Study on Thyroid Dysfunction in Patients with Type-2 Diabetes

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ABSTRACT

BACKGROUND

Diabetes mellitus is one of the leading endocrine disorders worldwide. Thyroid dysfunction is a common endocrine disorder affecting the general population next to diabetes. The objective of this study was to determine the prevalence of thyroid dysfunction among patients with Type 2 diabetes.

METHODS

This analytical cross sectional study was conducted from June 2019 to Dec 2019. One hundred and fifty type–2 diabetes patients who attended the outpatient clinic of General Medicine Department, ACS Medical College and Hospital were included in the study. A detailed history and examination was done after getting informed consent. Blood samples were collected and sent to the laboratory for the evaluation of thyroid profile.

RESULTS

Thyroid dysfunction was found in 27 % of the patients with diabetes. Subclinical hypothyroidism was the most common thyroid dysfunction reported (14.7 %) followed by clinical hypothyroidism (10 %), subclinical hyperthyroidism (2 %) and clinical hyperthyroidism (0.6 %).

CONCLUSIONS

Thyroid dysfunction is common in patients with type-2 diabetes. A substantial proportion of the diabetic patients with thyroid dysfunction have subclinical hypothyroidism. Unidentified thyroid dysfunction could negatively impact diabetes and its complications. Therefore, early and routine screening of thyroid is recommended in all patients with diabetes to reduce the burden of the disease.

KEYWORDS

Type-2 Diabetes Mellitus, Thyroid Dysfunction, Hypothyroidism

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BACKGROUND

Diabetes mellitus (DM), a common endocrine metabolic disorder, and is a leading cause of death worldwide.[1] In 2013 the prevalence of DM was estimated as to be 382 million people, of whom majority of the patients, nearly 90 % to 95 % presented with type-2 diabetes and it is anticipated to increase to 592 million by 2035. The reason behind this increasing prevalence of T2D worldwide is probably due to unhealthy lifestyles and the increasing aging population.[2]

India is home to 69.1 million people with DM and is estimated to have the second highest number of cases of DM in the world after China in 2015. The prevalence of DM in India ranges from 5 – 17 %, with higher levels found in the southern part of the country and in urban areas.[3]

Among the endocrine disorders, diseases of the thyroid gland are the most common disorders worldwide second only to diabetes and India is no exception. Recent report shows that 300 million people in the world are suffering from thyroid disorders and among them about 42 million people reside in India.[4]

Thyroid diseases and diabetes mellitus are the two most common endocrine disorders encountered in clinical practice which have been shown to mutually influence each other, and association between both the conditions have been long reported.[5,6,7] The prevalence of Thyroid Dysfunction (TD) is commonly reported in patients with Type 2 Diabetes than in the general population and it can adversely influence the metabolic control. Goiter has been identified as the risk factor for Thyroid dysfunction in diabetic patients when compared to the non-diabetics.[8] The relationship between TD and DM is characterized by a complex interaction of interdependence. Thyroid hormones contribute to the regulation of carbohydrate metabolism and pancreatic function and on the other hand, diabetes also affects thyroid function tests to a variable extent.[9]

Uncontrolled type-2 diabetes mellitus affects thyroid hormone levels, plasma tri-iodothyronine (T3) as well as thyroxine (T4) levels.[10,11] However, in most of the cases underlying thyroid disorders may go diagnosed because of the similarity in the clinical presentation of thyroid disorders and diabetes and can be overlooked or attributed to other medical disorders.[9] Several reports have indicated a higher prevalence of thyroid disorders in type-2 diabetes mellitus patients, with hypothyroidism being the most common disorder.[10,12] The possible reasons postulated for an association between diabetes mellitus and hypothyroidism could be genetic, biochemical, or of hormonal origin.[13]

Early screening of TD in patients with DM is justified because majority of the patients especially those with Subclinical hypothyroidism remains asymptomatic. Several epidemiological studies have reported that the patients with subclinical and overt hypothyroidism have significantly increased cardiovascular risk. Therefore the onset of TD in diabetic patients can further increase the long-term morbidity and mortality associated with diabetes.

Increased systemic vascular resistance, arterial stiffness, altered endothelial function, increased atherosclerosis, and altered coagulability have been reported to be associated with subclinical hypothyroidism and they are the major risk factors responsible for the increased cardiovascular mortality associated with TH deficiency. The coexistence of both diabetes and thyroid disorders may worsen the risk of diabetic retinopathy and diabetic nephropathy in patients with diabetes.[2] Current guidelines are neither clear nor specific about the frequency of thyroid function monitoring in Type 2 DM patients. Recognition and treatment of thyroid disorder in patients with diabetes may benefit glycemic control, attenuate cardiovascular risk, and improve general well-being. Therefore the current study was conducted to determine the prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus.

METHODS

This analytical cross sectional study was conducted in the Department of General Medicine, A.C.S Medical College and Hospital from June 2019 to Dec 2019. The study was approved by the institutional ethics committee of ACS Medical College and Hospital. A total of 150 patients with type-2 diabetes who regularly attend the outpatient diabetic clinic were included in the study.

Diagnosis of type-2 diabetes was done as per the American Diabetes Association criteria.

- Symptoms of diabetes plus random blood glucose concentration of ≥ 200 mg / dL (11.1 mmol / L) or
- Fasting plasma glucose ≥ 126 mg / dL (7.0 mmol / L) or
- Two-hour plasma glucose of ≥ 200 mg / dL (11.1 mmol / L) during oral glucose tolerance test. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.[14]

Known Type–2 diabetic patients were included in the study after getting informed consent. Patients with type-1 diabetes, diabetic nephropathy, known history of thyroid dysfunction, pregnant women, patients with recent interventions: pulse corticosteroids and / or radioiodine, history of receiving any drug that may have caused thyroid dysfunction and with a history of hospitalisation for less than 6 months were excluded.

All the patients underwent clinical and laboratory evaluation. A brief clinical history regarding diabetes, glycaemic control, any long-term illness, previous thyroid dysfunction, family history of diabetes and thyroid disorders, treatment history of oral hypoglycaemic drugs or insulin along with duration were taken. Blood samples were collected for thyroid function tests: Free T3, free T4 and thyroid stimulating hormone (TSH). Free T3 and free T4 were estimated using chemi luminescence immuno assay (CLIA) and TSH was estimated using ultra-sensitive CLIA method. Normal values are free T3: 2.0 - 4.0 pg / mL, free T4: 0.9 - 1.7 ng / mL and TSH: 0.35 - 5.50 μ IU / mL.

Based on the thyroid function profile, the target subjects were categorised into two main groups. The first group categorised as euthyroid included diabetic patients who had normal thyroid function profile (normal levels of fT3, fT4 and TSH), and the second group included diabetic patients with

abnormal thyroid profile. According to their thyroid profiles, the latter were categorised into four groups as follows:

1. Subclinical Hypothyroidism: Study participants with raised TSH levels (> 5.50 µ IU / mL) and normal fT3 and fT4 levels.
2. Clinical / Overt Hypothyroidism: Study participants with raised TSH levels (> 5.50 µ IU / mL) and low fT3 and fT4 levels
3. Subclinical Hyperthyroidism: Study participants with low TSH level (< 0.3 µ IU / mL) and normal fT3 and fT4 levels
4. Clinical / Overt Hyperthyroidism: Study participants with low TSH levels (< 0.3 µ IU / mL) and raised fT3 and fT4 levels.[15]

Statistical Analysis

The data was tabulated and analysed. Statistical analysis was performed using SPSS version 15. Categorical variables were described as frequency (percentage), mean ± 1.96 * standard deviation were used for continuous parameters. Epi Info software was used to calculate chi square values and p values. Mantel-Haenszel values were used. Two tailed p values were used to find associations.

RESULTS

A total of 150 patients with type-2 diabetes were included in the study. Socio demographic data of the studied population is presented in Table 1. Among the 150 type–2 diabetic patients included in the study, 43 (28.7 %) were males and 107 (71.3 %) were females. Most of the study patients belong to the age group of ≥ 50 years (56 %) with the mean age of 50.69 ± 11.48 years. Out of the 150-study population, 72.7 % (n = 109) was categorised as euthyroid and the remaining 27.3 % (n = 41) had thyroid dysfunction. (Figure 1) The distribution of various thyroid dysfunctions is depicted in Table 1. The prevalence of subclinical hypothyroidism was 14.7 %, clinical hypothyroidism was 10 %, sub clinical hyperthyroidism was 2 % and clinical hyperthyroidism 0.6 %.

Variable (Classification of the Variable)	Number of Diabetic Patients n = 150	Percentage (95 % C.I.)
Gender		
Male	43	28.7 (21.6 - 36.6)
Female	107	71.3 (63.4 - 78.4)
Age		
< 50 years	66	44 (35.9 - 52.3)
≥ 50 years	84	56 (47.7 - 64.1)
Duration of type 2 diabetes Mellitus		
< 5 years	98	65.3 (57.1 - 72.9)
≥ 5 years	52	34.7 (27.1 - 42.9)

Table 1. Socio–Demographic Profile of the Study Subjects

Association of thyroid disorders with gender, age and duration of diabetes among the study population is shown in Table 3. In the current study among the patients with thyroid disorders, 70.7 % were females and 29.3 % were males. In our study, 68.3 % of the patients who had thyroid disorders were above the age group of ≥ 50 years. Considering the duration of diabetes, 63.4 % of the patients who had thyroid disorders were diabetic for less than 5 years. However, there was no statistical significance.

Thyroid Characteristics	Total N (%)
Euthyroid	109 (72.7 %)
Subclinical Hypothyroidism	22 (14.7 %)
Clinical Hypothyroidism	15 (10 %)
Subclinical Hyperthyroidism	03 (2 %)
Clinical Hyperthyroidism	01 (0.6 %)
Total	**150 (100 %)**

Table 2. Distribution of Thyroid Status among Type-2 Diabetes Patients

Variable	Grouping of Variable (Number)	Number of Diabetics with Thyroid Disorders (n = 41)	Number of Diabetics without Thyroid disorders (n= 109)	Odds Ratio	Chi Square Value	p-Value
Gender	Males (n = 43)	12 (29.3 %)	31 (28.4 %)	1.04 (0.47 – 2.3)	0.01	0.92
	Females (n = 107)	29 (70.7 %)	78 (71.6 %)	1.00		
Age	≥ 50 years	28 (68.3 %)	56 (51.4 %)	2.04 (0.76 –4.35)	3.46	0.06
	< 50 years	13 (31.7 %)	53 (48.6 %)	1.00		
Duration of Diabetes	≥ 5 years	15 (36.6 %)	37 (33.9 %)	1.12 (0.53 -2.37)	0.09	0.76
	< 5 years	26 (63.4 %)	72 (66.1 %)	1.00		

Table 3. Correlation of Thyroid Disorders with Gender, Age and Duration of Diabetes among Type 2 Diabetes Patients

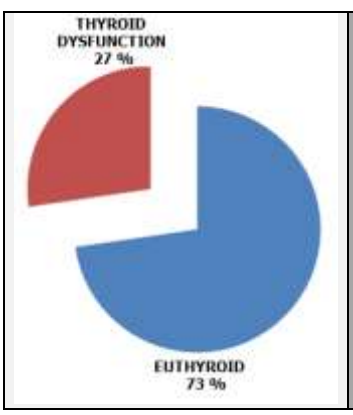

Figure 1. Thyroid Status among the Diabetic Patients

DISCUSSION

Diabetes mellitus represents a spectrum of metabolic disorders, which has become a major health challenge worldwide. In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India.[16,17] Diabetes Mellitus and thyroid dysfunction (TD) are the two endocrine disorders most

commonly encountered in clinical practice. Both Type 2 DM and TD are chronic diseases that require lifelong treatment and have a long-lasting effect on cardiovascular health. Several studies conducted showed a greater variability in the prevalence of thyroid dysfunction in general population ranging from 6 % to 13.4 %.[18] Also in diabetic patients, the prevalence is still greater and varies from 10 to 24 %.[18,19]

Type 2 diabetes mellitus has an intersecting underlying pathology with thyroid dysfunction. DM appears to influence thyroid function in two sites; firstly at the level of hypothalamic control of TSH release and secondly at peripheral tissue by converting T4 to T3. Hyperglycaemia causes reduction in hepatic concentration of T4-5 deiodinase, low serum concentration of T3, raised levels of reverse T3 and low, normal, or high level of T4. Thyroid hormone regulate metabolism and diabetes can alter metabolism.[20]

This study has showed a high prevalence (27 %) of thyroid dysfunction in patients with type 2 diabetes. The results of the present study was in accordance with the reports of Agrawal et al, Ghazali et al, Singh et al and Demitrost et al with prevalence of 27.8 %, 29.7 %, 30 % and 31.2 % respectively.[21,22,23,24] However in another South Indian study by Jali MV et al. the prevalence of thyroid dysfunction among diabetic patients was found to be 16.2 %.[25] In his study, Mehalingam et al has reported a prevalence of 17.5 %.[26] A study in Jordan by Radaideh et al found the overall prevalence of thyroid disease in type 2 DM to be 12.5 %.[27]

In the current analysis of type-2 diabetic patients, we observed a frequency of 14.7 % of subclinical hypothyroidism and 10 % of clinical hypothyroidism. This frequency reported is similar to the findings of Demitrost et al who has reported subclinical hypothyroidism in 16.3 % and clinical hypothyroidism in 11.4 % of the diabetic patients.[24] Another study done by Agrawal et al reported a prevalence of 15.2 % subclinical hypothyroidism and 10.6 % clinical hypothyroidism which is similar to our findings.[21] Explanation of variability in hypothyroidism prevalence in different diabetes populations can be made by several parameters such as adequacy of iodine intake which can affect the baseline thyroid status of population and presence of goiter, metabolic determinants like population glycemic achievement, metabolic syndrome, several comorbidities which related to thyroid dysfunction, and in epidemiology perspective, the total prevalence of diabetes in the population.[28] Hypothyroidism can also affect diabetes control. Hypoglycaemic episodes can occur due to the decreased production of glucose from the liver, meaning that hypothyroidism may mask the clinical signs and symptoms of diabetes. This also explains why diabetes patients with hypothyroidism may require less insulin than their counterparts without thyroid disease.[29]

It has been observed from earlier studies that T2DM patients with Subclinical hypothyroidism and hypothyroidism are more likely to develop complications such as diabetic nephropathy, diabetic retinopathy, peripheral arterial disease and diabetic peripheral neuropathy.[30] In a systematic review and meta-analysis, it has been noticed that the prevalence of subclinical hypothyroidism was higher in patients with T2DM as compared to healthy controls (OR = 1.93); and the similar trend was observed with studies focused on overt hypothyroidism.[31] Detecting thyroid dysfunction in type 2 diabetes patients will inform clinicians to give optimal treatment for metabolic conditions since thyroid condition such as hypothyroidism will delicate achievement of glycaemic target and other comorbidities.[28]

Early detection and treatment of hypothyroidism in type-2 diabetic patients helps in better control of other associated co-morbidities. The ability to diagnose and treat subclinical hypothyroidism in these patients may greatly enhance the quality of life.

This study reported a prevalence of 2 % of subclinical hyperthyroidism and 0.6 % of clinical hyperthyroidism in the study group which is comparable to the study done by Demitrost et al who has reported a prevalence of 2 % subclinical hyperthyroidism and 1.5 % clinical hyperthyroidism.[24] Similarly in the study done by Agrawal et al, 2 % of hyperthyroidism was reported.[21] Several other studies has shown a higher prevalence of hyperthyroidism in patients with diabetes when compared to the general population; it was found in 4.4 % of adult patients with Type 2 diabetes, while Subclinical Hyperthyroidism was present in ~2 % to 4 % of Type 2 diabetic patients.[2]

In the present study among the patients with thyroid disorder, 63.4 % had diabetes for less than 5 years of duration and 36.4 % had diabetes for more than 5 years of duration. However it was not found to be statistically significant. (Table 3) This is consistent with the results of Diez et al who also reported that there is no significant association between thyroid disorders and duration of diabetes.[8]

The following factors support the benefits of early screening for thyroid dysfunction in patients with type–2 Diabetes: (i) Thyroid dysfunction is frequently reported in patients with type-2 diabetes and the most common being hypothyroidism; (2) Even in the presence of overt hypothyroidism, majority of the patients with type 2 diabetes were asymptomatic; (2i) Clinical symptoms of TD may be masked by a poor metabolic control, which is more frequent when TD develops; (iv) Undetected thyroid disorders may compromise the metabolic control and increases the cardiovascular risks in patients with Type 2 Diabetes; and (v) Early screening of TD results in early treatment, preventing high cardiovascular and metabolic complications.[3]

In its guidance for 2000, the American Thyroid Association recommended that adults who were at least 35 years old should be screened for thyroid disorders by measuring serum thyrotropin every 5 years irrespective of whether they were diabetic or non-diabetic.[32] However, the 2015 Thyroid Dysfunction: Screening Guidelines of the US Preventive Services Task Force conclude that there is insufficient evidence to recommend TD screening in non-pregnant or asymptomatic adults.[33] The recommendations for thyroid function screening of T2DM patients are not clear. However, studies has shown that unrecognized thyroid dysfunction may impair metabolic control i.e. glycaemic control and lipid profile, by causing

hypoglycaemia or hyperglycaemia and it can cause an additional cardiovascular disease risk in patients with diabetes.[34] Therefore early screening for thyroid disorders is recommended to reduce the morbidities in patients with diabetes.

Small sample size was a limitation of this study.

CONCLUSIONS

In the current study, the prevalence of thyroid disorders was high (27 %) in patients with type–2 diabetes. Among the thyroid disorders, subclinical hypothyroidism was the most common. Duration of diabetes had no significant impact on thyroid disorders. Therefore, considering the higher prevalence of thyroid disorders, early and routine screening for thyroid disorders is suggested to reduce the morbidity and mortality among the diabetic patients.

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