Original Article:

Study of subclinical hypothyroidism among patients with type 2 diabetes mellitus

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ABSTRACT

Background: The clinical association between type 2 diabetes mellitus (T2DM) and subclinical hypothyroidism is important as both of these conditions are common in patients with metabolic syndrome who are prone to develop cerebrovascular and cardiovascular complications.

Methods: In this cross-sectional study, the burden of subclinical hypothyroidism defined as elevated thyroid stimulating hormone (TSH) (>4.2μIU/mL) with normal concentrations of serum total thyroxin (T_4) and free T_4 (FT_4) in 50 patients with T2DM and 50 age-and gender-matched healthy control subjects.

Results: We observed a significantly higher proportion of patients with T2DM had subclinical hypothyroidism compared to healthy control subjects [9/50 (18%) Vs 3/60 (6%); p=0.009]. We also observed a statistically significant positive correlation between the fasting plasma glucose and serum TSH levels (p<0.001).

Conclusion: Our observations suggest that screening for subclinical hypothyroidism may be beneficial in patients with T2DM and may help in detecting the condition early.

Key words: *Subclinical hypothyroidism, Type 2 Diabetes mellitus*

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INTRODUCTION

Diabetes mellitus (DM) is a group of aetiologically different metabolic defects characterized by hyperglycaemia resulting from defect in insulin secretion as well as insulin action or both.[1] The number of people with diabetes is increasing because of population growth, aging, urbanization and the increasing prevalence of obesity and physical inactivity.[2]

It has been observed that thyroid dysfunction is common in patients with Type 2 DM.[3] Thyroid disorders are also very common in the general population and is second most common condition affecting the endocrine system after diabetes mellitus.[4] Thyroid disease is a pathological state which adversely affects diabetic control and is commonly found in patients with type 2 DM.[5,6]

Thyroid hormones exert profound effects in the regulation of glucose homeostasis. These effects include modifications of circulating insulin levels and counter-regulatory hormones, intestinal absorption, hepatic production and peripheral tissue uptake of glucose.[7] Both insulin and thyroid hormones are involved in cellular metabolism and excess or deficit of any one can result in functional derangement of the other.[8] DM may affect thyroid function either at the level of hypothalamic control of TSH release or at the conversion of T_4 to tri-iodothyronine (T_3) in the peripheral tissues.[6] Hyperglycaemia causes reduction in hepatic concentration of T_4 deiodinase, low serum

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concentrations of T_3 and low, normal, or high levels of T_4. Thyroid hormones regulate metabolism of carbohydrates, lipids and proteins which are altered in DM.[9]

Subclinical hypothyroidism is defined as an elevated serum TSH level and normal concentrations of free T_3 (FT_3), free T_4 (FT_4), T_3 and T_4.[4] Several studies have reported the prevalence of subclinical hypothyroidism to be 10% -17% in patients with DM,[10-12] while the prevalence was found to be about 5% in another study.[6]

The present study was undertaken to evaluate subclinical hypothyroidism in patients with type 2 DM.

MATERIAL AND METHODS

Patients presenting with diabetes mellitus to the medicine out-patient clinic and patients admitted to the medical wards at S.S. Institute of Medical Sciences and Research Centre, Davangere, Karnataka State from December 2013 to November 2014 were screened for inclusion in the study. A written informed consent was obtained from the study subjects. The study was approved by the Institutional Ethical Committee.

Fifty patients with type 2 DM in the age group of 40-70 years whose disease duration was 5 years or more; and 50 age-and gender-matched healthy controls [fasting plasma glucose (FPG) <110 mg/dL on 2 occasions] were studied. The study excluded subjects with type 2 DM with complications like nephropathy, retinopathy, peripheral neuropathy; patients aged less than 18 years, patients with type 1 DM, patients receiving thyroid hormone replacement therapy, patients with gestational diabetes, rheumatoid arthritis, tuberculosis, collagen vascular disorders, liver diseases, renal diseases, cardiac failure and gout.

Under aseptic precautions, 4 mL of peripheral venous blood was drawn from the antecubital vein after an overnight fasting of 12 hours. Two mL of blood was collected in a fluoride vial for estimation of FPG and another 2 mL was collected in a plain vial for estimation of thyroid hormones. Plasma glucose was estimated by glucose oxidase peroxidase method using commercially available kit, (Human GmbH, Germany).[13] TSH and T_4 were estimated by electrochemiluminescence immunoassay (ECLIA); FT_4 was estimated by a microplate chemiluminescence immunoassay (CLIA) technique (Monobind Inc. USA).

Primary hypothyroidism was diagnosed when TSH (normal range 0.4-4.20 μIU/mL) was more than 4.2 μIU/mL and T_4, FT_4 were less than the normal values.[14] Subclinical hypothyroidism was diagnosed when TSH was more than 4.2 μIU/mL and T_4, FT_4 were within the normal range.

Statistical analysis

Continuous variables with normal distribution were compared using students t-test. Categorical variables were compared using chi-square test. Correlation between FPG, TSH, T_4 and FT_4 were studied using Pearson's correlation coefficient. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 20 (SPSS Inc., Chicago IL, USA). A p-value less than 0.05 was considered statistically significant.

RESULTS

Table 1 shows the age and gender distribution of the study subjects. Table 2 shows comparison of FPG, TSH, T_4 and FT_4 between type 2 DM patients and healthy control subjects. Patients with type 2 DM had a significantly higher TSH levels (p=0.003) compared to healthy control subjects. There were no statistically significant differences in the T_4 (p=0.173) and FT_4 (p=0.342) levels between patients with T2DM and healthy controls.

A significantly higher proportion of patients with T2DM had evidence of subclinical

Table 1: Age and gender distribution

Variable	Type 2 DM	Healthy control subjects
Age (years)*	56.1±8.5	55.3±9.8
Gender		
Males	28	31
Females	22	19

*expressed as mean ± standard deviation
DM = diabetes mellutus

Table 2: Comparison of serum concentrations of FPG, TSH, T_4 and FT_4 in 50 patients with type 2 DM and 50 healthy control subjects*

Variable	Type 2 DM	Healthy control subjects	p-value
FPG (mg/dL)	188.9 ± 62.9	95 ± 14.6	< 0.001
TSH (μIU/mL)	4.7 ± 2.8	3 ± 2.2	0.003
T_4 (μg/dL)	6.3 ± 2.2	5.7 ± 1.8	0.173
FT_4 (ng/dL)	1.3 ± 0.4	1.2 ± 0.3	0.342

* data are presented as mean ± standard deviation
FPG = fasting plasma glucose; TSH = thyroid stimulating hormone; T_4 = thyroxin; FT_4 = free T_4; T_3 = tri-iodothyronine
DM = diabetes mellitus

hypothyroidism compared to healthy control subjects (9/50 vs 3/50; p=0.009).

We also observed a statistically significant positive correlation between FPG and TSH (Table 3).

DISCUSSION

Poorly controlled DM is accompanied by an alteration in the thyroid function.[15] Thyroid hormones affect glucose metabolism along with lipids and proteins and conversely can be affected by hyperglycaemic status.[6] Altered thyroid hormone status has been described in patients with DM.[4]

This may be due to the presence of thyroid hormone binding inhibitor, inhibitor of T_4 to T_3 conversion, dysfunction of hypothalamo-pituitary-thyroid axis and the influence of poorly controlled DM on thyroid hormone levels.[1]

Further, abnormal thyroid hormone levels may be due to various medications that the patients with DM were receiving. It is known that insulin, an anabolic hormone enhances the level of FT_4 while it suppresses the level of T_3 by inhibiting hepatic conversion of T_4 to T_3[6] on the other hand, some of the oral hypoglycaemic agents such as the sulphonylureas are known to suppress the level of FT_4 and T_4 while causing raised levels of TSH.

In the present study, the frequency of subclinical hypothyroidism was 18% in type 2 DM compared to 6% in healthy controls.

Observations of the present study are in agreement with the earlier reports of 13.8%[4]

Table 3: Showing the correlation matrix of FPG, TSH, T_4 and FT_4 in type 2 DM

	FPG mg/dL	TSH μIU/mL	T_4 μg/dL	FT_4 ng/dL
FPG mg/dL	1	–	–	–
TSH μIU/mL	0.516 (0.001)	1	–	–
T_4 μg/dL	0.158 (0.117)	0.043 (0.674)	1	–
FT_4 ng/dL	0.019 (0.854)	0.110 (0.274)	0.066 (0.516)	1

FPG = fasting plasma glucose; TSH = thyroid stimulating hormone; T_4 = thyroxin; FT_4 = free T_4; T_3 = tri-iodothyronine
DM = diabetes mellitus

and 14%[6] subclinical hypothyroidism reported in patients with type 2 DM in other studies. Our figure of 18% subclinical hypothyroidism in patients with type 2 DM is higher than the 4.8% reported in one study[8] but lesser than the 48.3% reported in another study.[16]

Larger epidemiological studies are required to identify the reasons for these differences and understand the burden of subclinical hypothyroidism in type 2 DM.

Failure to recognize the presence of abnormal thyroid hormone levels in patients with type 2 DM may be a primary cause of poor management. Therefore, routine assessment of thyroid hormone levels in patients with type 2 diabetes will enable the efficient management of these patients.

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