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TO ASSESS FREE THYROID HORMONES (FT3 & FT4) AND THYROID STIMULATING HORMONE (TSH) IN TYPE 2 DIABETIC PATIENTS: RELATION WITH GLYCEMIC CONTROL

Biochemistry

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ABSTRACT

Introduction: Diabetes and thyroid disorders have been shown to mutually influence each other and higher prevalence of thyroid dysfunction is found in diabetes.

Materials and Methods: The present case-control study included 100 type 2 diabetic patients and 50 apparently healthy controls. Serum levels of free triiodothyronine (fT3), thyroxine (fT4) and thyroid stimulating hormone (TSH) were assayed in all subjects.

Results: Serum level of TSH in type 2 diabetic patients were significantly increased in comparison to apparently healthy controls and serum levels of fT3 and fT4 were significantly low in comparison to apparently healthy controls.

Conclusion: Regular screening of thyroid disorder in all type 2 diabetic patients should be done to achieve healthy life.

KEYWORDS

Low Ft3 State, Type 2 Diabetes Mellitus, Thyroid Disorder.

INTRODUCTION:

Thyroid diseases and diabetes mellitus are the two most common endocrine disorders encountered in clinical practice, affecting mutually each other.[1] The association between the two endocrine disorders had come in light since 1979 after the study done by Hecht A et al[2] that emphasized on the importance of screening of diabetic patients for thyroid diseases.[3] The preceding studies observed higher prevalence of thyroid dysfunction in diabetes as 31% and 46.5%.[4] The term 'thyroid diabetes' reflects the impact of alterations of thyroid hormones in the worsening of glycemic control.[5] There is a complex intertwining biochemical, genetic, and hormonal factors for the association. 5'-adenosine monophosphate-activated protein kinase (AMPK) is a central target for modulation of insulin sensitivity and feedback of thyroid hormones associated with appetite and energy expenditure.[6]

Altered thyroid hormones (TH) synthesis is seen in thyroid diseases – hyperthyroidism (excess production of the TH) and hypothyroidism (diminished TH production).[7] 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.[8] Poorly controlled diabetes, both Type 1 and Type 2, may induce a "Low T3 state" characterized by low serum total and free T3, increase in reverse T3 (rT3) but near normal serum T4 and TSH concentrations.[9] In the light of above discussion, present study was designed to assess serum free thyroid hormones (fT3 & fT4) and TSH among patients of type 2 diabetes mellitus (T2DM), and to correlate, if any with the glycemic status.

MATERIALS AND METHODS:

The present case-control study was conducted with a total of 150 subjects in the age range of 35 –70 years from the OPD and wards of medicine department of Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana-Ambala, Haryana, India.

Subjects included for the study were categorized into 2 groups:

Group 1: Hundred (100) diagnosed subjects with type 2 diabetes mellitus.

Group 2: Fifty (50) age and sex matched healthy subjects as controls. The cases were diagnosed as diabetes mellitus collaboratively by the Department of Medicine and the Department of Biochemistry. Informed consent, both in English as well as vernacular language, were taken from the participants included in the study. The study was approved by Institutional Ethics Committee.

Inclusion Criteria

I. OPD and IPD patients with the history of type 2 diabetes mellitus.
II. Age 35-70 years of either sex.

Exclusion Criteria

I. Patients below age 35 years.
II. Type 1 diabetic patient.
III. Known case of thyroid disorder and Patients on medication that modifies the thyroid functions.
IV. Patients who have undergone surgery of the thyroid gland.
V. Patients of drug-induced hyperglycemia like steroid therapy etc.

Sample Collection

2 ml fresh venous blood was collected in a vial containing anticoagulant, Ethylenediaminetetraacetate (EDTA). After homogenous mixing, sample was analyzed for glycosylated hemoglobin (HbA1c) by ion exchange method.[10]

Serum was collected for the analysis of thyroid hormones (fT3 & fT4) and TSH by chemiluminiscence method.[11-13]

Statistical Analysis

The data analysis was done with SPSS (Statistical Package for the Social Sciences). The 'p' value between 0.05 and 0.01 was taken as statistically significant; $p < 0.01$ as highly significant.

RESULTS

In the study, mean age of T2DM and apparently healthy controls were 56.76 ± 8.94 years and 55.22 ± 6.71 respectively. There were 37 T2DM categorized under good glycemic control i.e. HbA1c having < 7.5% whereas, there were 63 type 2 diabetic patients categorized under poor glycemic control i.e. HbA1c having ≥ 7.5%. It was clear that there were more poorly controlled type 2 diabetic patients. The mean HbA1c of type 2 diabetic patients was $8.60 \pm 1.95\%$ as compared to healthy controls ($4.75 \pm 0.66\%$) which was statistically highly significant having p value 0.00 i.e. $p < 0.001$.

Table 1: Comparison of fT3, fT4 and TSH between Diabetic cases and Healthy controls.

PARAMETER	GROUP	N	MEAN ± S. D.	P VALUE
fT3	Diabetic cases	100	1.68 ± 0.95	0.000
	Controls	50	2.71 ± 0.35	
fT4	Diabetic cases	100	1.04 ± 0.37	0.000
	Controls	50	1.31 ± 0.42	
TSH	Diabetic cases	100	4.45 ± 6.03	0.000
	Controls	50	1.89 ± 0.855	

Table 2: Distribution of subjects according to thyroid disorder.

THYROID DISORDER	NUMBER	PERCENTAGE
Normal	38	38%
Low fT3 State	33	33%
Hypothyroidism Primary Hypothyroidism Subclinical Hypothyroidism	28 09 19	28%
Clinical Hyperthyroidism	01	1%
Total	100	100%

Table 3: Correlation of TSH with fT3 and fT4 According to Glycemic Status.

GLYCEMIC STATUS	PARAMETER		fT3	TSH
GOOD GLYCEMIC CONTROL HbA1c < 7.5%, N = 37	fT4	Pearson Correlation	0.176	-0.452**
		Sig. (2-tailed)	0.297	**0.005**
POOR GLYCEMIC CONTROL HbA1c ≥ 7.5%, N = 63	fT4	Pearson Correlation	0.597**	-0.341**
		Sig. (2-tailed)	**0.000**	**0.006**

DISCUSSION

Diabetes mellitus is a global health problem affecting millions of population, which is associated with defective production or unbalanced action of insulin hormone, thereby, affecting intermediary metabolism. The predisposing factors may include sedentary life style, unbalanced diet and genetic transmission.[14] Thyroid hormone, secreted from thyroid gland through hypothalamic-pituitary-thyroid gland axis is essential for normal growth and development, neural differentiation and metabolic regulation in mammals.[15,16] Insulin and thyroid hormones are involved in cellular metabolism and excess or deficient of either of these hormones reflect the functional derangement of the other.

In present study, greater proportions of type 2 diabetic patients (63%) were poorly controlled. This might be due to various associated factors like socioeconomic status, lack of approach to the hospital, increased body mass index (BMI), obesity, sedentary life style etc. This finding was in consistent with the study done by M Khattab et al[17] which stated that 65.1% had HbA1c ≥ 7 % according to demographic, anthropometric and clinical characteristics.

In present study, Mean HbA1c was statistically highly significant among T2DM cases as compared to healthy control ($p < 0.000$). Also, Mean serum fT3 and fT4 levels were found to be decreased among T2DM patients as compared to healthy control which were statistically highly significant between the groups ($p < 0.000$). These findings were in consistent with the study done by Acharya et al.[18] who revealed that low serum fT3 and fT4 activities found in T2DM patients as compared to normal individuals. There was increased in serum TSH level among T2DM patients as compared to control which was also found to be statistically highly significant ($p < 0.000$). This finding was in accordance with the result displayed in the studies done by Acharya et al.[18] and Panneerselvam et al[19] indicating that serum TSH was significantly higher in T2DM patients than in normal individuals (Table 1).

In present study, low fT3 state was found as 33% among T2DM patients. 28% of the patients were suffering from hypothyroidism, of which greater proportions of patients had subclinical hypothyroidism (19 out of 28) (Table 2).

In present study **(Table 3)**, in good glycemic control group, only fT4 was correlated negatively with TSH which was statistically highly significant. In poor glycemic control group, fT4 was positively correlated with fT3 which was statistically highly significant ($p<0.01$), and was negatively correlated with TSH, which was also statistically significant. Also, negative correlation of fT3 with TSH was found to be statistically significant (Pearson correlation = -0.243, $p = 0.05$).

Derangement of thyroid hormones (including low T3 state) and TSH were more pronounced in poor glycemic control as compared to good glycemic control. Glycemic status in T2DM strongly affects serum T3 levels, basal TSH levels and TSH response to thyrotropin releasing hormone (TRH).[20,21] Type 2 diabetic patients with poor glycemic control had low T3, low T4 and raised TSH as compared to good glycemic control.[22]

CONCLUSION

The present study clearly highlighted the impact of hyperglycemia in type 2 diabetic patients on functioning of thyroid gland. Low fT3 state and derangement of thyroid hormone levels were more pronounced in poorly controlled diabetic patients. So, it is strongly recommended to all patients of type 2 diabetes mellitus for screening of their thyroid function and glycemic status to decrease the morbidity and mortality.

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