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EVALUATION OF THYROID DYSFUNCTION IN TYPE 2 DIABETES MELLITUS

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Abstract
Thyroid diseases and diabetes mellitus (DM) are two major endocrine disorders often seen in the clinics. Thyroid disorders are known to alter glycemic status of which hyperthyroidism potentially enhances blood glycemic levels and hypothyroidism enhances the risk to develop hypoglycemic episodes. Thus, the aim of this study was to evaluate thyroid dysfunction encountered among Type 2 DM patients. A comparative cross-sectional study was conducted in 40 type 2 diabetes mellitus (Group 1) patients either attending diabetic clinic or admitted in the medicine ward for metabolic control of diabetes in Government medical college, Kozhikode for a period of one year. 40 apparently healthy control controls were segregated in group 2. Thyroid function test (Free T3, Free T4 and TSH) was measured using chemiluminescence method and fasting blood sugar (FBS) with glucose oxidase-peroxidase method. Statistically analysis was done with Independent't' test and chi square test with p-value <0.05, considered significant. 58% DM subjects had low normal Free T3 levels (4.19+1.5pmol/L, p<0.001); 45% had high TSH levels (3.61+1.4µIU/ml, p<0.001) indicating subclinical hypothyroidism. However, 60% of patients had normal free T4 (18.1+4.17 pmol/L, p=0.98). Based on this study, the prevalence of thyroid disorder (Subclinical and overt hypothyroidism) was significantly higher in type 2 DM. Type 2 DM can be associated with thyroid dysfunction especially subclinical hypothyroidism which can have deleterious effects on cardiovascular and metabolic function hence warranting regular screening.
Keywords: *Thyroid, Dysfunction, Diabetes, Mellitus.*

I. INTRODUCTION

Diabetes mellitus is an important health problem affecting major populations worldwide. It is characterized by absolute or relative deficiencies in insulin secretion or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism. Metabolic dysregulation associated with diabetes mellitus causes secondary pathophysiologic changes in multiple organ systems that affect individual with diabetes mellitus. Type 2 diabetes mellitus is characterized by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production. Most patients with type 2 diabetes mellitus are obese when they develop diabetes; obesity aggravates insulin resistance. Insulin levels of Type 2 Diabetes mellitus patients are within normal range because of insulin resistance and therefore there is relative insulinopenia. Insulin resistance improves with weight reduction or pharmacologic interventions and hence results in normal blood glucose levels.

The influence of other endocrine and non-endocrine organs other than pancreas on diabetes mellitus is documented (3),(4),(5).Occasionally other endocrine disorders such as abnormal thyroid hormones levels are found in diabetes mellitus(.6) The physiological and biochemical relationship between insulin and the influence of both insulin and iodothyronines on the metabolism of carbohydrates, proteins and lipids were recorded. Diabetes mellitus and hyperthyroidism are metabolic disorders that affect the levels of carbohydrates, proteins and 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 tissues (fat and muscle) uptake of glucose. It has long been known that thyroid hormones act differentially in liver, skeletal muscle and adipose tissue the main targets of insulin action. While thyroid hormones oppose the action of insulin and stimulate hepatic gluconeogenesis and glycogenolysis, the former also increases the expression of GLUT-4 and phosphoglycerate kinase thereby enhancing intracellular glucose transport and glycolysis in tandem with insulin synergistically

Thyroid disorders have a major impact on glucose control. Insulin resistance, mainly associated with increased hepatic gluconeogenesis, is characteristic of an excess of thyroid hormones and explains why glucose control deteriorates when diabetic patients develop hyperthyroidism. Although glucose uptake in peripheral tissues has been described as either normal or increased reduced insulin stimulated peripheral glucose utilization is demonstrated in hyperthyroidism. Hypothyroidism results in unimpaired or decreased liver glucose output thereby compensating for insulin resistance present in peripheral tissues and accounting for the diminished insulin requirement for glycemic control in hypothyroid diabetic patients. Insulin resistance has also been reported in subclinical hypothyroidism, adding one more possible mechanism to the association of sub- clinical hypothyroidism and cardiovascular risk. Furthermore it has been shown, both in euthyroid non-diabetic and diabetic adults that small variations in TSH levels of insulin sensitivity might exert a marked effect on lipid levels. The interaction between insulin resistance and lower thyroid function might be a key determinant for a more atherogenic lipid profile in these populations. It has been earlier reported that long standing uncontrolled type 2 DM increases the risk for developing subclinical hyperthyroidism. Furthermore, thyroid dysfunction can increase the risk for cardiovascular diseases in Diabetes Mellitus by disequilibrium of lipid homeostasis and endothelial function (18). The coexistence of both diabetes and thyroid disorders has been associated with increased long term morbidity and mortality. The coexistence of both diabetes and thyroid disorders has been associated with increased long term morbidity and mortality.

II. MATERIALS AND METHODS

Study design-Comparative study design

Duration of study-1 year

Inclusion Criteria

Study was conducted among the patients attending the diabetic clinic or admitted in the medicine ward for metabolic control of diabetes in medical college, Kozhikode. Two study groups are selected

GROUP 1

40 consecutive type 2 diabetic patients including both male and female on oral hypoglycemic drugs/insulin and drugs /insulin in age group 30-65 years.

Exclusion criteria for group 1(Case)

Patientsvery ill and having advanced complications of diabetes mellitus.

Patients having a previously established thyroid dysfunction.

Patients not giving written consent.

GROUP 2

40 consecutive non-diabetic, healthy persons in same age group from bystanders of other patients, medical paramedical staff and bystanders

genetically unrelated to same patient taken as case.

Exclusion criteria for group 2 (control)

Patients having thyroid dysfunction.

Pregnant ladies.

Patients taking drugs like amiodarone.

Persons not giving written consent

Not matched to age.

Bystanders genetically related to same patient as case.

DATA COLLECTION

Study was conducted in 80 subjects of either sex with prior informed consent. Detailed clinical history was taken considering age, sex, duration of illness, history of hypertension.

Blood pressure was recorded.

Body mass index was calculated as weight in kilogram/ (height in m2)

The following blood parameters were compared in both the study groups.

Estimation of FT3

Estimation of FT4 Chemiluminiscence method

Estimation of TSH

Estimation of FBS- Glucose-oxidase method

RESULTS

A comparative cross sectional study was conducted among 80 subjects, with females comprising 67.5% and males 32.5%. First group included 40 patients (cases) who were diagnosed to have type 2 DM on oral Hypoglycemic agents(OHA)/insulin with mean age of 56.05 years and a second group(control) included 40 age and sex related apparently healthy individuals free of these events with mean age being 40.28years. All data analysis g Microsoft excel and statistical package of social sciences (spss-version16) software for windows. Results were analyzed statistically for significance by Independent's' test and chi square test. At p value <0.05 results were considered significant. Table 1.: Sociodemographic characteristics and study parameters.

Variable	Cases (Group 1)	Control (Group 2)	*p*-value
Age	40.78±7.16	56.05±7.12	
Gender			
Male	12	14	0.63
Female	28	26	
Average BMI	25.13	22.87	0.32
FBS	179.1	86.4	<0.001
Thyroid function test			
Free T3			
Hypothyroid	8	1	
Euthyroid low normal	15	4	<0.001
Euthyroid high normal	11	31	
Hyperthyroid	6	4	
Free T4			
Hypothyroid	3	0	0.98
Euthyroid	12	2	
Hyperthyroid	25	38	
TSH			
Hypothyroid	18	4	
Euthyroid low normal	8	23	0.02
Euthyroid high normal	13	8	
Hyperthyroid	1	2	

Figure 1: FBS levels and BMI between cases and control.

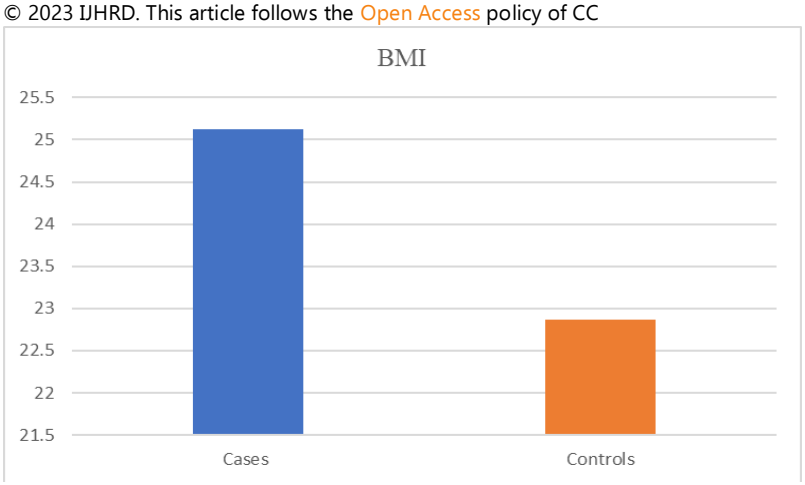
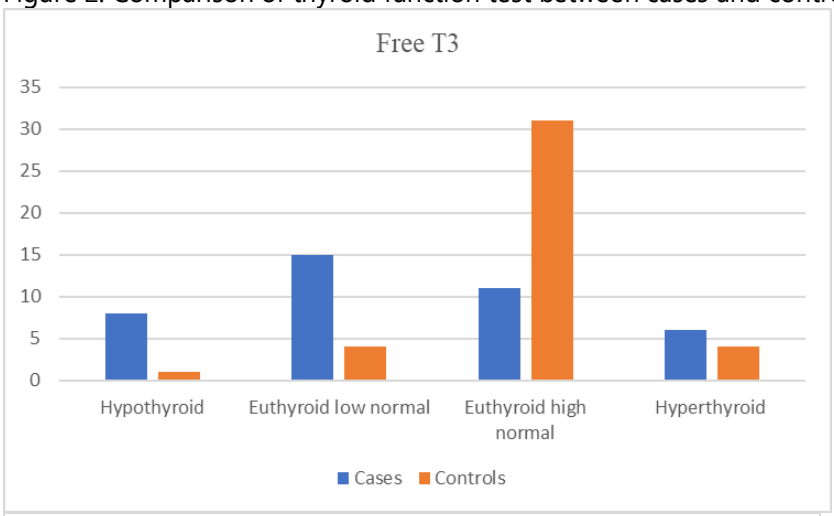
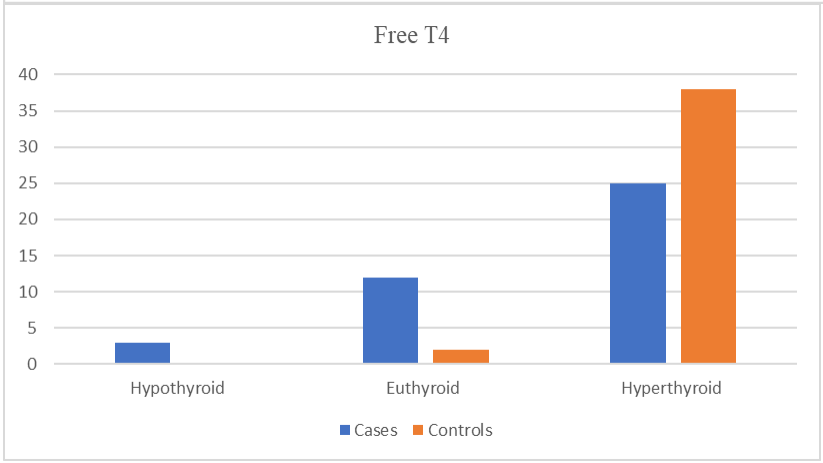
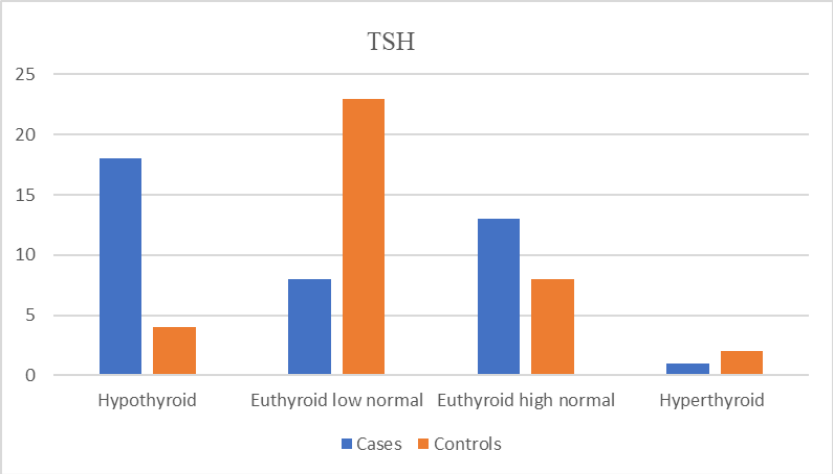


Figure 2: Comparison of thyroid function test between cases and controls







III. DISCUSSION

Thyroid disorders are highly prevalent in patients with Diabetes Mellitus. Abnormal thyroid hormone levels found in diabetes is due to the presence of Thyroid Hormone Binding Inhibitor (THBI)(19), an inhibitor of extra thyroidal conversion of enzyme of T4 to T3, and dysfunction of hypothalamus-hypophyseal-thyroid axis. The presence of subclinical hypothyroidism and hypothyroidism may result from hypothalamus-hypophyseal-thyroid axis disorders altered thyroid hormone levels due to the outcome of various medications the diabetic patients were receiving (20). Insulin an anabolic hormone enhances level of FT4, while it suppresses the level of T3 by inhibiting hepatic conversion of T4 to T3(21) On the other hand, some of the OHA (oral hypoglycemic agents) suppresses the level of FT4 while raises the level of TSH(22),(23).These situations explain the findings of low or raised thyroid hormone levels in euthyroid diabetics. Higher TSH level in patients with metabolic syndrome compared to that in the non-metabolic syndrome group suggesting that subclinical hypothyroidism may be a risk factor for metabolic syndrome (24). Increased risk of nephropathy was shown in type 2 diabetic patients with subclinical hypothyroidism (25) which could be explained by the decrease in cardiac output and increase in peripheral vascular resistance seen with hypothyroidism and the resulting decrease in renal flow and glomerular filtration rate.

Thyroid hormones may influence carbohydrate mechanisms via its interaction with adipocytokines and gut hormones. Adiponectin and thyroid hormones share some biological properties including reduction in body fat by increasing thermogenesis and lipid oxidation (26). Adiponectin might influence thyroid hormone production through its interaction with gC1q receptor found in thyroid mitochondria.

IV. CONCLUSION

The prevalence of thyroid disorder was quite high in type 2 diabetes mellitus. Hypothyroidism with low FT3 levels and subclinical hypothyroidism with raised TSH and normal FT4 levels were found in type 2 diabetes mellitus patients. Increased frequency of thyroid dysfunction in diabetic patients and its likely deleterious effects on cardiovascular and metabolic function calls for a systematic approach to thyroid disease screening in diabetes. . A higher frequency of retinopathy and nephropathy was observed in diabetic patients with subclinical hypothyroidism and more severe retinopathy was noted as well. Therefore, management of subclinical hypothyroidism in patients with diabetes may prove beneficial.

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