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Prevalence of Thyroid Dysfunction in Type 2 Diabetes Mellitus: A Cross Sectional Study

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Abstract

Background: Diabetes mellitus (DM) and thyroid dysfunction (TD) are two common endocrine disorders. Type 2 diabetes mellitus (T2DM) is a major health burden worldwide with many patients encountering thyroid dysfunction later in their life. Various studies have found that diabetes and thyroid disorders mutually influence each other and both disorders tend to coexist. However, the prevalence of thyroid dysfunction and associated clinical variables in these patients is an important correlation to study. The unrecognized TD may adversely affect the metabolic control and add more risk to an already predisposing scenario for cardiovascular diseases. **Aim & Objective:** The objective of this study was to investigate the prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus. **Study Design:** Observational cross sectional study. **Methodology:** Subjects with (T2DM) attending OPD in medicine department of GMC Aurangabad and some subjects with known history of T2DM from social circle were included in this study. Whereas those diabetic patients with known thyroid disorders, complications of diabetes mellitus, history of other illnesses, and hyperlipidaemia as well as on corticosteroids therapy and medications affecting thyroid levels were excluded from this study. **Method of sample analysis:** Serum freeT3 , freeT4 , TSH were estimated in the central clinical laboratory on cobas e411 biochemistry immunoassay analyser which used the principle of electrochemiluminiscence for estimating these hormones. **Method of statistical analysis:** The statistical analysis was performed using SPSS software. The statistical data was systematically analysed and was represented in form of mean + S.D. Unpaired t-test was used to compare between two means of all parametric continuous variable and p-value < 0.05 was considered as statistically significant. **Result:** Prevalence of thyroid dysfunction among T2DM patients was found to be 13.4%. Gender-specific prevalence was found to be higher in females as compared to males.**Conclusion:** We conclude that screening for thyroid disease among patients with diabetes mellitus should be routinely performed considering the incidence of new cases diagnosed and the possible aggravation of the classical risk factors such as hypertension and dyslipidemia, arising from an undiagnosed thyroid dysfunction.

Key words: Thyroid dysfunction, Prevalence, Diabetes mellitus.

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Introduction

Diabetes mellitus and thyroid dysfunction are the two most common endocrine disorders seen in outpatient care with reported global prevalence ranging from 2 to 17%. Thyroid dysfunction is a spectrum of disorders of the thyroid gland which manifests either as hyper or

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hypothyroidism and is reflected in circulating levels of TSH. There is a deep, fundamental relation between diabetes mellitus and thyroid dysfunction.[1] Studies have found that thyroid dysfunction is much common in diabetic population compared to non-diabetic population, diabetes and thyroid disorders have been shown to influence each other mutually because of intersecting pathology.[2] Thyroid hormones cause an increase in the hepatocyte concentration of glucose-6-phosphate and glucose transporter 2 (GLUT 2) thereby leading to increased hepatic glucose output and abnormal glucose metabolism giving rise to the overproduction of lactate entering Cori's cycle and further promotes hepatic gluconeogenesis.[3] Thyroid hormones also cause an increase in gut glucose absorption and increased lipolysis which further promotes hepatic gluconeogenesis. Thus, thyroid dysfunction may lead to the development of insulin resistance. Diabetes mellitus also influences thyroid function at two different sites. Firstly, at the level of hypothalamic control of TSH release and next at the level of peripheral tissue by converting T4 to T3.[4] Hyperglycaemia causes a reduction in the hepatic concentration of T4-T5 deiodinase, low serum concentration of T3, raised, normal or low T4. A possible genetic interaction has also been noted between the development of thyroid dysfunction and type-2 Diabetes Mellitus. Few genes like protein kinase B, Inhibitory G protein, GLUT2,[3] phosphoenolpyruvate kinase have been identified. Hence, assessment of thyroid function in the uprising diabetic patient number may be helpful in identifying cases of clinical and subclinical thyroid dysfunction thereby assisting in mitigating the harmful effects due to low thyroid hormones. There is a deep unexplored relation between thyroid dysfunction and diabetes mellitus. Thyroid hormones influence the regulation of carbohydrate metabolism and pancreatic function, whereas diabetes also affects thyroid function tests to a variable level. A number of studies have stated an array of complex intertwining biochemical, genetic, and hormonal abnormalities mirroring this patho-physiological association.[5]

Aim and Objective

The objective of this study was to investigate the prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus.

Material and Methods

Study subjects: This study was a observational cross sectional study in which 230 Subjects with T2DM were enrolled for this study.

Inclusion Criteria: The subjects having T2DM were enrolled from those attending the OPD in medicine department of GMC Aurangabad and some volunteer subjects with known history of T2DM were also included from social circle in this study. Among these subjects 124 were females and 106 were male subjects. All these subjects were ageing within a range of 40 to 60 years.

Exclusion Criteria: Those diabetic patients with known thyroid disorders, complications of diabetes mellitus, history of other illnesses, and hyperlipidaemia as well as on corticosteroids therapy and medications affecting thyroid levels were excluded from this study.

Laboratory Assessment: This study was done over a period of 12 months from January 2022 to December 2022 in GMC Aurangabad. After written consent of the study subjects fasting blood samples were taken and were analysed for serum freeT3 , freeT4 , and TSH. Serum freeT3 , freeT4 & TSH were estimated in the central clinical laboratory on cobas e411 biochemistry immunoassay analyser which used the principle of electro-chemiluminiscence for estimating these hormones.

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Study-related definitions

Overt hypothyroidism: A patient was classified to have overt hypothyroidism if the level of TSH was >4.50 μIU/mL, fT4 <0.7 ng/dL, and fT3 <1.4 pg/mL.[6]

Subclinical hypothyroidism (SCH): A patient was classified to have SCH if the level of TSH was >4.50 μIU/mL, fT4 was 0.7–1.4 ng/dL& fT3 was 1.4–4.2 pg/mL[6]

Hyperthyroidism: A patient was classified to have hyperthyroidism if the level of TSH was < 0.30 μIU/mL, fT4 was > 1.8 ng/dL, and fT3 was 1.4–4.4 pg/mL.[6]

Study statistical analysis: The data generated from the study were entered into MS Excel and analysed using SPSS statistical package version 20.0. The statistical data was systematically analysed and was represented in form of mean + S.D. Unpaired t-test was used to compare between two means of all parametric continuous variable and p-value < 0.05 was considered as statistically significant.

The following serum thyroid hormone values were considered as normal according to the kit insert information sheet:

Table 1: Reference values of serum freeT3, freeT4 & TSH

Thyroid Hormone	**Reference Values**
free T3(fT3)	1.4-4.2 pg/ml
free T4(fT4)	0.7-1.4 ng/dl
TSH	0.34-4.25 μIU/ml)

Results

The mean duration of these study subjects having T2DM was found to be 2 years and seven months. The results of this study had been summarised in following tables.In table 2 the reported values of fT3, fT4 & TSH in male and female T2DM study subjects are summarised.

Table 2

Thyroid Hormone	**Reported value in** T2DM **Males**	**Reported value in** T2DM **Females**	**p value**
	Mean ± SD	**Mean ± SD**	
free T3(fT3)	4.0±10.69	1.3±9.04	0.043*
free T4(fT4)	1.1±0.68	0.8±0.37	0.0001*
TSH	3.3±7.04	5.9±8.25	0.011*

*p value < 0.05 whis is statistically significant.

In table 3 the prevalence rates of thyroid dysfunction were reported in male and female T2DM study subjects.

Table 3

Thyroid Dysfunction	**Total T2DM Subjects**		**Male T2DM subjects**		**Female T2DM subjects**	
	Number	**Prevalence**	**Number**	**Prevalence**	**Number**	**Prevalence**
Overt Hypothyroidism	06	2.6%	1	2.5%	2	4.1%
Subclinical Hypothyroidism	24	10.83%	3	7.9%	5	15.6%
Hyperthyroidism	0	0	0	0	0	0

This study reported the thyroid dysfunction prevalence of 13.5% among the study subjects having T2DM. Of these 10.83% were found to be having subclinical hypothyroidism, 2.6% were found to be having overt hypothyroidism whereas hyperthyroidism was not reported in any of the subjects under this study. Gender-specific prevalence was found to be higher in females as compared to males.

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Discussion

This study demonstrated a 13.5 % prevalence of thyroid dysfunction in the diabetic patients studied. Subclinical hypothyroidism was the most frequent dysfunction found corresponding to 10.83% of the patients which was similar to studies already described in the literature[7-9] but higher than that reported in studies with non-diabetics.[10,11] Our observations were in consistence with the previous similar studies performed in India and other countries. First, of its kind, the Wickham study (UK) in 1977 reported 6.6% prevalence of thyroid dysfunction in T2DM patients.[12] The CTDP study (USA) reported the prevalence of 11.7%. The NHANES III study documented the prevalence of 5.9% in T2DM patients.[13] A study in Jordan by Radaideh *et al.* found the prevalence of thyroid dysfunction to be 12.5%.[14] In another study by Papazafiropoulouet *et al.* in Greece, prevalence was shown to be 12.3%.[15] Another study by Akbar *et al.* estimated that prevalence of thyroid dysfunction to be 16%.[16] Higher prevalence of 29.7%, 32.4% documented in Nigeria by Ghazalis *et al.*[17] and in Spain by Diez *et al.*[18] respectively. Studies were done in India by Vikhe *et al.*[19] in Pune and Demitrost *et al.*[20] in Manipur showed a higher prevalence of 30% and 31.2% respectively. This study also reported the higher prevalence of subclinical hypothyroidism as compared to its overt counterpart. This finding of the study is consistent with previous studies such as Chen.G etal[21] & Tamez-Perez etal[22] which have shown that the subclinical hypothyroidism is the predominant thyroid dysfunction in patients with T2DM.[21] The reason for subclinical hypothyroidism being more common than overt hypothyroidism among diabetics is uncertain but some studies have attributed this to a complex interdependent interaction.Thes studies had suggested that leptin was greater in many diabetics,[23,24] which might stimulate synthesis of TSH by affecting the hypothalamic-pituitary-thyroid(HPT) axis via Janus activating kinase (JAK)-2/signal transduction and activation of transcription (STAT) 3 factor *in vitro* and *in vivo*.[25] Hyperinsulinemia was also prevalent in T2DM population and insulin might influence thyrotropin releasing hormone (TRH) and TSH when modulating glycemic status[26], thus, diabetics might have higher TSH. In other studies conducted by Roos Ac etal and Mehran L etal the proposed mechanisms suggests that changes in serum TSH and fT4 levels correlate with changes in HbA1C and result in increased insulin resistance, ultimately leading to T2DM.[27,28] On the other hand, another study suggested that an increase in serum TSH characterizes subclinical hypothyroidism, and those TSH molecules bind to their corresponding receptors on adipocytes leading to altering their homeostasis, rendering them dysfunctional, which decreases the secretion of insulin-sensitizing adipokines and adiponectin, ultimately leading to insulin resistance.[29]

Some limitations of our study must be discussed. This study was a cross-sectional with internal validity and we used a convenience sample of diabetic patients already treated in an university hospital. Some types of selection bias may have occurred because these patients were already under medical care.

Conclusion: We suggest routine screening for thyroid disease among patients with diabetes mellitus type 2. Considering the incidence of new cases diagnosed with T2DM and the present load of prevalence the screening of thyroid function in T2DM becomes crucial as timely screening may prevent the possible aggravation of the classical risk factors such as hypertension and dyslipidemia, arising from an undiagnosed thyroid dysfunction.

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