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Original Research Article

Study of correlation of hypothyroidism with diabetic microvascular complications in type 2 diabetic adult Indian females

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ABSTRACT

Background: Patients with type 2 diabetes mellitus are more prone to thyroid disorders. Hypothyroidism in them leads to an aggravation of microvascular complications. Screening for thyroid dysfunction in diabetic patients will allow early treatment of hypothyroidism. The aim of this study is to assess the correlation of hypothyroidism with diabetic microvascular complications.
Methods: This is a cross-sectional study that was conducted at department of medicine GSVM Medical College, Kanpur. 200 female patients with type 2 diabetes mellitus attending the out-patient department were included. Subjects with any prior history of thyroid disease, chronic liver disease, or acute illness were excluded from the study.
Results: Our study describes 14% prevalence of hypothyroidism (subclinical hypothyroidism 13.5%) among 200 diabetic subjects. Among hypothyroid patients 64.29% patients had nephropathy, 60.71% patients had neuropathy, 64.29% patients had retinopathy whereas euthyroid patients had 26.74%, 25% and 29.07% nephropathy, neuropathy, and retinopathy respectively.
Conclusions: The prevalence of hypothyroidism was 14% among female patients with type 2 diabetes mellitus in this study. Overt hypothyroidism was 0.5 % and subclinical hypothyroidism was more common (13.5%) among the study subjects. Patients having hypothyroidism were more likely to be having diabetic nephropathy, neuropathy, and retinopathy.

Keywords: Hypothyroidism, HbA1c, BMI, Microvascular complications

INTRODUCTION

Patients with type 2 diabetes mellitus are at higher risk to develop thyroid disorders. Many diabetic patients show features of thyroid dysfunction over a period of time.[1] Uncontrolled type 2 diabetes mellitus affects plasma T3 as well as T4 levels. The possible reason postulated for an association between diabetes mellitus and hypothyroidism could be genetic biochemical or of hormonal origin. Resistance to insulin has an important role in the development of hypothyroidism in patients with type 2 diabetes mellitus. The prevalence of hypothyroidism in India is 11%, compared with only 2% in the UK and 4.6% in the USA. women are affected more commonly with overall prevalence of about 85% of affected subjects. In diabetic patients hypothyroidism leads to an aggravation of hypertension, dyslipidaemia, and cardiovascular disease.[2] Thus, in diabetic females it is important to recognize and treat hypothyroidism to slow down the progression of diabetic complications.[3] A simple blood test is enough to diagnose hypothyroidism which can be ordered by the primary care physician who is treating diabetic patients. Early treatment of hypothyroidism in diabetic females may help in improving their glycaemic control and lipid profile. Sub-clinical hypothyroidism in diabetic patients have been reported to be associated with an increased risk of microvascular and macrovascular complications.[4,5] Microvascular complications of diabetes

like retinopathy, nephropathy and neuropathy can worsen in the presence of co-existing hypothyroidism due to dyslipidaemia. Screening for thyroid disorders in diabetic patients may allow early treatment of sub clinical and overt hypothyroidism.[6] This study was done to find out the prevalence of hypothyroidism in adult Indian female population with type 2 diabetes mellitus and find out its correlation with diabetic microvascular complications.

METHODS

This is a cross-sectional study that was conducted at department of medicine GSVM Medical College, Kanpur from December 2020 to October 2022 after having clearance from the institutional ethics committee (IEC Ref. No. EC/123/May/2022). Considering a prevalence of 32% of thyroid dysfunction in diabetic subjects seen in a previous study with an absolute precision of 5% at 5% level of significance, the sample size was calculated to be 200 (using the sample size formula for proportions).

Convenient sampling technique was used to include diabetic patients attending the medicine OPDs of the hospital.

Inclusion criteria

Adult Indian females, known or newly diagnosed case of type-2 diabetes mellitus, patients who gives consent to be part of study, and patients willing to give written signed informed consent to participate in the study were included.

Exclusion criteria

Pregnancy/lactation, type-1 DM and other types of diabetes mellitus, gestational dm, critically ill patient, pre-existing thyroid disorder/patient on antithyroid medications, history of thyroid surgery, history of radiotherapy, systemic auto-immune diseases, and patients on medication which affect thyroid function e.g., lithium, amiodarone, phenytoin, carbamazepine were excluded.

Data regarding age and duration of diabetes were noted in the proforma of the study subjects. Assessment of body mass index (BMI) was done in all the subjects. Body weight was measured using an electronic scale to the nearest 0.1 kg. Subjects were asked to stand straight and relaxed with minimum clothing. Height was measured to the nearest 0.1 cm by using the wall-mounted stadiometer. The height of the subjects was taken in the standing position, without footwear keeping head in the Frankfurt plane. BMI was subsequently calculated dividing the body weight in kilograms by the square of height in meters. BMI between 25 and 29.9 kg/m^2 was taken as overweight while BMI above 30 kg/m^2 was taken as obesity for the purpose of this study. The laboratory investigations that were performed were glycosylated haemoglobin, fasting blood sugar, lipid profile and urine routine microscopy and urine albumin-creatinine ratio, complete blood count, liver function test, kidney function test. Screening for diabetic retinopathy was done by dilated fundus examination. Diabetic retinopathy was classified as non-proliferative (NPDR) or proliferative (PDR) in the study subjects. NPDR was further sub-divided into mild, moderate, and severe categories. Twelve lead electrocardiogram (ECG) was taken for evaluation of cardiovascular disease. Study subjects with changes suggestive of ischemia on ECG were considered to have ischemic heart disease. Monofilament test was performed in subjects clinically suspected to have diabetic neuropathy. Diabetic nephropathy was considered to be present if there was albuminuria. Microalbuminuria was defined as urinary albumin excretion of 30-300 mg/day while macroalbuminuria was defined as presence of urinary albumin of more than 300 mg/day.

Serum thyroid stimulating hormone (TSH), free triiodothyronine (T3) and free thyroxine (T4) were assessed in the fasting serum samples of the study subjects using chemiluminescent immunoassay method technology. The normal range of TSH was 0.5-5.5 U/ml, 1.4-4.4 pg/ml for free T3 and 0.7-1.8 ng/dl for free T4. Sub-clinical hypothyroidism was defined as subjects with TSH value >5.5 U/ml and normal free T3 and T4 levels.

Statistical analysis

Analysis of data was performed using statistical package for the social sciences (SPSS) version 20.0. Continuous variables were expressed as means and standard deviation. Categorical variables were expressed as percentages. Comparison between variables was done by using appropriate statistical tests of significance. Association between variables was considered statistically significant if p value was less than 0.05.

RESULTS

Mean age of study subjects was 52.53±9.7 years. Among the 200 diabetics patients, 26 (13%) were aged <40 years, 51 (25.5%) were aged 40-49 years, 62 (31%) were aged 50-59 years, 58 (29%) were aged 60-69 years and only 3 (1.5%) were aged above 70 years (Table 1).

Table 1: Age distribution of study subjects.

Age group (years)	Number	Percentage
<40	26	13
40-49	51	25.5
50-59	62	31
60-69	58	29
70-79	3	1.5
Total	200	100
Mean±SD	52.53±9.7 years	

Mean BMI of study subjects was 26.41±1.62 kg/m^2. Among the 200 diabetics patients, BMI of 35 (17.5%) was <25 kg/m^2, 163(81.5%) was 25-30 kg/m^2, and only 2 (1%) were having 30-35 kg/m^2 (Table 2).

Table 2: Distribution of study subjects according to their BMI.

BMI (kg/m^2)	Number	Percentage
<25	35	17.5
25-30	163	81.5
30-35	2	1
Total	200	100
Mean±SD	26.41±1.62	

Mean duration of diabetes of study subjects was 11.25±6.91 years. Among the 200 diabetics patients, 45 (22.5%) were having duration of <5 years, 47 (23.5%) were having duration of 5-9 years, 35 (17.5%) were having duration of 10-14 years, 39 (19.5%) were having duration of 15-19 years, 24 (12%) were having duration of 20-24 years and only 10 (5%) were having duration of 25-30 years (Table 3).

Table 3: Distribution of study subjects according to duration of diabetes.

Duration of diabetes (years)	Number	Percentage
<5	45	22.5
5-9	47	23.5
10-14	35	17.5
15-19	39	19.5
20-24	24	12
25-30	10	5
Total	200	100
Mean±SD	11.25±6.91 years	

Mean HbA1c level of study subjects was 8.23±1.65%. Among the 200 diabetics patients, 24 (12%) were having HbA1c <7%, 137 (68.5%) were having HbA1c 7-9%, 24 (12%) were having HbA1c 9-11%, and 15 (7.5%) were having HbA1c 11-13% (Table 4).

Table 4: Distribution of study subjects according to HbA1C levels.

HbA1C levels (%)	Number	Percentage
<7	24	12
7-9	137	68.5
9-11	24	12
11-13	15	7.5
Total	200	100
Mean±SD	8.23±1.65	

Among 200 diabetic subjects, 64 (32%) were having nephropathy, 60 (30%) were having neuropathy, 68 (34%) were having retinopathy.

Among 200 diabetic subjects, 27 (13.5%) were having subclinical hypothyroidism and 1 (0.5%) was having clinical hypothyroidism.

Prevalence of nephropathy was more among hypothyroid patients seen in 18 out of 28 (64.29%) patients as compared to euthyroid patients seen in 46 out of 172 (26.74%) patients, and this difference was found to be statistically significant (p<0.001) (Table 5).

Table 5: Distribution of study subjects according to complications.

Complications	Number	Percentage
Nephropathy	64	32
Neuropathy	60	30
Retinopathy	68	34

Prevalence of neuropathy was more among hypothyroid patients seen in 17 out of 28 (60.71%) patients as compared to euthyroid patients seen in 43 out of 172 (25%) patients, and this difference was found to be statistically significant (p<0.001) (Table 6).

Table 6: Thyroid dysfunction in relation to nephropathy.

Parameters	No. nephropathy	Nephropathy
Euthyroid	126	46
Hypothyroid	10	18

Prevalence of retinopathy was more among hypothyroid patients seen in 18 out of 28 (64.29%) patients as compared to euthyroid patients seen in 50 out of 172 (29.07%) patients, and this difference was found to be statistically significant (p<0.001) (Table 7).

Table 7: Thyroid dysfunction in relation to neuropathy.

Parameters	No. nephropathy	Nephropathy
Euthyroid	129	43
Hypothyroid	11	17

Table 8: Thyroid dysfunction in relation to retinopathy.

Parameters	No. retinopathy	Retinopathy
Euthyroid	122	50
Hypothyroid	10	18

DISCUSSION

Diabetes mellitus is a multi-factorial disorder and a complex interaction between diabetes mellitus and thyroid disorder. Because of insulin and thyroid hormones are closely involved in cellular metabolism, any abnormality of one of them may result in the functional derangement of other.

Insulin resistance that is typically seen in patients with type 2 diabetes mellitus plays a major role in the development of thyroid dysfunction in such patients. Thyroid dysfunction can occur in the form of hypothyroidism and hyperthyroidism. Sub-clinical hypothyroidism can also occur in diabetic patients and can contribute to diabetic complications like retinopathy, neuropathy, and cardiovascular disease.

Multiple studies revealed the increased prevalence of thyroid disorders in type 2 diabetics. A recent meta-analysis Han et al of 61 studies performed worldwide described adjusted pooled prevalence of subclinical-hypothyroidism in type 2 diabetes mellitus patients was 10.2%.[8] Meanwhile, type 2 diabetes mellitus was associated with a 1.93-fold increase in the risk of subclinical-hypothyroidism.

Wu et al was the meta-analysis investigating the association between DR and SCH and it demonstrated that DM patient suffering from SCH could increase the risk of DR.[9] In this research, the pooled effect estimated from eight included papers demonstrated a 2.13-fold (95% CI=1.41–3.23, p<0.001) increased risk of DR in SCH patients compared with non-SCH individuals. But it differed from those of Chen et al and Yongqiang et al.[10,11]

However, the studies from India showed the much higher prevalence of thyroid disorders. For example, Gurjeet reported 15% prevalence of subclinical-hypothyroidism in type 2 diabetics in Punjab; Demitrost from Manipur reported the same to be 16.3%; Anil et al from South India found this prevalence to be 11.25% and recently Chaturvedi et al from Meerut reported this prevalence as high as 27%.[1,12-14] Most of the studies from India also reported the prevalence of subclinical hypothyroid is higher in diabetics as compared with nondiabetics.[5,14]

Our study describes 14% prevalence of hypothyroidism (subclinical hypothyroidism 13.5%) in people with diabetes. This is consistent with the results of previously published reports. We did not have any control arm.

Results from previous meta-analysis Han et al reported subclinical-hypothyroidism might affect the development of diabetic complications with an overall odds ratio of 1.74 (95% CI: 1.34, 2.28) for diabetic nephropathy, 1.42 (95% CI: 1.21, 1.67) for diabetic retinopathy, 1.85 (95% CI: 1.35, 2.54) for peripheral arterial disease, and 1.87 (95% CI: 1.06, 3.28) for diabetic peripheral neuropathy.[8] Chen et al that found sub-clinical hypothyroidism to be a risk factor for nephropathy and cardiovascular disease among type 2 diabetic patients.[4] In our study we found a trend towards higher diabetic microvascular complications (neuropathy, retinopathy, and nephropathy) with rising TSH. Among hypothyroid patients 64.29% patients had nephropathy, 60.71% patients had neuropathy, 64.29% patients had retinopathy whereas euthyroid patients had 26.74%, 25% and 29.07% nephropathy, neuropathy, and retinopathy respectively. These results are consistent with previous studies.

Thyroid dysfunction is a common occurrence among patients with type 2 diabetes mellitus. It is more pronounced in patients with long-standing diabetes and female gender. Treatment of thyroid dysfunction in diabetic patients can improve their morbidity and prevent worsening of diabetic complications.

Limitations

We did not perform anti-thyroid peroxidase (anti TPO) antibody test in our study. Thus, autoimmune hypothyroidism could not be assessed.

CONCLUSION

The prevalence of hypothyroidism was 14% among female patients with type 2 diabetes mellitus in this study. Overt hypothyroidism was 0.5 % and subclinical hypothyroidism was more common (13.5%) among the study subjects. Type 2 diabetic subjects having hypothyroidism are more likely to have diabetic microvascular complications like diabetic nephropathy, neuropathy and retinopathy.

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