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Original Research

PREVALENCE AND ASSOCIATION OF SUBCLINICAL HYPOTHYROIDISM IN ADULT PATIENTS WITH DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL

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Abstract:

Introduction: Diabetes and thyroid disease are two of the most common types of endocrine metabolic diseases.The prevalence of SCH is more in patients with T2DM (2.2% to 17%) than the general population (4 to 10%). Research have shown that the thyroid hormone plays a role in controlling glucose metabolism and pancreatic function, while diabetes can alter thyroid function. However,the link between T2DM and related thyroid disorders remains highly debatable and human research have shown conflicting results.Hence the current study was undertaken to estimate the prevalence of SCH in type 2 DM patients also the association between the two endocrine disorders which will help in better management.**Material and methods:**An analytical cross-sectional study was done in 300 adult Type 2 Diabetes mellitus patients in a tertiary care during December 2021 to May 2023 after institutional ethical approval.Convenient sampling method was used. Data collection was done in a semistructured questionnaire which includes, age, sex, weight, BMI, Medical and relevant surgical and personal history. Clinical examination was done and complications if any were recorded.Statistical analysis was done using SPSS version 23. Statistical tests applied were chi square test, t test, spearmans correlation and multiple logistic regression with $P<0.05$ was considered as statistically significant. **Results:**The prevalence of subclinical hypothyroidism in this study was 16% (58/300 patients). Mean age of patients was high in patients with SCH (54.2) compared to euthyroid patients (52.7) but was not significant statistically. More proportion of females (21.6%) compared to males (12%) have SCH which was significant. Mean HbA1C, free T4 and total cholesterol was significantly more in patients with SCH

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compared to euthyroid patients.Spearmans rho was used to assess correlation which shows weak association of HbA1C with TSH (r=0.14/p>0.05) which was not statistically significant. **Conclusons**: The prevalence of subclinical hypothyroidism in this study was 16% (58/300 patients).After adjusting for age, gender, BMI, duration of diabetes mellitus, dyslipidaemia and complications due to diabetes mellitus multiple logistic regression shows the odds of having SCH is 0.9 times and 1.2 times in patients with HbA1C 7-9%and >9%, when HbA1C <7% was considered as reference which was significant statistically.

Keywords: Subclinical hypothyroidism, Diabetes Mellitus, Adult, correlation, multiple logistic regression

INTRODUCTION

As per recent evidence more than half a billion people are living with diabetes worldwide. In the year 2021, it is estimated that 537 million people have diabetes, which is projected to reach 643 million by 2030, and 783 million by 2045.[1,2]Diabetes and thyroid disease are two of the most common types of endocrine metabolic diseases. Both diseases are multifactorial in origin and have been implicated in the causation of dyslipidemia, dermatological diseases, atherosclerosis, and myocardial dysfunction, as well as endothelial dysfunction [3,4,5]. Type 2 diabetes mellitus (T2DM) has been associated with subclinical hypothyroidism (SCH) [6,7]. The prevalence of SCH is more in patients with T2DM (2.2% to 17%) than the general population (4 to 10%) [8,9,10,11]. Research have shown that the thyroid hormone plays a role in controlling glucose metabolism and pancreatic function, while diabetes can alter thyroid function. However,the link between T2DM and related thyroid disorders remains highly debatable and human research have shown conflicting results.

The proportion of patients with T2DM with thyroid disease is significantly higher than that of healthy people (12,13,14), and subclinical hypothyroidism (SCH) accounts for the largest proportion of these cases (15,16). SCH is a pathological condition in which the levels of thyroid stimulating hormone (TSH) in the blood are increased and the levels of thyroid hormones (FT3 and FT4) are in the normal range. [17]

Presently, controversy persists about indications for treatmentof SCH and whether individuals should beroutinely screened for this dysfunction. Hence the current study was undertaken to estimate the prevalence of SCH in type 2 DM patients also the association between the two endocrine disorders which will help in better management.

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METHODOLOGY

An analytical cross-sectional study was done in adult Type 2 Diabetes mellitus patients in a tertiary care during December 2021 to May 2023 after institutional ethical approval. Patients ≥ 18years with T2DM and/or hypertension (who were already receiving antidiabetic/antihypertensive therapies or with fasting plasma glucose (FPG) ≥ /dl or HbA1c ≥ 6.5% (in newly diagnosed T2DM cases[18] or with blood pressure (BP) ≥ 140/90mmHg were included in the study. the exclusion criteria were unwillingness to participate in the study, known history of thyroid disease, surgery of the thyroid gland, other thyroid disorders diagnosed recently, radiation exposure to the thyroid gland, pregnancy, patients on medications known to modify the thyroid functions such as glucocorticoids, lithium, and amiodarone, unstable cardiac disease, renal impairment, liver cirrhosis, malignancies, and other types of DM such as secondary DM, gestational DM, or type 1 DM. after obtaining their written informed consent.

Sample size was calculated based on a study by Pragnasharma et al in which prevalence of subclinical hypothyroidism in type 2 DM adults in India was 24.3%.[18] With 5% absolute precision and 95% confidence to estimate 23% of SCH in study population, the sample size required was 273.Convenient sampling method was used.

Data collection was done in a semistructured questionnaire which includes, age, sex, weight, BMI, Medical and relevant surgical and personal history. Clinical examination was done and complications if any were recorded (complications included Diabetic retinopathy, nephropathy, neuropathy, vascular complications and peripheral artery disease). Under aseptic conditions 20ml of Fasting venous blood sample was collected and analysed in RandoxImola a Fully automated analyser. Haemoglobin estimation, lipid profile (including Total cholesterol, LDL, HDL, Triglycerides), creatinine, urea, was estimated. Serum TSH, free T3, and free T4 were estimated using the enhanced chemiluminescence method on i1000 SR from Abbott. SCH was defined as an elevated level of serum thyroid-stimulating hormone (>5.0 μIU/mL) with a normal level of free T3 and T4. HbA1C was estimated in Wondfofinecare fully automated analyser, which was supplied with finecare HbA1C test kits.

Statistical analysis was done using SPSS version 23. Statistical tests applied were chi square test, t test, spearmans correlation and multiple logistic regression with $P<0.05$ was considered as statistically significant.

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RESULTS

Out of the 300 patients in the study, there were 175(58.3%) male and 125(41.7%) female patients.Age ranges from 22-75 years with mean ± Standard deviation (SD) of age being 55.14 ± 15.82, with majority belonging to 40-60(47%) years age group. With respect to duration of Type 2 DM, mean was 6.45±2.51. About 44% were suffering from Type 2 DM for ≥5 years. (shown in table 1)

TABLE 1: PATIENTS BY AGE, SEX AND DURATION OF TYPE2 DM

Socio-demographic detail	Category	Frequency (n=300)	Percentage
Age in years	18-40	63	21%
	41-60	141	47%
	>60	96	32%
Sex	Male	175	58.3%
	Female	125	41.7%
Duration Of Type 2 DM	< 5 year	168	56%
	≥ 5 year	132	44%

The range forBMIwas18.3–31.6withmean21.73 ±1.98,range forFBSwas76- 315mg/dl withmean of 161.58±62.75, range for PPBSwas97-328withmean294.6±96.75, range for HbA1c was5.7 –12.7 withmean 7.75 ± 1.91. Mean and SD of TSH, free T3 and T4 was 3.17±2.9 (range 0.25-6.5), 2.82±1.2 pg/dl (range1.12-4.9) and 2.69±0.61 µg/dl(range 1.7-5.4).Total cholesterol of study patients ranges from 87 to 431 with a mean of 156 ±49.31, LDL cholesterol ranges from 81 - 272with mean 102.9 ±45.6,HDLranges from 15 to 72 with mean33.3±10.7, Triglyceride ranges from 97-419 with mean 4 3.3±199.4, creatinine ranges from0.60 - 1.20 with mean 0.94 ± 0.14, CRP ranges from 0.6 – 12.2 with mean 2.94 ± 3.14. Haemoglobin ranges from 5.6gm/dl - 15.8 gm/dl, with mean 11.1±4.31.(Shown in the table 2)

TABLE 2: MINIMUM, MAXIMUM MEAN AND STANDARD DEVIATION OF VARIABLES STUDIED.

Parameters (n=300)	Minimum	Maximum	Mean	SD

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Bodymass index	18.30	31.6	21.73	1.98
FBS mg/dl	76	315	161.58	62.75
PPBS mg/dl	97	328	294.6	96.75
HbA1c %	5.7	12.7	7.75	1.91
Total cholesterol mg/dl	87	431	156	49.31
Ldl-cholesterol mg/dl	81	272	102.9	45.6
Hdl-cholesterol mg/dl	15	72	33.3	10.7
Triglyceride mg/dl	97	419.00	43.3	19.40
Creatinine	0.60	12.2	2.94	3.14
Hemoglobin g/dl	5.6	15.8	11.1	4.31
TSH	0.25	6.5	3.17	2.9
Free T3 pg/dl	1.12	4.9	2.82	1.2
Free T4 µg/dl	1.7	5.4	2.69	0.61

The prevalence of subclinical hypothyroidism in this study was 16% (58/300 patients). Mean age of patients was high in patients with SCH (54.2) compared to euthyroid patients (52.7) but was not significant statistically. More proportion of females (21.6%) compared to males (12%) have SCH which was significant. Mean HbA1C, free T4 and total cholesterol was significantly more in patients with SCH compared to euthyroid patients. Distribution of mean of duration of diabetes mellitus, freeT3, HDL cholesterol, LDL cholesterol and proportion of patients with complications of DM was not significant statistically. (shown in table 3)

Table 3: Distribution of variables in euthyroid versus subclinical hypothyroid patients

Characteristics		Euthyroid (242)	Subclinical hypothyroid (58)	Chi-square or t test/ P value
Age in years (mean ± SD)		52.7±11.9	54.2±12.8	0.84/0.39
Gender	Male	154 (88%)	21(12%)	5/0.02
	Female	88 (70.4%)	37 (29.6%)	

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Duration of diabetes in years (mean ± SD)		5.7±2.9 years	6.1±3.4 years	1.36/0.17
HbA1c (%)		7.5±1.2	8.1±3.5	2.19/0.03
Free T3 (pg/ml) (mean ± SD)		3.11±2.1	2.9±1.5	0.71/0.473
Free T4 (μg/dl) (mean ± SD)		5.6±2.7	6.7±1.1	3.03/0.002
Total cholesterol (mg/dl) (mean ± SD)		156±19.8	163±21.7	2.37/0.01
HDL cholesterol (mg/dl) (mean ± SD)		37±16.7	35±19.1	0.79/0.42
LDL cholesterol (mg/dl) (mean ± SD)		106.2±14.7	109.9±15.4	1.7/0.08
Complications of DM	Yes	60	19	1.53/0.216
	No	182	39	

Spearmans rho was used to assess correlation which shows weak association of HbA1C with TSH (r=0.14/p>0.05) which was not statistically significant. (shown in table 4)

Table 4: Correlation of HbA1C with TSH

		TSH
Hb1AC(%)	Spearmans rho	0.144
	Sig. (2-tailed)	0.318
	N	300

After adjusting for age, gender, BMI, duration of diabetes mellitus, dyslipidaemia and complications due to diabetes mellitus multiple logistic regression shows the odds of having SCH is 0.9 times and 1.2 times in patients with HbA1C 7-9%and >9%, when HbA1C <7% was considered as reference which was significant statistically. (shown in table 5)

Table 5: Multiple logistic regression of SCH versus HbA1C

SCH versus HbA1C	OR (95% CI)	P
HbA1C <7%	Reference	
HbA1C 7-9%	0.9 (0.7-1.5)	0.034
HbA1C >9%	1.2 (0.6-2.6)	0.027

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DISCUSSION

In this study prevalence of SCH was 16% where as in study by Pragya et al done, in Indian diabetic patients, the prevalence of SCH was 23.4%.[18]Study by Ghosh et al., reported a 23% prevalence of SCH in T2DM patients in Eastern India.[19] Our finding was similar to study by Akbar et al., who reported that thyroid dysfunction was present in 16% of Saudi T2DM patients.[20]

In this study 58.3% were females with male to female ratio 1:1.2. In study by Pragya et al females constituted 53.66% of the type 2 diabetic population with maletofemale ratio being 1 :1.16.[18] In our study female preponderance (females/males=63.8%/36.2%) was seen in the SCH group this difference was statistically significant, which was similar to study by Pragya et al where females were 69% compared to 31% males.[18]In this study mean age of T2DM patients in subclinical thyroid group was slightly higher than the euthyroid group (54.2 vs 52.7) which was not significant, where as in study by Pragya et al it was similar (55.25 vs. 55.23 years).[18]

The mean duration of T2DM in SCH group was slightly higher but was not significant statistically, (5.7years versus 6.1 years), Like in study by Ezeani et al. who found that the mean duration of diabetes in the SCH group was higher (9.5 years) than that in the euthyroid group (6.0 years).[21] where as in study by Pragya et al it was 7.3 years in the euthyroid group and 6.1 years in the SCH group.[18] No significant relationships were found between the presence of SCH and age or duration of T2DM.

In this study mean HbA1C was 7.3 in euthyroid and 8.1 in SCH group and this difference was significant. In study by Pragya et al mean HbA1c in the euthyroid group was 7.89%, whereas it was higher (8.33%) in the SCH group, but the difference was statistically not significant ($p = 0.09$).[18]

In our study HbA1C and TSH were weakly correlated which was not significant (spearmans rho 1.4 with p value =0.318). Multiple logistic regression after adjusting for age, gender, BMI, duration of diabetes mellitus, dyslipidaemia and complications due to diabetes mellitus shows the odds of having SCH is 0.9 times and 1.2 times in patients with HbA1C 7-9%and >9%, when HbA1C <7% was considered as reference

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which was not significant statistically. Similar findings were seen in study by Pragya et al where the linear regression model showed a weak significant correlation between the HbA1c categories and the TSH (r = 0.156; p = 0.026). However, in multivariate logistic regression analysis, after adjustment of age and duration of diabetes, for the HbA1c> 9% category when compared with the HbA1c < 7% category, high TSH was not a significant predictor.[18] Whereas in Study by Fakhroo et al shows 64% higher odds of having T2DM in participants with subclinical hypothyroidism (OR=1.64, 95% CI (0.79, 3.40), p=0.181). After adjusting for covariates, there was an increase in the odds of having T2DM in participants with subclinical hypothyroidism (OR=2.82, 95% CI (1.13, 7.02), p=0.026). The age category 50–85 was associated with the highest increase in the odds of having T2DM (OR=29.52, 95% CI (12.27, 71.03), p=0.000).[22]Incontract a systematic review and meta-analysis of cross-sectional studies have established that T2DM was associated with a 1.93-fold increase in the odds of subclinical hypothyroidism.[23]

Recommendation: Thus a multicentric study is recommended to address these controversies.

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