

Original Research Article

Prevalence of hypothyroidism in patients with type 2 diabetes mellitus attending a tertiary care hospital in a rural area of Bihar, India

Abhishek Kamendu¹, Ahmad Nadeem Aslami^{2*}

¹Department of General Medicine, ²Department of Community Medicine, NMCH, Sasaram, Bihar, India

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*Correspondence:

Dr. Ahmad Nadeem Aslami,

E-mail: ahmadnadeemaslami@gmail.com

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ABSTRACT

Background: Diabetes has become a major health challenge all over the world. Previous studies have found that diabetes and thyroid disorders mutually influence each other and both disorders tend to coexist. The aim of this study was to find out prevalence of hypothyroidism and its associated factors in type 2 diabetes mellitus patients.

Methods: Consecutive 200 patients with type 2 diabetes mellitus attending outpatient department of medicine in a tertiary care centre in Sasaram, Bihar were evaluated clinically and biochemically. Subclinical hypothyroid and overt hypothyroidism was diagnosed as per standard definitions. The results obtained were statistically analysed by using chi square test and finding odds ratio.

Results: Out of 200 patients, 75.5% were euthyroid while 24.5% were hypothyroid. Out of 49 hypothyroid patients, subclinical hypothyroid (SC-Hypo) was present in 41 patients and overt hypothyroid (C-Hypo) was present in only 8 patients. The prevalence of hypothyroidism was found more in males, age ≥ 60 years, patients with HbA1c value $\geq 7\%$, patients with diabetes duration less than 5 years and in hypertensive patients.

Conclusions: Thyroid dysfunction screening should be done in all type 2 diabetic patients periodically and appropriate individualized treatments in addition to thyroid function test should be given to diabetes mellitus patients with subclinical hypothyroidism as well.

Keywords: Diabetes mellitus, Hypothyroidism, Prevalence

INTRODUCTION

There were an estimated 61 million Diabetes Mellitus (DM) patients in India in 2016. The prevalence of DM is increasing worldwide, with the global prevalence expected to double by 2030 while in India, the prevalence of DM is estimated to be 7.3%.¹

DM is the most common chronic endocrine disease characterized by hyperglycemia resulted from impaired insulin secretion and/or insulin action. Chronic diabetic hyperglycemia is associated with long-term organ damage, dysfunction and failure. Numerous epidemiological studies indicated the higher prevalence

of overt hypothyroidism in type 2 diabetes mellitus (T2DM) population than in general population. However, the relationship between subclinical hypothyroidism and T2DM is controversial. A meta-analysis showed that type 2DM (T2DM) patients are more likely to have hypothyroidism when compared with healthy population and hypothyroidism may be associated with increased diabetic complications.² The prevalence and its associated factors of hypothyroidism is not much studied in India.

The aim of this study was to find out prevalence of hypothyroidism in type 2 DM patients. The secondary objective was to access if hypothyroidism was associated with other characteristics of diabetic patients.

METHODS

An observational cross-sectional study was conducted in medicine department of a tertiary care centre in Sasaram, Bihar, India after getting ethical clearance from institutional ethical committee. The period of study was from April to August 2018. Consecutive two hundred patients with diabetes who attended our out-patient department were evaluated. Diabetes was defined as per American Diabetes Association (ADA) criteria. Written informed consent for the study was obtained from all the patients. Pregnant women and those taking glucocorticoid or amiodarone were excluded.

All patients went through clinical evaluation, followed by laboratory tests. Fundus photography was taken by ophthalmologist and retinal staging was done as per Early Treatment Diabetic Retinopathy Study (ETDRS) research group diabetic retinopathy classification system.

Blood samples were obtained for biochemical analysis: HbA1c, lipid profile, creatinine, free thyroxine (FT4) and thyrotropin (TSH), anti-thyroperoxidase antibody (anti-TPO) and urine for albumin-creatinine ratio (ACR). All tests were done by standard methods available in the hospital. A reference ranges were fixed for laboratory tests: 0.4-4 μ IU/ml for TSH and 0.8-1.9ng/dl for FT4 and the inter-assay coefficients of variation (CV) for the assays were 8.9% and 5.5% for TSH and FT4, respectively.

Clinical hypothyroidism (C-Hypo) was defined if TSH levels were >4 μ IU/mL and FT4 levels were lower than 0.8ng/dL while sub-clinical hypothyroidism (SC-Hypo) was defined if TSH levels were >4 μ IU/ml and FT4 levels ranged from 0.8ng/dl to 1.9ng/dL. Anti-TPO levels more than 35IU/mL was considered to be positive.

Data were entered in MS Excel Data and it was analysed by SPSS version 16. Data were presented in percentages. Chi-square statistics were used to compare categorical variables in both groups. Odds ratio was calculated along with confidence intervals. The statistical significance was considered as $p < 0.005$.

RESULTS

In this study, 200 patients were included for final analysis. The demographic and clinical data are presented in table1. Out of 200 patients, 61% were male and mean age was 55.4 ± 10.5 years. According to BMI classification, 41.5% patients were overweight and 27% were obese while mean BMI was $27.1 \pm 4.28 \text{ kg/m}^2$. According to the duration of diabetes, 70.5% were of less than five years period while the mean duration of diabetes was 4.12 ± 3.42 years. 51.5% patients had HbA1c value less than or equal to seven while mean HbA1c was $7.91 \pm 1.78\%$. Positive family history of DM was found in 36% patients and positive family history of thyroid was found in only 4% patients. Overall, 27% (54/200) patients

had an addiction of tobacco. Out of these, 38 (29%) had chewable habit of tobacco addiction, 29 (14.5%) were smokers while 13 (6.5%) had both forms of tobacco addiction. Addiction of alcohol was found in 42 (21%) patients, all males.

Clinically, 46.5% patients had features of insulin resistance (acanthosis nigricans) and 4% has goitre of grade 1B or more. Co morbidities included hypertension (57.5%) and dyslipidemia (87.5%). Out of 115 hypertensive patients, only 42.6% (49/115) were on treatment while out of 175 dyslipidemia patients, only 22.8% (40/175) of them were on treatment.

Table 1: Demographic and clinical data of study population (n=200).

Characteristics	Values
Age (in years)	55.4 ± 10.5
Gender	
Males	132 (61%)
Females	68 (39%)
BMI	
Underweight (<18.5 kg/m ²)	14 (7%)
Normal (18.5-24.9 kg/m ²)	49 (24.5%)
Overweight (25.0-29.9 kg/m ²)	83 (41.5%)
Obesity ($\geq 30 \text{ kg/m}^2$)	54 (27.0%)
Duration of diabetes	
<5 years	141 (70.5%)
≥ 5 years	59 (29.5%)
Family history of diabetes	138 (69%)
Family history of hypothyroidism	8 (4%)
History of smoking	54 (27%)
History of alcohol	42 (21%)
Goitre (any grade)	8 (4%)
Acanthosis nigricans	93 (46.5%)
Retinopathy	22 (11%)
Neuropathy	32 (16%)
HbA1c	
<7%	97 (48.5%)
$\geq 7\%$	103 (51.5%)
Hypertension	115 (57.5%)
Dyslipidemia	175 (87.5%)

Prevalence of diabetes complications are listed in Figure 1. Out of 200 patients, 23% (46/200) of them had distal symmetrical peripheral neuropathy, 37% (74/200) had moderate increased proteinuria, 6% (12/200) had severely increased proteinuria, 9% (18/200) had mild retinopathy and 1% (2/200) had moderate retinopathy.

Table 2 shows prevalence of thyroid dysfunction in study population. Out of 200 patients, 75.5% (151/200) were euthyroid while 24.5% (49/200) were hypothyroid. Out of 49 hypothyroid patients, subclinical hypothyroid (SC-Hypo) was present in 41 patients and overt hypothyroid (C-Hypo) was present in only 8 patients. Anti-TPO antibody was positive in 12.5% (25/200) patients.

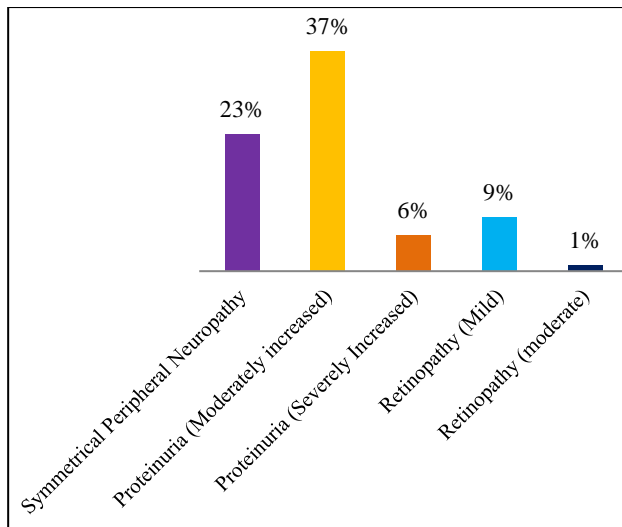


Figure 1: Diabetes complications in the study population (n=200).

Table 2: Prevalence of thyroid dysfunction in type 2 DM.

Thyroid status	Total
Euthyroid	151 (75.5%)
Hypothyroid	49 (24.5%)
Subclinical hypothyroidism	41 (20.5%)
Clinical hypothyroidism	8 (4%)

Table 3 shows prevalence of hypothyroidism according to different characteristics. The prevalence of hypothyroidism was found more in males (61.2%; 30/49) as compared to females (38.8%; 19/49), more in age ≥ 60 years (65.3%; 32/49), more in patients with HbA1c value $\geq 7\%$ (83.7%; 41/49) than in patients with HbA1c value $< 7\%$ (16.3%; 8/49), more in patients with a diabetes duration less than 5 years (71.4%; 35/49) than in patients with a diabetes duration more than or equal to 5 years (28.6%; 14/49) and more in hypertensive patients (65.3%; 32/49) than in non-hypertensive (34.7%; 17/49).

Table 3: Prevalence of hypothyroidism and its association with other characteristic.

Characteristics	Hypothyroidism		Total	OR	95% CI of OR	Statistics
	Present	Absent				
Gender						
Females	37 (54.4%)	31 (45.6%)	68	11.93	5.57- 25.55	χ^2 <0.001, df = 1, p= 0.417; Highly Significant
Males	12 (9.1%)	120 (90.9%)	132	1		
Age Group						
<60 Years	17 (20.7%)	65 (79.3%)	82	0.70	0.35 – 1.37	χ^2 =1.07, df = 1, p=0.300; Not significant
≥ 60 years	32 (27.1%)	86 (72.9%)	118	1		
HbA1c						
≥ 7%	41 (39.8%)	62 (60.2%)	103	7.35	3.22 –16.77	χ^2 =26.9, df = 1, p< 0.0001; highly significant
< 7%	8 (8.2%)	89 (91.8%)	97	1		
Diabetes Duration						
≥ 5 years	14 (23.7%)	45 (76.3)	59	0.94	0.46- 1.91	χ^2 =0.03, df = 1, p=0.862; Not Significant
< 5 years	35 (24.8%)	106 (75.2%)	141	1		
Hypertension						
Present	32 (27.8%)	83 (72.2%)	115	1.54	0.78- 3.01	χ^2 =1.62, df = 1, p=0.203; Not significant
Absent	17 (20.0%)	68 (80.0%)	85	1		

χ^2 = Chi square; df= degree of freedom; p= p value; OR=Odds ratio; CI= Confidence Interval

Table 4: Correlation between TSH and diabetic complications.

Correlation	With urine ACR	With eGFR	With VPT	With retinopathy
p	0.16	0.041	0.032	0.22
r	0.19	-0.35	0.64	0.08

r: Co-efficient of relation, TSH: Thyroid stimulating hormone, VPT: Vibration perception threshold, ACR: Albumin creatinine ratio, eGFR: Estimated GFR

TSH had a significant positive correlation with vibration perception threshold (p=0.032, r=0.64) and significant

negative correlation with estimated GFR (p=0.041, r= - 0.35) although TSH did not have a significant correlation with urine ACR or retinopathy (Table 4).

DISCUSSION

The demographic and clinical data of 200 diabetic patients shows preponderance of males of older age. Most of the patients had high BMI and nearly two third were of diabetes duration of less than five years period. Positive family history of DM was found in one third patients. Co-morbidities included hypertension and dyslipidemia. Pramanik S et al, did a study among 100

patients in a tertiary care hospital in Eastern India found similar features in their study.³

In this study, prevalence of hypothyroidism was 24.5%. However, the studies from different parts of India showed much higher prevalence of thyroid dysfunction. Demitrost L et al, Gurjeet S et al, Anil KR et al and Chaturvedi S et al reported 15%, 16.3%, 11.25% and 27% prevalence.⁴⁻⁷ In these studies, the prevalence of subclinical hypothyroidism is higher in diabetics as compared with non-diabetics. In this study, subclinical hypothyroid (SC-Hypo) was present in 20.5% patients. Many studies did abroad have revealed the increased prevalence of hypothyroidism in type 2 DM. A meta-analysis done by Han C et al of 61 studies described adjusted pool prevalence of SC-hypo in T2DM was 10.2%.²

In present study, prevalence of hypothyroidism in diabetic patients was found more in males as compared to females, more in advancing age, more in patients with high HbA1c value, more in patients with a high duration of diabetes and more in hypertensive patients. Similar kind of results are seen in different studies done by Papazafiropoulou A et al, Whitehead C et al, Ardekani MA et al, Diez JJ et al and Roos A et al.⁸⁻¹²

Authors founded a trend towards higher diabetic complications (neuropathy and nephropathy) with rising TSH. Zhao W et al, showed that TSH level is independently associated with diabetic peripheral neuropathy in Chinese population with T2DM and A high serum TSH level may be a potential risk factor for DPN.¹³ Udiong CEJ et al and Pasupathi P et al, showed in their articles that DM affects other organs than pancreas and there are alterations in the hypothalamus-pituitary-thyroid axis. TSH secretions are in return decreased and TSH response to Thyroid releasing hormone (TRH) is also reduced. Despite normal peripheral TSH metabolism, T3 and T4 hormone production and iodine uptake by the thyroid are diminished. There is marked changes in the structure of thyroid and pituitary gland that influences their secretions. T4 deiodination to T3 in peripheral tissues is decreased. These situations are prevalent in diabetics and will be aggravated in poorly controlled diabetics.^{14,15}

CONCLUSION

Authors have seen that hypothyroidism among T2DM affects a considerable amount of patients. Further studies on larger population will give more information about the relationship between different parameters of thyroid function tests and DM. In the management of DM, it is necessary to recognize the presence of hypothyroidism otherwise prognosis of treatment will be poor. There is a need for routine tests of thyroid hormone in T2DM in order to improve quality of life among T2DM patients and also to reduce morbidity.

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