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Research Article

THYROID HORMONE PROFILE AND THYROID AUTOIMMUNITY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS - A CROSS SECTIONAL STUDY FROM A TERTIARY CARE CENTRE IN NORTH KERALA

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A B S T R A C T

Introduction: Diabetes mellitus and thyroid dysfunction are common endocrine disorders encountered in clinical practice. Prevalence of thyroid dysfunction in type II diabetes mellitus have not been studied much. **Objective:** To determine the thyroid hormone profile and thyroid autoimmunity in patients with type 2 diabetes mellitus. **Design**: Cross sectional study. **Setting**: 116 patients with type 2 diabetes mellitus who attended the Diabetes clinic, Government Medical College, Kozhikode, Kerala during a period of 1 year was included in the study group. **Results:** Mean TSH levels were 6.39± 13.97 and 4.86 ± 10.93 among the diabetics and non-diabetics respectively, which was statistically significant (p value 0.018). Biochemical thyroid dysfunction was detected in 31.03 %(36) of the diabetic group, which was statistically significant (p value: 0.008).Of these 32 individuals were hypothyroid (p value: 0.008), of which 19 had subclinical and 13 had overt hypothyroidism.4 diabetic individuals were hyperthyroid, of which 3 had overt and 1 had subclinical hyperthyroidism; this was not statistically significant.37 % of the study group and 34 % of the control group were anti TPO antibody positive, but no statistical significance was detected (p value: 0.88). **Conclusions**: The prevalence of Thyroid dysfunction is common in Type 2 diabetics, subclinical hypothyroidism being most common.

INTRODUCTION

Diabetes mellitus and thyroid dysfunction are two common endocrine disorders encountered in clinical practice. While the key pathology described in diabetes mellitus type 1 is autoimmune destruction of insulin secreting beta cells of pancreas, the etiology of type 2 diabetes is often multifactorial, including genetic and environmental factors that affect the beta cells or produce tissue resistance towards insulin.

Thyroid hormones are known to produce calorigenic effect through its nuclear-mediated regulation of the synthesis of respiratory genes and mitochondrial transcription factors, and also by direct action on mitochondria[1].The pathogenesis of diabetes mellitus and thyroid dysfunction are intertwined as 5′ adenosine monophosphate-activated protein kinase (AMPK) is an important target for modulation of insulin sensitivity and feedback of thyroid hormones ,and hence associated with appetite and energy expenditure[2].

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Thus coexisting thyroid dysfunction could be contributing to the worsening of diabetes mellitus. Often the clinical symptoms and signs of thyroid diseases and diabetes mellitus could mimic each other and lead to the underestimation of either of them in many patients. It could be that untreated thyroid disease may be a potential cause of poor glycemic control and appearance of frequent hypoglycemia episodes in many patients on treatment for diabetes.

While many have inquired into the association between type1 diabetes and thyroid diseases, there have been not many studies on the thyroid hormone status and thyroid autoimmunity in type 2 diabetes patients, especially in Kerala. In the current study we have evaluated the thyroid hormone profile & thyroid autoimmunity in patients with type 2 diabetes mellitus in patients from a tertiary care center in south India.

MATERIALS AND METHODS

This cross sectional study was conducted in Government Medical College, Kozhikode, Kerala-a tertiary care teaching hospital in South India. A random sample of 116 patients with

type 2 diabetes mellitus who attended the Diabetes clinic under the Department of General Medicine during a period of 1 year was included in the study group. The study group constituted patients who were diagnosed with diabetes mellitus after the age of 35 years and started with life style modification therapy, oral hypoglycemic agents or insulin. 119 age and sex matched controls were also included in the study. All patients with previously diagnosed thyroid disorders, history of neck irradiation, renal failure, recent myocardial infarction or on drugs which interfere with thyroid hormone metabolism such as beta blockers, amiodarone were excluded.

A written informed consent was obtained from all participants and the study was approved by the institutional ethical committee.

Venous blood samples were obtained and assessed for thyroid hormone status, anti-thyroid peroxidase antibody (anti TPO Ab) and blood sugar values. Fasting and postprandial (2 hour) blood sugar values were estimated directly from the hospital clinical laboratory. T3, T4 and TSH and anti TPO antibody levels were estimated using Enzyme immune technique in the department of Nuclear Medicine.

Normal ranges for the assays were as follows

FBS is 70-110- mg/dL ,PPBS (2 hour) : <200mg/dL
T3: 0.8-2ng/dL
T4, 55-135ng/dL
TSH: 0.2-4.2 µIU/mL

A titre of <30 IU/ml was taken as normal for anti TPO antibody levels.

Criteria for classifying thyroid hormone status were as: euthyroid when T3, T4 and TSH were in normal range; primary hypothyroidism when TSH more than 4.2 mIU/ml with T3 and T4 below normal; primary hyperthyroidism when TSH is < 0.2 IU/ml and T3,T4 levels above normal.

Subclinical hypothyroidism was defined as TSH more than 4.2 IµU/ml and T3, T4 levels within normal range. Subclinical hyperthyroidism was defined as TSH less than 0.2µIU/ml and T3, T4 levels within normal limits.

Data and Statistical Analysis

The results were entered in Excel format and expressed as mean ± SD. Statistical significance was assessed by student't' test. All data were analyzed using SPSS version18.0.A p value of 0.05 or less was considered to be statistically significant

RESULTS

116 diabetic and 120 apparently healthy individuals were recruited for this study. We analyzed the blood sugar values, thyroid hormone profile (T3, T4, and TSH) and anti TPO antibody levels in Type 2 diabetes mellitus patients and compared them with the non-diabetic control group. The mean age of the diabetic group was 54.08 ±9.28 years and 50.7±12.64 years in the control group. Persons of age group 50- 59 years comprised the most of both study and control group (Table 1).The diabetic group included67(56.9 %) females and 49 males (43.1%)(n=116) whereas the non-diabetic group had 68 (56.8%) females and 52 males (43.2 %)(n=120) .In the diabetic group, 18 % (21) had diabetes for less than 5 years, 22%(25) had diabetes for 5- 10 years, 41%(48) patients had diabetes mellitus since 10-19 years and nearly 19 % (22) had its onset since more than 20 years. Mean duration of type II diabetes mellitus among the study group was 11.7±7.34 years (Range 1-30 years). There was no significant association between duration of diabetes mellitus and TSH values.

Around 54 % patients were only on oral hypoglycemic agents (OHAs) and 11 % only on insulin treatment apart from lifestyle modification; 34% were on both OHA and insulin. Only 1 patient was managed with lifestyle changes only.

The mean T3 level in the diabetic group was 1.05± 0.63ng/ml and 1.06 ±0.4 in control group. The mean T4 levels were 75.47±32 and 77.67±22 in the study and control group respectively. Whereas TSH levels were 6.39± 13.97 and 4.86 ± 10.93 among the diabetics and non-diabetics respectively, which was statistically significant (p value 0.018). Mean anti TPO levels were 152.88± 310.48 and 152.08 ± 312.86 respectively among the diabetic and no diabetic group.(Table 2).

Biochemical thyroid dysfunction could be detected in 36 subjects (31.03 %) of the diabetic group, which was statistically significant (p value: 0.008).Among these patients with thyroid dysfunction, 32 individuals were hypothyroid (p value: 0.008), of which 19 had subclinical and 13 had overt hypothyroidism. Correlation between subclinical hypothyroidism and diabetes mellitus was statistically significant (p value: 0.044).4 individuals from the study group were hyperthyroid, of which 3 were overt and 1 had subclinical hyperthyroidism; this was not statistically significant. 37 % of the study group and 34 % of the control group were anti TPO antibody positive, but no statistical significance was detected (p value: 0.88) (Table 3).

Among diabetics, 21 (18.1%) had goitre and in control group 3 (2.5%) had goitre (pvalue : 0.000).

Table 1 showing age distribution of cases and controls

Age distribution of subjects				
Age group (in years)	Cases		Control	
	No.	Percentage	No.	Percentage
30-39	10	8.6	13	10.8
40-49	19	16.4	18	16.2
50-59	52	44.8	53	45
60-69	31	26.7	32	25.3
≥ 70	4	3.4	4	3.5
TOTAL	116	100%	120	100%
Mean age	54.08 ±9.28 years		50.7±12.64 years	

Table 2 showing the mean values of T3, T4, TSH, anti TPO antibody levels among cases and controls

Mean T3, T4, TSH and anti-TPO antibody levels among cases and controls			
Parameters	Cases(n=116)	Controls(n=120)	p-value (student 't' test)
T3	1.058	1.06	0.15
T4	75.475	77.628	0.23
TSH	16.39	4.8	0.018
anti-TPO	152.879	152.083	0.64

Table 3 showing thyroid dysfunction in cases and controls

	T2DM (n=116)	Controls (n= 120)	p-value (student 't' test)
Biochemical thyroid dysfunction	36 (31.03%)	17 (14%)	0.008
Hypothyroidism	32 (27.8%)	16 (13.2%)	0.025
• Overt	19 (16%)	6 (5%)	0.375
• Subclinical	13 (11.2%)	10 (8.3%)	0.044
Hyperthyroidism	4 (3.4%)	1 (0.8%)	0.207

• Overt	3 (2.5%)	0(0%)	0.117
• Subclinical	1 (0.9%)	1 (0.8%)	1.0
Anti-TPO positivity	43 (37%)	41 (34%)	0.88

DISCUSSION

116 diabetics and 120 controls were evaluated in the present study. Age distributions among subjects of both groups were similar, maximum individuals in the range of 50- 59 years. Number of females was more than males.

In our study 31 % of diabetic patients had evident biochemical thyroid dysfunction which was found to be statistically significant (p value: 0.008).This prevalence is more than that reported by other studies.16 % prevalence was reported by Khurana *et al* (2016) and 28 % prevalence by Raghuwanshi *et al*(2014)[3,4].

27.8% of the diabetics had hypothyroidism (16% overt and 11.2 % had subclinical hypothyroidism) in the present study. This prevalence is comparable to many other studies[4,5]. Most authors across the world have agreed that hypothyroidism is the most common thyroid dysfunction detected in type II diabetes mellitus[4,5,6,7,8]. Prevalence of subclinical hypothyroidism in diabetics reported by us is comparable to a similar study from south India by Anil *et al* (11.25 %)[9]. There are studies that reported that subclinical hypothyroidism was more common than overt disease in type 2 diabetes mellitus[3,5,10] .

In the present study, TSH levels were significantly higher in diabetics as compared to non-diabetics. No significant difference was detected in the levels of T3 and T4 between the 2 groups in our study. In most other studies, TSH levels were significantly high and T3, T4 levels were significantly lower in diabetics[5,11].Altered thyroid hormone levels have been described to be associated with poor glycemic control. It has been suggested that the presence of thyroid hormone binding inhibitor (THBI), the presence of inhibitor of extrathyroidal T4 to T3 (IEC) and dysfunction of the hypothalamo-hypophysial-thyroid axis are considered to be involved in abnormal thyroid function in diabetic patients[12]. In addition there is less activation of AMPK (5'-Adenosine Mono Phosphate activated Protein Kinase) in type 2 diabetes which also causes decreased formation of thyroid hormones[1].In diabetic patients, it is found that nocturnal TSH peak is blunted or abolished, and the TSH response to Thyrotropin releasing hormone (TRH) is impaired[13].

Recognition of subclinical hypothyroidism in diabetes mellitus is very important. Han *et al* (2015) in his systematic review and meta-analysis found out type II diabetes was associated with a 1.93-fold increase in the risk of subclinical hypothyroidism [10].They also found that subclinical hypothyroidism might produce an increased risk of development of diabetic complications like diabetic nephropathy, diabetic retinopathy, peripheral arterial disease, diabetic peripheral neuropathy[10].

In our study we had detected diabetic patients with TSH value as high as 100 µIU/mL, but not diagnosed previously. This could be because symptoms of hypothyroidism would have been camouflaged by the clinical features of diabetes mellitus. This highlights that physicians may need to be well aware of the coexistence of hypothyroidism not only in type 1 but also in type II diabetes.

We found that 3.4 % of the cases had hyperthyroidism which is comparable to results obtained in other studies too[3,5].But in our study this association did not show statistical significance. Insulin resistance has been a proven condition in hyperthyroidism as well as hypothyroidism[2].Thus insulin resistance could be the linking factor between hyperthyroidism and diabetes mellitus.

Among diabetics, 21 (18.1%) had goitre which was statistically significant (p value: 0.000).Higher levels of circulating insulin associated with insulin resistance have shown a proliferative effect on thyroid tissue resulting in increased formation of nodules and goiter[14,15].

Regarding Anti TPO levels, our study revealed no significant difference in the mean anti-TPO levels between diabetics and controls with any form of thyroid dysfunction. These results are in agreement with previous reports that suggest that thyroid dysfunction in type II diabetes may not be solely immunologically mediated[16]. The high prevalence of anti TPO antibody detected in both case and control group conforms with the current increasing anti TPO prevalence in Indian population[17,18].

Our study was conducted in Government Medical College, Kozhikode a tertiary care teaching hospital in northern Kerala which caters to the needs of nearly 6 districts of our state. So the results would represent a broader population. As far as our knowledge, there have been only limited studies from southern part of India investigating the thyroid dysfunction in type II diabetic patients. There is a hospital based cohort study from Kerala in which the prevalence of thyroid disorders is similar in type 2 diabetic and non-diabetic subjects in their population[19].

The limitation of our study was that evaluation of predictors of thyroid dysfunction in diabetes mellitus was not done. No follow-up was done in diabetic euthyroid patients whether they developed thyroid disease later.

CONCLUSION

Nearly 31.03 % of diabetics have biochemical thyroid abnormality in our study. Subclinical hypothyroidism was the most common dysfunction, followed by overt hypothyroidism. Further studies need to be carried out to investigate how hyperglycemia could be causing impairment of thyroid function.

Clinicians should be aware of this high prevalence ofthyroid dysfunction and type II diabetes mellitus in addition to our previous knowledge of type I diabetes-thyroid disease association.TSH screening of patients with diabetes may be advised at regular intervals to detect thyroid dysfunction especially subclinical hypothyroidism. This would aid the physician to prevent complications like nephropathy, retinopathy, neuropathy and arterial diseases in type II diabetes patients. Clinical features of diabetes mellitus could be camouflaging the symptoms of hypothyroidism and hence do not receive appropriate treatment. Hyperthyroidism is known to produce hyperglycemia. Early detection and management of thyroid disorders may help attain better quality of life in diabetic patients. Hence thyroid function tests may be done as part of routine evaluation of patients with type II diabetes mellitus.

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Conflict of Interest: Nil

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