmugam et al.* [13] on 186 Indian diabetic patients to investigate the prevalence of TD in DM patients which reported high prevalence of TD (47.5%) in the age group of <50 years compared to patients with the age group of >60 years (35%). However, there are studies performed by *Vikhe VB et al.* [14] and *Bharath et al.* [15] that provide evidence that the risk of TD proportionately increases with advancing age. Therefore, it is important to emphasize that the patients with TD are older than the general population which was specifically mentioned as the age group of 51-70 years showing the highest prevalence on an average basis.

The study is limited by a smaller sample size, non-randomized patient pool that is mix of both newly diagnosed diabetics as well as patients already on treatment at the hospital. Nevertheless, the available data emphasizes the previously reported findings to determine the prevalence of TD in DM patients in India and includes a higher number of T2DM patients whose prevalence was poorly described in previous studies. These study findings may be more favorable to the subclinical abnormalities that could explain the higher frequencies found in DM patients and hence the benefit of screening for TD in them.

CONCLUSION

The overall prevalence rate of TD in patients with diabetes was 24.52%. The prevalence of TD was high in type 1 compared to type 2 DM patients and showed slightly more association with female gender

and was highest in middle age group. Although, it is clearly evident that TD has a strong co-relation with DM, the association between the type of DM and TD is still debatable. Therefore, it is highly recommended that all diabetic patients are screened for TD, which may aid in secondary prevention, as well as primary prevention and early diagnosis and treatment of associated complications.

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COMPETING INTERESTS

The authors declare that they have no competing interests related to this manuscript.

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