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Original Article

Sub-clinical Hypothyroidism in Type 2 Diabetes Mellitus Patients in a Tertiary Care Hospital, Mysore

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Abstract

Thyroid diseases and type 2 diabetes mellitus are the two most common endocrine disorders encountered in clinical practice. Diabetes mellitus and thyroid disorders are shown to mutually influence each other. The present study was done to assess and compare the thyroid function tests in diabetes mellitus patients and normal healthy volunteers. This is a cross-sectional, age-matched, comparative, hospital based study. Type 2 Diabetes mellitus patients without hypothyroidism attending the medicine outpatient department (OPD) or admitted in the medicine wards were screened and then included as cases (30 patients). The normal healthy volunteers without diabetes mellitus or hypothyroidism were screened and included for control group (30 Patients).

In this study the mean and standard deviation (S.D.) of thyroid stimulating hormone (TSH) was statistically, significantly higher in the diabetes mellitus group (5.48±2.32 mIU/dl), when compared to control group (2.91±1.44 mIU/dl). This sub clinical hypothyroidism leads to dyslipidemia. The results also showed elevated total cholesterol, low density lipoprotein (LDL) in diabetes mellitus group, when compared to control group. Thus, subclinical hypothyroidism in type 2 diabetes mellitus can aggravate the classical risk factors such as hypertension and dyslipidemia, arising from an undiagnosed thyroid dysfunction and can lead to an increased cardiovascular risk in these patients.

Introduction

Thyroid diseases and type 2 diabetes mellitus are the two most common endocrine disorders encountered in clinical practice. Diabetes mellitus and thyroid disorders are shown to mutually influence each other. Diabetes mellitus appears to influence thyroid function in two sites; firstly at the level of hypothalamic control of TSH release and secondly at the conversion of T4 to T3 in the peripheral tissue(1). Subclinical hypothyroidism is more common in type 2 diabetes mellitus patients (2).

There is great variability in the prevalence of thyroid disorders in general population, ranging from 6.6% to 13.4% (3). In diabetic patients, the prevalence is still greater and varies from 10 to 24% (3, 4). These differences can be explained by the degree of iodine

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intake among different regions, and the diversity in the population (5). Chronic hyperglycemia from any route of cause leads to hypothyroidism and elevated thyroid stimulating hormone, dyslipidemia, cardiovascular diseases (6). Till date not much data is available about subclinical hypothyroidism in diabetes mellitus in the Mysore city population.

Objectives of the study

The present study was done to assess and compare the thyroid function tests in diabetes mellitus patients and normal healthy volunteers.

Materials and Method

It is a hospital based cross-sectional, age matched, comparative study done on 30 diabetes mellitus patients (taken as cases) and 30 normal healthy volunteers (taken as controls).

Control group:

A total of 30 normal healthy volunteers aged between 35-70 years without diabetes mellitus and without history of hypothyroidism were included as control group. Patients aged above 70 years or below 35 years or patients with history of chronic illness/diabetes mellitus were excluded from the study.

Diabetes mellitus group:

A total of 30 patients aged between 35-70 years with type 2 diabetes mellitus of less than 5 years duration and without history of hypothyroidism were included as case group. Patients aged above 70 years or below 35 years or patients with history of chronic illness were excluded from the study.

Type 2 diabetes mellitus, is defined by fasting glucose >126 mg/dl, or post–prandial glucose >200 mg/dl, or HbA1c level >6.5 gm/dl (7). The normal TSH value used is 1 to 4 mIU/dl. Sub-clinical hypothyroidism is diagnosed, if TSH value is 4 to 10 mIU/dl (8).

Ethical Clearance:

Institutional ethical committee clearance for this study was obtained from JSS Medical College, Mysore. All the study subjects were explained about the study procedure and informed consent was obtained from them.

Biochemical investigations:

The parameters included were: Diabetic profile- fasting blood sugar (FBS), post-prandial blood sugar (PPBS), glycosylated hemoglobin (HbA1c), serum creatinine, thyroid function tests- tri-iodothyronine (T3), tetra-iodothyronine (T4), TSH and lipid profile- total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) were estimated in both the groups. The venous blood from antecubital vein was collected after overnight fasting. Two ml of blood was collected in fluoride vial for estimation of fasting blood glucose and another 2 ml in plain vial for thyroid hormone estimation. It was centrifuged at 4000 rpm for separation of serum. Serum creatinine was measured by enzymatic method. Two ml of venous blood was collected again in fluoride vial 2 hours after the patient has taken his/her regular breakfast for estimation of post prandial blood glucose level. Blood glucose was estimated by Glucose oxidase peroxidase method. TSH, T3, T4 was estimated by electrochemiluminiscence method. HbA1c was assessed by high performance liquid chromatography (HPLC) method. Total cholesterol was estimated by cholesterol oxidase method, HDL by direct immuno inhibition method, LDL by direct measurement.

Statistics:

Mean and Standard deviation (S.D.) of the parameters in diabetic profile (FBS, PPBS, HbA1c, serum creatinine), thyroid profile (TSH, T3, T4), lipid profile (total cholesterol, LDL, HDL), were calculated, for both groups. Unpaired‘t’ test was applied to know

the statistical significance of difference for these values between the two groups.

Results

From the Table I, we can observe that mean and S.D. value of biochemical parameters FBS, PPBS, HbA1c, TSH, serum creatinine, total cholesterol and LDL were significantly higher among the cases (diabetes mellitus group) when compared to control group. The High density lipoprotein (HDL) was significantly lower in cases when compared to control group. However T3 and T4 levels were similar in both the groups.

TABLE I : Diabetic profile, lipid profile and thyroid profile in control and diabetes mellitus groups.

S. No.	*Parameter*	*Control group*	*Diabetes mellitus group*	*'p' value*
1	FBS (mg/dl)	90.7±10.53	162±57.6	<0.05*
2	PPBS (mg/dl)	160.43±20.60	224.63±73.60	<0.05*
3	Total cholesterol (mg/dl)	159.7±29.84	197.78±48.04	<0.05*
4	LDL (mg/dl)	93.53±30.89	119.12±38.35	<0.05*
5	HDL (mg/dl)	45.1±1.13	41.57±11.62	<0.05*
6	TSH (mIU/dl)	2.91±1.44	5.48±2.32	<0.05*
7	T3 (µg/dl)	0.90±0.21	0.91±0.33	NS
8	T4 (µg/dl)	6.18±2.75	5.96±2.33	NS
9	HbA1c (%)	6.09±0.67	8.54±1.43	<0.05*
10	Serum creatinine (mg/dl)	0.90±0.18	1.07±0.30	<0.05*

* 'p' value less than 0.05 is statistically significant. NS = 'p' value more than 0.05 statistically not significant.

Discussion

In our study the mean and S.D. of TSH was higher in the diabetes mellitus group when compared to control group as shown in Table-I. This sub clinical hypothyroidism leads to dyslipidemia. Our results also showed elevated total cholesterol, LDL in diabetes mellitus group when compared to control group. It indicates that patients with diabetes mellitus are more prone to have complication when hypothyroidism associates with diabetes which is in agreement with the findings of many researchers (9, 10). Similarly in our study HbA1c, serum creatinine was increased in diabetes mellitus group. Thus subclinical hypothyroidism can aggravate the classical risk factors such as hypertension and dyslipidemia, arising from an undiagnosed thyroid dysfunction and can lead to an increased cardiovascular risk and nephropathy in these patients.

It is well known that increase in FBS, PPBS and HbA1c leads to abnormal glycaemia and atherogenic dyslipidemia. This causes increased risk of micro and macro-vascular complications such as nephropathy, retinopathy, neuropathy, coronary artery disease, cerebrovascular disease and peripheral vascular disease. Increased levels of LDL, low levels of HDL cholesterol and high levels of triglycerides are found in diabetes mellitus. This atherogenic lipoprotein profile contributes to 2–4 fold excess risk of cardiovascular disease in diabetics (11). HDL is

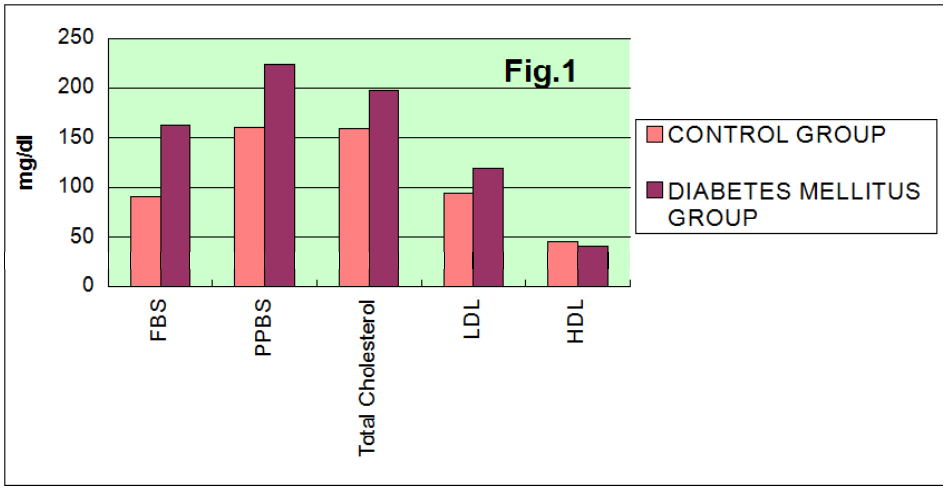

Fig. 1 : Figure showing mean value of FBS, PPBS, total cholesterol, LDL, and HDL between the control and diabetes mellitus groups.

atheroprotective and low HDL is independent risk factor for cardiovascular disease risk even when the LDL is normal or low. Thus both insulin and thyroid hormones are involved in cellular metabolism and excess or deficiency of any one can result in functional derangement of the other (12).

As per the earlier studies both clinical and subclinical hypothyroidisms are recognized as insulin resistant states (13-15). In vivo and in vitro studies have shown that this is due to impaired insulin stimulated glucose utilization in peripheral tissues (13, 14). A recent study involving subjects from a Chinese population found a 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 (16). Furthermore, an increased risk of nephropathy was shown in type 2 diabetic patients with subclinical hypothyroidism (17) 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 (18).

In 2005, Den Hollander et al. reported that treating hypothyroidism improved renal function in diabetic patients (19). As for retinopathy, Yang et al. demonstrated recently that diabetic patients with subclinical hypothyroidism have more severe retinopathy than euthyroid patients with diabetes (20). Altered thyroid hormones have been described in patients with diabetes especially those with poor glycemic control. In diabetic patients, the nocturnal TSH peak is blunted or abolished and the TSH response to TRH is impaired (21). Reduced T3 levels have been observed in uncontrolled diabetic patients. This “low T3 state” could be explained by an impairment in peripheral conversion of T4 to T3 that normalizes with improvement in glycemic control (1). Furthermore, it is shown, both in euthyroid non-diabetic (22) and diabetic adults, (23) that small variations in TSH at different 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.

Conclusion

Thus this study shows the prevalence of subclinical hypothyroidism among type 2 diabetes mellitus patients. Failure to recognize the presence of sub-clinical hypothyroidism in diabetes mellitus patients may be a primary cause of poor management often encountered in treated diabetics. Therefore, routine assessment of thyroid hormone level in addition to other biochemical parameters in the early stage of diabetes mellitus will help in the management of diabetes mellitus particularly in those patients, whose conditions are difficult to manage.

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