ABSTRACT

Introduction: Diabetes mellitus (DM) is one of the important health problems affecting the major populations worldwide. Diabetes mellitus, endocrine disorder which involves multiple organ systems and leads to significant morbidity and mortality due to accompanying complications. Thyroid diseases and diabetes mellitus are common endocrine disorders. The present study is carried out for the assessment of thyroid dysfunction in type 2 diabetic patients by measurement of serum T3, serum T4 and serum TSH levels.

Materials & method: This study was conducted in Department of Physiology in association with Department of Endocrinology, JNU Institute for Medical Sciences & Research Center, Jaipur. A total of 100 subjects were enrolled into the study. They were divided into 2 groups, 50 age and sex matched healthy subjects were taken as group I (controls) (HbA1c: 5.5 to 6.5 %) and 50 type 2 diabetes mellitus subjects were taken as group II (HbA1c: >7.5 %). Age of the study subjects was 35 to 65 years. Under aseptic conditions, 5 mL random venous blood sample is collected from all subjects in vacutainers, 2 mL in plain tube and 3 mL in EDTA tube. Serum sample was used for the estimation of random sugar (GOD-POD method) by using ERBA chemistry analyzer, thyroid profile by ELISA method, using mini VIDAS and EDTA sample is used for estimation of HbA1c by using BIORAD-D10. Data were expressed as mean ±SD. P value <0.05 is considered as statistically significant.

Results: Random blood sugar and HbA1c levels were significantly increased in T2DM (group II) subjects compared with controls (group I). T3 levels were significantly decreased and TSH levels were significantly increased in T2DM subjects compared to controls. HbA1c is positively correlated with TSH.

Conclusion: In this present study, we have observed that the abnormal thyroid hormone levels among type 2 diabetics. Therefore there is a need for the routine assay of thyroid hormones in type 2 diabetes mellitus inorder to improve the quality of life and reduce the morbidity.

Keywords: Diabetes mellitus, Hypothyroidism, Glycated hemoglobin

INTRODUCTION

Diabetes mellitus (DM) is one of the important health problems affecting the major population worldwide1. Diabetes mellitus, endocrine disorder which involves multiple organ systems and leads to significant morbidity and mortality due to accompanying complications2. Diabetes mellitus is characterized by absolute or relative deficiency in insulin secretion or insulin action or both, associated with hyperglycemia, and disturbances in carbohydrate, lipid and protein metabolism. Thyroid diseases and diabetes mellitus are common endocrine disorders3. Diabetic patients have increased prevalence of thyroid disorder, with hypothyroid being the most
In diabetic patients, thyroid dysfunction varies from 2.2% - 17%. Diabetic women are more commonly affected than men. Hypothyroidism is a clinical syndrome occurs from a deficiency of thyroid hormones. It is very common thyroid problem in diabetic patients.

Thyroid hormones and insulin are the antagonists, and involved in metabolism of carbohydrates, proteins, and lipids. The functional impairment occurs in thyroid hormone as well as insulin if their levels are altered. Thyroid disorders adversely affect diabetic control. 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. Increased hyperglycemia causes reversible reduction of the activity and hepatic concentration of T4-5'-deiodinase, low serum T3, increase in reverse T3 and also variation in the level of T4. Failure to identify the imbalance of thyroid hormones in patients with type 2 diabetes may be a major cause of poor management and diagnosis of diabetic patients. Therefore, there is need to consider the thyroid hormones in type 2 diabetic patients as routine investigations and serum T3, T4 and TSH are more reliable and sensitive tests for thyroid dysfunction in the management of type 2 diabetic patients. Therefore, the present study is carried out for the assessment of thyroid dysfunction in type 2 diabetic patients by measurement of serum T3, serum T4 and serum TSH levels.

**MATERIALS & METHOD**

This is a prospective, case-control study, conducted in Department of Physiology in association with Department of Endocrinology, JNU Institute for Medical Sciences & Research Center, Jaipur. After obtaining permission from Institutional Ethical Committee and written informed consent from study participants, a total of 100 subjects were enrolled into the study. They were divided into 2 groups, 50 age and sex matched healthy subjects were taken as group I (controls) (HbA1c: 5.5 to 6.5 %) and 50 type 2 diabetes mellitus subjects were taken as group II (HbA1c: >7.5 %). Age of the study subjects was 35 to 65 years. Patients with a history of hypertension, renal impairment, autoimmune disorders, cerebrovascular diseases, acute respiratory failure, previous vascular events (angina, myocardial infarction and acute arterial occlusion) were excluded from the study. A detailed clinical and physical examination was done for all study participants. Under aseptic conditions, 5 mL random venous blood sample is collected from all subjects in vacutainers, 2 mL in plain tube and 3 mL in EDTA tube. The blood samples were centrifuged at 2500 rpm for 10 minutes to obtain serum. The separated serum sample was used for the estimation of random sugar (GOD-POD method) by using ERBA chemistry analyzer, thyroid profile (serum T3, T4 and TSH) by ELISA method, using mini VIDAS and EDTA sample is used for estimation of HbA1c by using BIORAD-D10.

**Statistical Analysis:**

Data were expressed as mean ±SD. P value <0.05 is considered as statistically significant. Pearson’s correlation coefficient for correlation of TSH and HbA1c. Statistical analysis was done by using SPSS 20.0, Stata 8.0.

## RESULTS

Random blood sugar and HbA1c levels were significantly increased in T2DM (group II) subjects compared with controls (group I). T3 levels were significantly decreased and TSH levels were significantly increased in T2DM subjects compared to controls (Table 1). HbA1c is positively correlated with TSH (Table 2). T4 levels were not significant.

### Table 1: Comparison of study parameters between T2DM cases and controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls (n=50)</th>
<th>T2DM (n=50)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>Random Blood sugar (mg/dL)</td>
<td>94.02±10.121</td>
<td>169.10±46.658</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Glycated Hemoglobin (%)</td>
<td>5.4±0.29</td>
<td>7.31±1.67</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Total T3 (ng/mL)</td>
<td>3.04±1.04</td>
<td>1.50±0.46</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Total T4 (mg/dL)</td>
<td>6.49±3.35</td>
<td>6.37±1.91</td>
<td>0.824</td>
</tr>
<tr>
<td>TSH (mIU/mL)</td>
<td>1.06±0.38</td>
<td>3.80±1.14</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

* Statistically significant
Table 2: Spearman’s rho correlation between HbA1c and TSH

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Correlation Coefficient(r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>0.468**</td>
</tr>
</tbody>
</table>

**Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

The present study is carried out for the assessment of thyroid dysfunction in type 2 diabetic patients. The thyroid hormones, total T3, total T4 are insulin antagonists. These hormones potentiate the insulin action indirectly TRH synthesis decreases in diabetes. These could be responsible for the occurrences of low thyroid hormone levels in some diabetics.

The study showed that the serum total T3 levels decreased and serum TSH levels were increased in type 2 diabetics when compared to controls. A study by Singh G et al., reported that type 2 diabetes mellitus patients had abnormal thyroid hormone levels. The level of T3, T4, FT3 and FT4 were significantly lower while the levels of TSH were significantly higher in type 2 diabetics as compared to non-diabetics, which agrees with the findings of this study.

Diabetes Mellitus and hypothyroidism, both are closely related endocrine disorders, and are associated with several metabolic abnormalities. The effect of thyroid hormones, T4 and T3, on body homeostatic energy and metabolic regulation is explained by its action on peripheral tissues. Secretion of insulin is influenced by thyroid hormones. Hypothyroidism causes decrease in glucose-related β-cell insulin secretion. Gene array studies in hypothyroid patient’s skeletal muscle have shown a classical effect on sugar transporter expression by down-regulating the GLUT5 in hypothyroidism. On the contrary, expression of GLUT4 is not changed, but model animals showed altered translocation of GLUT4 to the cell membrane and negative alteration of enzyme-baseddegradation of intracellular sugar in hypothyroid state. In diabetes mellitus there is influence of endocrine and non-endocrine organs other than pancreas and there are alterations in the hypothalamus-pituitary-thyroid axis. Hypothalamic plasmaTRH, pituitary and plasma TSH, as well as TSH secretion rates are reduced, and the TSH response to TRH is decreased.

Despitenoormal peripheral TSH metabolism T3 and T4 production andiodide uptake by the thyroid are diminished. There are important structural changes in the thyroid gland and pituitary that are accompanied by marked alterations in their secretory activities. In the peripheral tissues, T4deiodination to T3 is decreased. Iodothyronines are insulin antagonist with high levels being diabetogenic, while absence of the hormone inhibits the development of diabetes. These situations may prevail in diabetics and would be aggravated in poorly controlled diabetics. Oxidative stress, which is associated withdiabetes, may also cause changes in the hypothalamus anteriorpituitaryaxis in diabetics.

In the present study, we found deceased T3 levels with significantly increased random blood glucose and HbA1c in type 2 diabetics. The level of TSH was significantly elevated in type 2 diabetics. The interaction between thyroid disorders and diabetes mellitus is a complex process. Low T3 state is described as low serum total and free T3 levels but near normal serum T4 and TSH concentrations. Low serum T3 is due to reduced peripheral conversion of T4 to T3. It is well known that insulin, an anabolic hormone enhances the levels of FT4 while it suppresses the levels of T3 by inhibiting hepatic conversion of T4 to T3. TRH synthesis decreases in diabetes mellitus and also there is loss of nocturnal TSH peak which is responsible for the occurrences of low thyroid hormone levels in some diabetics.

In the present study HbA1c was found to be significantly increased in patients with diabetes, and it was directly proportional to the bloodglucose levels. According to Kim et al., hypothyroidism falsely increases the HbA1c levels due to reduced erythropoiesis. Thyroid hormone replacement is associated with a decrease in HbA1c level, which is influenced by increased erythropoiesis rather than by changes in glucose level. It has recently been reported that T3 has an anti-apoptotic and protective effect on the pancreatic β-cells. T3 activates the PI-3 kinase pathway via thyroid hormone receptor on the β-cell, and stimulates insulin secretion. This may be related to an association between increased FT3 levels and decreased HbA1c i.e. low total T3. Our result of a positive correlation between HbA1c and TSH is consistent with the results by Velijasimi et al., They examined the effects of treatment of subclinicalhypothyroidism on metabolic control and hyperinsulinaemia and concluded that the correlation between TSH and HbA1c were positive and significant. Studies have reported that, there is increased prevalence of diabetics.
of thyroid dysfunction in diabetes mellitus patients, it is necessary to identify the people with greater risk like patients over 50 or 55 years of age, especially in clinically suspected patients or lipid abnormalities. So it is necessary to suggest that a testing of thyroid profile will help to analyze the development of hypothyroidism in patients with type 2 diabetes mellitus.

CONCLUSION

In this present study, we have observed that the abnormal thyroid hormone levels among type 2 diabetics. Failure to early identification of abnormal thyroid function may be a primary cause of poor management of diabetes mellitus. Therefore, there is a need for the routine assay of thyroid hormones in type 2 diabetics in order to improve the quality of life and reduce the morbidity. The study on a larger population will help to give further information about the relationship between the glycated hemoglobin and thyroid functions.

Conflict of Interest: Nil

Funding: Nil

Acknowledgement: Nil

REFERENCES
18. Kim MK, Kwon HS, Baek K, Lee JH, Park WC, Sohn HS, et al. Effects of thyroid hormone on


