

Thyroid Status in Diabetes Mellitus

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Abstract

The study was carried out to estimate thyroid hormones (T3, T4 and TSH) level in diabetic patients and to compare it with normal controls in an attempt to find out the importance of thyroid hormone estimation in diabetic cases. Sixty cases of diabetes mellitus who attended Diabetic Clinic, RIMS during the period from October 2008 to March 2010 were taken as the cases and 30 healthy individuals were selected as control group. Serum total Tri-iodothyronine (T3), thyroxine (T4), thyroid stimulating hormone and blood sugar were estimated in the cases and controls. The study showed that diabetes was more prevalent in the age group of 51-65 years, and more in males (52%). The mean fasting blood sugar (126.17 ± 37.92 mg%) and serum TSH level (4.58 ± 2.90 mIU/L) were increased significantly ($r=0.884$, $p>0.05$) whereas serum T4 level (5.79 ± 4.39 µg/dl) was decreased significantly in diabetic cases when compared with controls. Mean T3 level of diabetic cases was higher than controls but it was insignificant. Diabetes mellitus cases with statistically significant higher TSH value have complications like hypertension, retinopathy, nephropathy etc. A statistically significant, negative correlation ($r=-0.942$, $p<0.05$) was seen between Serum T4 and blood sugar in the cases. Therefore, routine assessment of thyroid hormone level in addition to other biochemical variables in the early stage of diabetes will help in the management of these patients.

Introduction

Diabetes mellitus is a group of aetiologically different metabolic defects characterized by hyperglycaemia resulting from defect in insulin secretion as well as insulin action or both. Occasionally other endocrine disorders like abnormal thyroid hormone level are found in diabetes [1]. Diabetes and thyroid disorders have been shown to mutually influence each other and associations between both conditions have long been reported [2]. In the NHANES III study, a survey of 17,353 subjects representing the US population, hypothyroidism was found in 4.6% and hyperthyroidism in 1.3% of subjects [3]. It was observed that there was an increased frequency of thyroid dysfunction with advancing age and a higher prevalence of thyroid disease in women compared to men and in diabetic subjects compared to non-diabetic. Several reports documented a higher than normal prevalence of thyroid dysfunction in the diabetic population. Particularly, Perros et al. [4] demonstrated an overall prevalence of 13.4% of thyroid diseases in diabetics with the highest prevalence in type 1 female diabetics (31.4%) and lowest prevalence in type 2 male diabetics (6.9%). Recently, a prevalence of 12.3% was reported among Greek diabetic patients [5] and 16% of Saudi patients with type 2 diabetes were found to have thyroid dysfunction [6]. In Jordan, a study reported that thyroid dysfunction was present in 12.5% of type 2 diabetic patients [7]. However, thyroid disorders were found to be more common in subjects with type 1 diabetes compared to those with type 2 diabetes. Additionally, a 3.5-fold increased risk of autoimmune thyroiditis was noticed in GADA positive patients [8]. Thyroid disorders remain the most frequent autoimmune disorders associated with type 1 diabetes. Physiological and biochemical interrelationship between insulin and the influence of both insulin and iodothyronines on the metabolism of carbohydrate, proteins and lipid are recorded [9]. Thyroid disease is a pathological state that adversely affects diabetic control and is commonly found in most forms of DM which is associated with advanced age in type 2 diabetes and autoimmune diseases in type 1 diabetes. DM 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. Marked hyperglycemia causes reversible reduction of the activity and hepatic concentration of T4-5-deiodinase, low serum concentration of T3, elevated levels of reverse T3 and low, normal, or high level of T4 [10]. Till date not much data is available about thyroid diseases in diabetes

in the Manipur. Therefore, this study has been carried out to find out any thyroid dysfunction in diabetic cases and hence the importance of its estimation in diabetic patients.

Materials and Methods

It was a cross sectional study conducted in the Department of Biochemistry in collaboration with the Department of Medicine, Regional Institute of Medical Sciences, Imphal (RIMS), during the period from October 2008 to March 2010. The Study Group consisted of 60 confirmed diabetic cases on Oral Hypoglycemic Agent or insulin or Diabetic diet attending Diabetic Clinic, Regional Institute of Medical Sciences, Imphal. Controls consisted of 30 age and sex matched healthy individuals. Those cases with known thyroid disorders, history of other illness, hyperlipidemia, other physical illness and physiological stress which induce alteration on the thyroid hormone were excluded from the study. Detailed history of each regarding age, sex, address, religion, occupation, marital status, personal history was taken. Informed consent of the patient was recorded in a proforma designed for the study. Approval from the ethical committee, RIMS was taken. Fasting as well as post prandial blood sugar was estimated to know the glycemic status.

A total of 4 ml of 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. Two ml of venous blood was collected again in

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fluoride vial 2 hours after the patient has taken his regular meal for estimation of post prandial blood glucose level.

Blood glucose was estimated by Glucose oxidase peroxidase Method as described by Trinder P using commercially available kit, Human GmbH, Germany [11]. TSH was estimated by classical sandwich Enzyme Linked Immunosorbant Assay (ELISA) technique [12]. T3 and T4 were estimated by using competitive binding ELISA technique [13]. Classification of the values was based on the following criteria.

- 1) Normal, when the total T4 and TSH are in the normal range (i.e., TSH=-0.69-2.02 ng/ml; T4=4.4-10 µg/dl for males and 4.8-11.6 µg/dl for females).
- 2) Hypothyroidism-when total T4<4.4 µg/dl and TSH>6.2 mIU/l.
- 3) Subclinical hypothyroidism when T4 is within normal limits but TSH>6.2 mIU/l.
- 4) Hyperthyroidism when serum TSH<0.3 mIU/l.

Statistical analysis

Data are expressed as Mean ± SD and percentage. Continuous variables of the 2 groups were compared by student's t test wherever suitable. These statistical analyses were performed using SPSS version 16. The study was approved by the institutional review board and all the participants gave written informed consent.

Results and Discussion

Table 1 presents the age and sex distribution of diabetic subjects and controls. Majority of the cases belong to the age group 51-65 years (40%) followed by 36-50 years (38.3%). Mean age ± SD of cases were 50 ± 11 years and of the controls group was 49 ± 13 years. Males comprised of 51.7% and females were 48.3% of the study group. Forty three percent of the study group cases have fasting sugar level above 120 mg/dl whereas 95% of the study group cases have postprandial blood sugar level above 140 mg/dl (Table 2). This indicates a poor glycaemic status in the study group. The onset of diabetes precedes the diagnosis of thyroid dysfunction by approximately one decade [14].

Table 3 shows the levels of various laboratory parameters in diabetic and non-diabetic subjects. Fasting blood sugar and serum TSH levels are increased significantly whereas the serum T4 level is decreased significantly in diabetes mellitus cases when compared with control. Serum T3 showed no significant change in study cases when compared with controls. Our study showed a clear picture of hypothyroidism in diabetes mellitus study group. Similar findings were seen in the study of Islam et al., Suzuki et al., and Baron [15-17]. The reported frequency of hypothyroidism has varied from 0.7-4% [18,19]. The abnormal thyroid hormone level may be due to various medication the diabetics

were receiving like phenylthiourea which suppress the level of FT4 and T4, while causing raised levels of TSH [20], insulin which enhances the level of FT4 while it suppresses the level of T3 by inhibiting hepatic conversion of T4 to T3, decreased TRH synthesis in diabetics [16], autoimmune diseases [21] and prevalence of thyroid antibodies in diabetic cases [17]. Glycaemic status is influenced by insulin which is known to modulate TRH & TSH level [22]. The abnormal hormone level in diabetes may be due to the presence of thyroid hormone binding inhibitor, inhibitor of T4 to T3 conversion, dysfunction hypothalamo-pituitary-thyroid axis and the influence of poorly controlled diabetes on thyroid hormone concentration [23].

Serum T4 level was found to be lower in male compared to females in the study group but the difference was found to be insignificant. However when serum T4 level was compared between the study group and controls it was found to be statistically lowered in the study group (Table 4). Comparison between male (3.62 ± 2.98 mIU/l) and female (5.61 ± 2.46 mIU/l) values of TSH in study group exhibited significantly (p<0.001) increased value among female cases. Also there is significant (p<0.001) increase of TSH among female cases of study group (5.61 ± 2.46 mIU/l) when compared with control female value (2.68 ± 1.66 mIU/l) (Table 5). The mean TSH level was significantly higher in cases and it was significantly higher in female's cases which is similar to the findings of Celani et al. [24]. Hypothyroid state was higher in females which are probably associated with the higher prevalence of obesity in diabetic female. Obesity causes an elevation of TSH due to central & peripheral mechanism [25,26]. Obese persons have increased levels of leptin and pro-opiomelanocortin which directly stimulate TRH neurons in the paraventricular nucleus leading to increased TSH.

The mean serum T3 and T4 was found to be insignificantly higher in the cases with complication like hypertension, coronary artery disease, nephropathy, neuropathy, retinopathy etc compared to those without complication; however, the mean serum TSH level in diabetes mellitus with complication was found to be significantly higher than those without complication (Table 6). It indicates that Diabetes mellitus cases are more prone to have complication when hypothyroidism associates with diabetes which is in agreement with the findings of many researchers [27,28]. The distribution of serum TSH over different blood sugar level shows insignificant positive correlation (r= 0.884, t=2.673, p>0.05); whereas the distribution of serum T4 over different blood sugar level shows significant negative correlation (r=-0.942, t=5.599, p<0.01). This is correlated with the findings of Dimitridis and Raptis and Ahren et al. [29,30]. Uncontrolled hyperthyroidism in diabetic patients may trigger hyperglycaemic emergencies while recurrent hypoglycaemic episodes have been reported in diabetic patients with hypothyroidism. Furthermore, thyroid dysfunction may amplify cardiovascular disease risk in diabetic patients through inter-relationships with dyslipidaemia, insulin resistance and vascular

group	Male	Mean age in years ± SD	females	Mean age in years ± SD	total	Mean age in years ± SD
Diabetes mellitus	31	54 ± 10	29	47 ± 12	60	50 ± 11
control	17	51 ± 13	13	47 ± 14	30	49 ± 13

Table 1: Mean age with standard deviation in both control and diabetes mellitus cases.

Fasting blood sugar (mg/dl)	Study group No (%)	Post-prandial blood sugar (mg%)	Study group No (%)
<90	17(28.3)	<110	0
91-100	5(8.3)	110-120	0
101-110	9(15)	121-130	2(3.4)
111-120	3(5)	131-140	1(1.6)
>120	26(43.3)	>140	57(95)

Table 2: Distribution of blood sugar levels in diabetes mellitus cases.

Parameters	Controls(n=30)	Cases(n=60)	P-value
Fasting blood sugar(mg/dl)	86.57 ± 8.14	126.17 ± 37.92*	0.0003
T3(nmol/dl)	1.29 ± 0.43	1.39 ± 0.59	0.3420
T4(µg/dl)	7.54 ± 1.94	5.80 ± 4.39*	0.0101
TSH(mIU/l)	3.08 ± 1.56	4.58 ± 2.90*	0.0020

*(p<0.05 - significant)

Table 3: Biochemical parameters in control and diabetic cases (values are expressed in mean ± S.D.).

Serum		NO OF CASES	Mean T4 ± SD (µg/dl)	Range
Controls	Males	17	7.52 ± 1.92	4.6-10.44
	Females	13	7.45 ± 2.01	4.5-10.4
	Total	30	7.55 ± 1.92	4.5-10.5
Diabetes	Males	31	5.49 ± 4.12	0.43-12.84
	Females	29	6.14 ± 4.69	0.58-13.49
	Total	60	5.80 ± 4.38*	0.43-13.49

P<0.05- significant

Table 4: Serum total thyroxine(T4) in control and study group.

Serum		NO OF CASES	Mean TSH ± SD (mIU/ml)	Range
Controls	Males	17	3.37 ± 1.47	0.78-5.45
	Females	13	2.68 ± 1.66	0.66-6.0
	Total	30	3.07 ± 1.56	0.66-6.0
Diabetes	Males	31	3.62 ± 2.98	0.41-9.00
	Females	29	5.61 ± 2.46(b**)	0.46-10.37
	Total	60	4.58 ± 2.90(a*)	0.41-10.37

P<0.05 –significant; a - comparison between TSH values of study and control group;

b** - comparison between TSH values of males and females of study group

Table 5: Serum thyroid stimulating hormone (TSH) in control and study group.

Parameters	DM without complications	DM with complications	P value
T4(µg/dl)	4.698 ± 2.883	7.459 ± 4.672	0.636
T3(nmol/ml)	1.308 ± 0.530	1.570 ± 0.677	0.109
TSH(mIU/l)	5.021 ± 4.080	7.459 ± 4.672	0.044

p- <0.05-significant

Table 6: Thyroid hormone level in diabetes mellitus with and without complications.

endothelial dysfunction. This is a preliminary study with a small sample size, larger epidemiological studies is required to find out the actual prevalence and incidence of thyroid abnormality in this part of the country.

Conclusion

Thus this study shows the prevalence of abnormal thyroid hormone level among diabetic subjects. The relationship between thyroid disorders and diabetes mellitus is characterized by a complex interdependent interaction. Failure to recognize the presence of abnormal thyroid hormone level in diabetes may be a primary cause of poor management often encountered in some treated diabetics. Therefore, routine assessment of thyroid hormone level in addition to other biochemical parameters in the early stage of diabetes will help in the management of diabetes particularly in those patients whose conditions are difficult to manage.

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