

Original Research Article

Study of prevalence of thyroid dysfunction in type 2 diabetes mellitus

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Received: 04 July 2018

Accepted: 31 July 2018

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is associated with increased incidence of thyroid dysfunction (TD). The coexistence of thyroid dysfunction in T2DM patient is an important barrier in achieving treatment goal. The study regarding prevalence of TD in T2DM has not been done in patients of Eastern Uttar Pradesh. The present study was aimed to know the prevalence of thyroid dysfunction in T2DM in patients of Eastern Uttar Pradesh.

Methods: This is an observational cross sectional prevalence study of thyroid dysfunction in 250 diagnosed T2DM patients delect diagnosed based on ADA criteria attending the department of medicine Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh, Study was India, done over a period of 1 year. Thyroid dysfunction was classified on the basis of ATA criteria. All subjects underwent a detailed history, clinical examination and relevant biochemical tests.

Results: The prevalence of thyroid dysfunction in T2DM patients was found to be 20.4% in this study.

Conclusions: The prevalence of thyroid dysfunction was found to be higher in type 2 diabetes mellitus patients in comparison to general population as mentioned in different literature.

Keywords: Type 2 diabetes mellitus (T2DM), Thyroid dysfunction (TD), Thyroid stimulating hormone (TSH), Triiodothyronin (T3), Tetraiodothyronin (T4)

INTRODUCTION

Thyroid disorders have a major impact on diabetes treatment, control and its complication. Hyperthyroidism impairs glycaemic control in diabetic subjects, while hypothyroidism may increase susceptibility to hypoglycaemias thus complicating diabetes management. A high frequency of diabetic retinopathy and nephropathy was observed in diabetic patients even with subclinical hypothyroidism.

It has been established that thyroid dysfunction is more prevalent in people with type 1 diabetes (T1DM). Autoimmune thyroid disease and T1DM are caused by similar mechanism of dysregulation of immune surveillance and tolerance. American Thyroid Association/American Association of Clinical Endocrinology (ATA/AACE-2012) and American

Diabetes Association (ADA-2005) has given a guideline for screening of thyroid dysfunction in type 1 diabetes patients.^{1,2} But no such guideline exists for screening of thyroid dysfunction in T2DM patients till date.

Coexistence of T2DM and thyroid dysfunction is prevalent worldwide. We also observed in our common clinical practice that many T2DM patients have obscured thyroid dysfunction. Controlling hyperglycemia in the presence of underlying thyroid dysfunction poses problem even when it is subclinical. Therefore, detection and management of thyroid dysfunction in T2DM patients may prove beneficial.

There are various studies on the prevalence of thyroid dysfunction in T2DM patients from different parts of globe that concluded increased prevalence of thyroid dysfunction in T2DM patients. Most of the studies have

been done overseas and other parts of India. However, no studies have been done to estimate the prevalence of thyroid dysfunction in T2DM patients in the Eastern U.P. region.

The aim of present study was to determine the prevalence of thyroid dysfunction in T2DM patients, attending the Department of medicine, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh, India, which is the only tertiary care health facility for Eastern UP and bordering Bihar and Nepal.

METHODS

This observational cross-sectional study was conducted over 250 already diagnosed T2DM patients (as per ADA³ guideline) attending the Department of medicine, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh, India, from December 2016 to December 2017.

ADA criteria to diagnose T2DM are as follows³

- A fasting plasma glucose (FPG) level of 126mg/dL (7.0mmol/L) or higher,
- A 2-hour plasma glucose level of 200mg/dL (11.1mmol/L) or higher during a 75-g oral glucose tolerance test (OGTT),
- A random plasma glucose of 200mg/dL (11.1mmol/L) or higher in a patient with classic symptoms of hyperglycemia or hyperglycaemic crisis.

We excluded non-consenting patients, type 1 diabetes mellitus patients, critically ill patients, diabetic nephropathy patients, gestational diabetes mellitus patients, patients on drug affecting thyroid function and patients who underwent thyroid gland surgery. Total 250 T2DM patients were recruited who met our inclusion and exclusion criteria.

A detailed clinical history such as age, sex, family history of diabetes, clinical history regarding diabetes mellitus (onset and duration), history of long term illness, previous history of thyroid dysfunction, previous history of hypertension and any kind of drug therapy, whether the patient was on oral hypoglycaemic agent (OHA) or insulin or both was recorded. A through personal history of smoking, alcohol or any illicit drug intake was taken.

A through clinical examination including general physical examination, vitals (pulse, blood pressure, temperature and respiratory rate), anthropometric measurement (weight, height, BMI and waist hip ratio), and systemic examination was carried out. BMI was calculated using Quetlet's index {BMI = weight in kg/(height in meters)²} and waist hip ratio was measured by Seca 203 Circumference Measuring Tape.

All selected T2DM patients were also subjected to estimation of HbA_{1c}, serum triglyceride, HDL, serum

urea, serum creatinine, and urine routine microscopic. All evaluation was done in the central pathology of the Nehru Hospital, B.R.D. Medical College. HbA_{1c} level was estimated by Ion Exchange High Performance Liquid Chromatography (HPLC) on BIO-RAD-D-10. Lipid profile by enzymatic colorimetric (CHOD-PAP) Trinder End point method on SELECTRA-PRO-M.

All the study subjects were evaluated for thyroid dysfunction by testing thyroid profile (Free T₃, Free T₄ and TSH) by Chemiluminescent Microparticle Immunoassay (CMIA) using ARCHITECT TSH ASSAY machine. Thyroid dysfunction was considered based on ATA guideline as.⁴

Table 1: Diagnostic criteria for thyroid dysfunction.

Disorder	TSH (mIU/mL)
Hypothyroidism	>10
Subclinical hypothyroidism	4.50 -10
Normal thyroid function	0.45-4.50
Hyperthyroidism	<0.45

The correlation of prevalence of thyroid disorder with gender distribution, age distribution, duration of diabetes, HbA_{1c}, BMI and Waist-hip ratio was then done. The observations and interpretations were recorded and results obtained were statistically analysed.

The results were presented in frequencies and percentages. The odds ratio (OR) with its 95% confidence interval (CI) was calculated. The between-group differences calculated using a two-sided paired t-test or Chi-squared statistic test. The p-value <0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

A total of 250 study subjects were studied out of which 127 were male (50.80%) and 123 were female (49.2%).

According to age, our study population included 8 patients of age <30 year (3.2%), 188 patients of age between 30- 60 year (75.2%), and 54 patients of age > 60 year (21.6%).

Table 2: Prevalence of thyroid dysfunction in study population.

Thyroid dysfunction	No. (n=250)	% of total study subjects
Present	51	20.4
Absent	199	79.6

We observed 51 out of total 250 study subjects with type 2 diabetes had thyroid dysfunction. In this study prevalence of thyroid dysfunction was found to be 20.4% in patients of type 2DM (95% CI=16-26%) (Table 2).

In this study, observed that out of 127 male subjects 16 had thyroid dysfunction and out of 123 female subjects 35 had thyroid dysfunction, therefore the prevalence of

thyroid dysfunction was significantly higher (OR=0.36, 95%CI=0.18-0.69, p=0.002) among females (28.5%) compared to males 16 (12.6%) (Table 3).

Table 3: Prevalence of thyroid dysfunction among study subjects according to gender.

Gender	No. of patients	%	Thyroid dysfunction				OR (95% CI)	p-value ¹
			Present		Absent			
			No.	%	No.	%		
Male	127	50.8	16	12.6	111	87.4	0.36 (0.18-0.69)	0.002*
Female	123	49.2	35	28.5	88	71.5	1.00 (Ref.)	0.82

Table 4: Prevalence of thyroid dysfunction among study subjects according to age.

Age (in years)	No. of patients	%	Thyroid dysfunction				OR (95%CI)	p-value ¹
			Present		Absent			
			No.	%	No.	%		
<30	7	3.2	1	14	6	75.0	0.73 (0.14-7.79)	0.71
30-60	188	75.2	37	19.7	151	80.3	0.85 (0.15-4.80)	0.86
>60	55	21.6	13	23.6	42	77.8	1.00 (Ref.)	

Table 5: Prevalence of thyroid dysfunction among study subjects according to duration of diabetes.

Duration of diabetes in years	No. of patient	%	Thyroid dysfunction				OR (95% CI)	p-value ¹
			Present		Absent			
			No.	%	No.	%		
<1	76	30.4	22	28.9	54	71.1	1.75 (0.84-3.66)	0.13
1-5	89	35.6	13	14.6	76	85.4	0.73 (0.33-1.64)	0.45
>5	85	34.0	16	18.8	69	81.2	1.00 (Ref.)	

Table 6: Prevalence of thyroid dysfunction among study subjects according to BMI.

BMI	No. of patient	%	Thyroid dysfunction				OR (95%CI)	p-value ¹
			Present		Absent			
			No.	%	No.	%		
<22.9	88	35.2	4	4.5	84	95.5	1.00 (Ref.)	
23-24.9	75	30.0	5	6.7	70	93.3	1.50 (0.38-5.80)	0.55
≥25	87	34.8	42	48.3	45	51.7	19.60 (6.60-58.15)	0.0001*

Table 7: Prevalence of thyroid dysfunction among study subjects according to WHR.

WHR	No. of patient	%	Thyroid dysfunction				OR (95%CI)	p-value ¹
			Present		Absent			
			No.	%	No.	%		
Central obesity	93	37.2	40	43	53	57.0	10.01 (4.79-20.94)	0.0001*
No central obesity	157	62.8	11	7	146	93.0	1.00 (Ref.)	

In this study we observed that out of 7 subjects who were less than 30 years of age only 1 had thyroid dysfunction, of the 188 subjects were between 30 to 60 years of age 37 had thyroid dysfunction and of the 55 subjects who were more than 60 years of age 13 had thyroid dysfunction. Therefore, prevalence of thyroid dysfunction was highest

in age group of >60 years (23.6%) followed by >30-60 years (19.7%) and <30(14%) years age group (Table 4).

In this study, out of 76 patients with <1 year of duration diabetes 22 patients had thyroid dysfunction; and 89 patients with 1-5-year duration of diabetes 13 patients had thyroid dysfunction; out of 85 patients with >5 years

duration of diabetes 16 patients have thyroid dysfunction. Therefore, this study showed that the prevalence of thyroid dysfunction among diabetic patients was insignificantly ($p>0.05$) associated with the duration of diabetes (Table 5).

Of the total 250 study subjects, 88 patients with BMI between 18 to 22.9, 4 patients had thyroid dysfunction; out of 75 patients with BMI between 23 to 24.9 5 patients had thyroid dysfunction, and out of 87 patients with BMI >25 , 42 patients had thyroid dysfunction. Therefore, in this study we found that the prevalence of thyroid dysfunction was significantly higher (OR=19.60, 95% CI=6.60-58.15, $p=0.0001$) among those with BMI ≥ 25 (48.3%) (Table 6).

In this study, 40 patients out of 93 patients with central obesity had thyroid dysfunction; and 11 patients out of 157 patients with no central obesity had thyroid dysfunction. Therefore, we found that the prevalence of thyroid dysfunction was higher among T2DM patients having central obesity (43%) (Table 7).

DISCUSSION

The present institutional observational cross-sectional study was conducted over 250 patients of T2DM, who attended the OPD of the department of medicine of B.R.D. medical college Gorakhpur, from December 2016 to December 2017. Patients were selected according to inclusion and exclusion criteria. Detailed history, clinical examination and required laboratory investigations were done. All the study subjects were receiving individualised treatment such as life style modification, medical nutrition therapy, OHA's, insulin or both.

In the present study, out of the 250 T2DM patients, 51 (20.4%) patients had thyroid dysfunction and 199 (79.6%) patients were found to be euthyroid.

Various studies across the globe with different methodologies and of varied study subjects concluded different prevalence of thyroid dysfunction in T2DM.

In two European studies by Perros et al, Smithson MJ et al (1998), Nobre et al (2002) and Papazafropoulou et al (2010) prevalence of thyroid dysfunction in T2DM were found to be 6.9%-12.7%.⁵⁻⁸ The higher prevalence of thyroid dysfunction in our study compared with European countries is possibly due to long-standing iodine deficiency in our country, which has only been partly corrected over the past 34 years despite the promotion of iodised salt since 1983. A second explanation may be that the iodine supplementation can also induce or aggravate autoimmunity, resulting in goitre and thyroid dysfunction.

However, in a study conducted by Díez JJ et al, in another European country (Spain) prevalence of thyroid dysfunction in T2DM patient was 32.4%, which was

significantly higher as compared to peer European studies.⁹

Paradoxically a large cross-sectional population based European study of Norway (HUNT 2 and 3) comprising 83044 participants concluded that T2DM was not strongly and gender neutrally associated with thyroid dysfunction in T2DM patients.¹⁰

Two studies from Middle East countries by Radaideh AR et al and Akbar DH et al found prevalence of thyroid dysfunction in T2DM patients from 5 to 7%.^{11,12} The logical explanation of the lower prevalence is due to iodine replete status of the middle east countries and difference in thyroid function assay methods.

Various studies from different parts of India by Laloo Demitrost et al, Vibha Uppal et al, Saroj Mishra et al, Ashok Khurana et al and Ajaz Ahmad Telwani et al found that the prevalence of thyroid dysfunction in T2DM patients was in range of 16 to 31.2%.¹³⁻¹⁷ The explanation of increased prevalence reported in most of the Indian studies may be due to our country is having mixed population with iodine deficient and iodine replete status. There may be a genetic or environmental (goitrogens) angle of explanation too.

In this study, overt hypothyroidism was found in 4.0% of the total 250 T2DM patients. This result is lower in comparison with the results of Pasupathi et al, 28.0% (Tamilnadu 2008), Díez JJ et al, 15.1% (New York 2011), Laloo Demitrost et al, 11.4% (Manipur 2012) and C. E. J. Udiong et al, 26.6% (Nigeria 2015).^{18,9,13,19} Our results are higher in comparison to the results of Perros et al, 0.9% (Scotland 1995), Ravishankar et al 1.0% (Bangalore 2013).^{5,20}

In this study, hyperthyroidism was found in 2.4% of the total 250 T2DM patients. This result is in concordance with the results of Demitrost L et al, 3.5% (Manipur 2012).¹³ This results are lower in comparison to the results of Pasupathi et al, 17.0% (Tamilnadu 2008), Díez JJ et al, 6.6% (New York 2011), Ravishankar et al, 13.0% (Bangalore 2013) and C. E. J. Udiong et al, 19.9% (Nigeria 2015).^{18,9,20,19}

The differences in outcome of prevalence of thyroid in different studies may be due to different ethnicity, BMI, population composition, variation in diagnostic criteria, sensitivity of pathological test used, exposure to goitrogens and variation in iodine intake.

In the present study, the prevalence of thyroid disorders was more in females as compared to males (28.5% vs. 12.6%) which when evaluated statistically was significant (p value < 0.05 , Table 6). Our results are consistent with studies of Papazafropoulou et al, Celani et al, Vondra et al, Pimenta et al, Babu et al and Michalek et al, in which they too reported higher prevalence of thyroid disorders in T2DM females as compared to T2DM males.^{8,21-25}

Thus, prevalence of thyroid disorders in T2DM patients is strongly influenced by female gender (Table 2).

Out of 51 T2DM patients who had thyroid disorders, 1(14%) patients belonged to <30 years age group, 37 (19.7%) patients belonged to age group of 30-60 years and 13(23.6%) patients belonged to age group >60 years. Thus, the age specific trend in the prevalence of thyroid disorder was found to be highest in the age group of >60 years. The results of this study are in accordance with the results of the studies Michalek et al, Whitehead et al, Feely et al, Vondra et al, Moulik et al and Johnson et al also found a higher prevalence of thyroid disorders in diabetic patients with advancing age (Table 3).^{25-27,22,28,29}

In this study, out of 51 diabetic patients who had thyroid disorders, 4 (4.5%) had BMI <22.9%, 5 (6.7%) had BMI between 23-24.9 and 42 (48.3%) had BMI >25. Thus, the prevalence of thyroid disorders was found to be more in patients who had BMI >25. This data when evaluated was statistically significant (Table 3, p value <0.05). The findings of this study are similar to the studies by Papazafiropoulou et al and Procs et al who also found prevalence of thyroid disorders to be significantly more in patients who had higher BMI (p values = 0.03 and 0.018 respectively (Table 5)).^{8,30}

In this study, out of 51 diabetic patients who had thyroid disorders, 40 had central obesity while 11 had no central obesity. When evaluated statistically it was found that there were significantly increased prevalence of thyroid dysfunction in patients having central obesity (p>0.05) which is consistent with findings of Kouidhi S et al and de Pergola G et al (Table 6).^{31,32}

Out of 51 T2DM patients who had thyroid disorders, 22 (28.9%) had duration of diabetes of <1 year, 13 (14.6%) had duration of diabetes between 1-5 years, 16 (18.8%) had duration of diabetes of >5 years. Thus, we found that the prevalence of thyroid disorders was not affected by the duration of diabetes (Table 4).

Some limitations of this study must be discussed. This study was a cross sectional hospital based observational study. The study subjects were recruited from the diabetic patients already being treated in the OPD of department of medicine, BRD Medical College, Gorakhpur, Uttar Pradesh. Hence, there is possibility of selection bias because these patients were already under regular medical care with us. However, all patients were submitted to the same study protocol.

The strength of this study is the greater number of the study subjects (n=250), which is more than that in any other Indian and overseas studies with T2DM patients. Another strength of this study is that we used ultrasensitive laboratory tests for estimation of TSH and FT4 in all study subjects (T2DM patients) leading to more efficient and accurate detection of thyroid dysfunction in comparison of pear studies.

CONCLUSION

This study, the first of its kind in Eastern Uttar Pradesh, showed higher prevalence of thyroid dysfunction in T2DM patients than that recorded in the general population. There is a high prevalence of thyroid disorders in patients with T2DM, which was further found to be more in females, elderly patients, and patients with BMI >25. No relation of thyroid disorder with duration of diabetes was found. We recommend that thyroid profile should be a routine screening test in all patients with T2DM at the time of initial diagnosis and at follow up visits, especially in females, elderly and those with BMI >25. However, we reinforce that prospective studies with more number of study subjects is necessary to clarify and established these recommendations.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Singh RK, Mittal M, Singh A, Kumar A. Study of prevalence of thyroid dysfunction in type 2 diabetes mellitus. *Int J Res Med Sci* 2018;6:3089-94.