Evaluation of thyroid profile status in case of type-2 diabetes mellitus in North Indian population

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ABSTRACT

Diabetes mellitus (DM) is a group of aetiologically different metabolic disorder characterized by hyperglycemia due to inadequate insulin secretion or defect in insulin action or both. There is strong correlation between DM and thyroid hormones. The aim of this study was to find out the association between hypothyroidism and type 2 diabetes mellitus in north Indian patients to evaluate the hyperglycemic effect by correlating fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c) and thyroid profile parameters. 50 type-2 DM patients and 50 controls were studied for their thyroid profile along with their fasting glucose levels and glycosylated hemoglobin (HbA1c). Analysis was performed by comparing the values with age and matched controls using student’s t test. Analysis showed that in type 2 diabetes mellitus patients and thyroid dysfunction prevalence rate in our study is high. Serum triiodothyronine (T3) and tetra-iodothyronine (T4) hormone concentrations were low and Thyroid Stimulating Hormone (TSH) concentrations were high in Type 2 DM when compared to controls. The T3 (p value <0.05), T4 and TSH (p value, <0.001) shows significant difference. FSG (p value, <0.05) also show significant correlations with thyroid profile parameters. Type 2 Diabetes Mellitus patients are at risk for hypothyroidism and hence have to be followed up with serum TSH levels. There was significant and inverse relation of HbA1c with thyroid hormone level whereas level of serum TSH was seen to have significant and direct relation with HbA1c. Insulin an anabolic
hormone metabolizes glucose enhances the level of freeT4 (FT4) while it suppresses the level of T3 by inhibiting hepatic conversion of T4 to T3. On the other hand some of the oral hypoglycemic agents such as the phenylthioureas are known to suppress the level of FT4 and T4, while causing raised levels of TSH.

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1. Introduction

Exiguobacterium was first described in 1983 by Collins et al. In 1994, Farrow et al. included the species formerly identified as Brevibacterium acetylicum incertae sedis into the genus Exiguobacterium, as E. acetylicum (Farrow et al., 1994). 11 new species have been added to the genus (Chaturvedi et al., 2008; Chaturvedi and Shivaji 2006; Crapart et al. 2007; Fruhling et al. 2002; Kim et al. 2005; Lopez-Cortes et al. 2006; Rodrigues et al. 2006; Yumoto et al., 2004). Exiguobacterium spp. These microorganisms have been detected in Siberian permafrost, temperate and tropical soils. have been isolated from, or molecularly detected in, a wide range of habitats including cold and hot environments with temperature range from -12 to 55 °C. The Exiguobacterium genus comprises psychrotrophic, mesophilic, and moderate thermophilic species and strains (Vishnivetskaya et al., 2005), with pronounced morphological diversity (ovoid, rods, double rods, and chains) depending on species, strain, and environmental conditions (Vishnivetskaya et al., 2007). Exiguobacterium acetylicum is a rhizospheric, Gram positive, rod shaped, yellow pigmented bacterium isolated Caspian Sea, on nutrient agar plates incubated at 4 °C. The strain was positive for siderophore and HCN production. In separate invitro assays it was found to inhibit the growth and development fungi and bacteria. As agricultural production has intensified over the past few decades, producers have become more dependent on agrochemicals,for plant disease management. The increased usage of such chemical in Diabetes Mellitus (DM) and thyroid dysfunction (TD) are the two most common metabolic and interrelated disorders in clinical practice (Hage et al., 2011). The total prevalence of DM is increasing and is projected to rise to 366 million worldwide in 2030, affecting 4-4% of all age groups. Today, an increase in prevalence is confirmed among individuals >65 years of age wild et a.,l 2004). Important factors contributed to diabetes are sedentary lifestyle, dietary modifications, ethnicity, hypertension and obesity especially in the 21st century (Mason et al., 1980). 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 1diabetes (Johnson 2006). 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 (Shah 2007) . 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. The association of the two endocrinal dysfunctions has been reported in different societies throughout the last two decades (Gloria-Bothini 2000). One way to assess the mean blood glucose levels is to monitor the HbA1c, which gives the average blood glucose level of the preceding 2-3 months. In uncontrolled or poorly controlled diabetes there is an increased glycosylation of a number of proteins, including hemoglobin and a-crystalline of the lenses. HbA1C was found to increase in patients with diabetes to approximately 16%, and the amount of increase was directly proportional to the fasting blood glucose level. During diabetes, the excess glucose present in blood reacts with hemoglobin (Sompson et al., 2002). In the present study, we noticed a marked increase in HbA1C levels in diabetic patients, which could be due to excessive glycosylation of hemoglobin.

2. Materials and Methods

One hundred cases of type 2 diabetes mellitus patients attending outdoor and indoor of medicine department, Indira Gandhi Institute of Medical Sciences, Patna, out of one hundred, fifty were taken as cases and fifty normal healthy subjects were taken as control. It was a cross sectional study conducted in the Department of
Biochemistry in collaboration with the Department of Medicine, during the period from Jan 2010 to March 2012. The inclusion criteria was duration of DM more than 7 months for patients with T2DM. Written informed consent for the study was obtained from all of the patients. Both case and control group had both male and female patient of 30 – 75 years of age group. Venous blood was collected from patient and control group after twelve hour fasting. Blood was taken in tubes containing fluoride oxalate, EDTA and plain tube for blood sugar, HbA1c and T3, T4, TSH estimation respectively. Blood sugar fasting (FBG) estimation was done within four hours by GOD-POD method. HbA1c was estimated using a fully automated clinical chemistry analyzer (Olympus AU-400). T3, T4 and TSH was estimated by chemiluminescence method of Access 2(Beckman Coulter, USA). The serum levels of T3 (normal range 0.87-1.8 ng/dl), T4 (normal range 5.5-12.2 μg/dl) and TSH (normal range 0.2-5.2 μIU/ml) FPG (normal range 70-110mg/dl), and HbA1c (normal range 4.2-6.2%). The following guidelines for detection of thyroid dysfunction were considered, 1) Normal – when FT3 FT4 T3, T4 and TSH were within the normal range. 2) Primary hypothyroidism – when TSH is more than 5.2 mIU/L and T3, T4 is less than the normal value. 3) Primary hyperthyroidism - when TSH is less than 0.2 mIU/L and FT4, FT3, T3, T4 is more than the normal values. 4) Subclinical hypothyroidism – when TSH is more than 5.2 mIU/L and FT3, FT4, T3, T4 is within the normal range. 5) Subclinical hyperthyroidism – when TSH is less than 0.2 mIU/L and FT3, FT4, T3, T4 are within the normal range.

2.1. Statistical analysis

The results obtained from the above investigation were analysed and expressed as mean ± SD. The comparison was done by student t test.

3. Results

Clinical and demographic data of the studied population are presented in Table 1. In our study, the TSH was significantly higher in diabetics than in non-diabetics (41.90 ± 29.60 mIU/mL vs 5.99 ± 1.77 mIU/mL, p<0.001). FBG and HbA1c were significantly higher in diabetic subjects as compared to non-diabetic subjects (p<0.001). T3 and T4 are also low in case of diabetics.

Table 1
Characteristics of non-diabetic and diabetic subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-diabetic subjects(Control)</th>
<th>Diabetic patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47 ± 7.0</td>
<td>51 ± 6***</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male 15</td>
<td>48.0±12</td>
<td>45±14.0</td>
</tr>
<tr>
<td>Female 35</td>
<td>47±15</td>
<td>49±17</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>94.6±10.4</td>
<td>170.8 ± 27.43***</td>
</tr>
<tr>
<td>Fasting (mg/dl)</td>
<td>5.27±0.37</td>
<td>7.70±0.79***</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>5.99±1.77</td>
<td>41.90 ± 29.60***</td>
</tr>
<tr>
<td>TSH</td>
<td>9.01±1.008</td>
<td>5.85±2.63***</td>
</tr>
<tr>
<td>T4</td>
<td>0.89±0.23</td>
<td>0.616±0.31**</td>
</tr>
</tbody>
</table>

**P<0.05, ***P<.0001.

4. Discussion

Hypothyroidism and diabetes mellitus are two endocrinal disorders associated with each other. Insulin resistance, an important factor in type 2 diabetes mellitus leads to production of free fatty acids, which activates the signaling enzyme protein kinase C, inhibits phosphatidylinositol-3 (PI-3) kinase (an endothelial Nitric oxide synthase agonist pathway), and increase the production of reactive oxygen species(ROS). This mechanism directly hinders nitric oxide (NO) production or decreases its bioavailability once produced (Libby et al., 1998) . In chronic hyperglycemia, there is non enzymatic glycation/oxidation of amino acids, lipid and lipoproteins. The formation of
advanced glycation end-products (AGEs) has long been recognized as a fundamental mechanism of cellular injury in diabetes. The accumulation of AGEs accelerates atherogenesis, increased vascular permeability, basement membrane thickening, increased extracellular matrix and mesangial fibrosis. This process leads the way to eventual glomerulosclerosis and renal failure (Salahudeen et al., 1992).

The association between DM and TD is widely known, with the first studies published in 1979 (Papazafiropoulou 2010). In this study we found that the level of TSH which changes in response to thyroid hormones was found significantly higher in diabetic group than control group. The level of these hormones was found significantly related to fasting blood sugar and glycated hemoglobin. Reduced glucose absorption from gastrointestinal tract accompanied by prolonged peripheral glucose accumulation; gluconeogenesis, diminished hepatic glucose output and reduced disposal of glucose are hallmarks of hypothyroidism (Suziki et al 1994). TRH synthesis decreases in diabetes, and this could be responsible for the occurrence of low thyroid hormone levels in diabetics (Smith et al., 1998). The abnormal thyroid hormone level may be due to various medications used by diabetes. Insulin an anabolic hormone enhances the level of FT4 while it suppresses the level of T3 by inhibiting hepatic conversion of T4 to T3. On the other hand some of the oral hypoglycemic agents such as the phenylthioureas are known to suppress the level of FT4 and T4, while causing raised levels of TSH (Whitley 1984).

5. Conclusion

Thus this study show high incidence of abnormal thyroid hormone level among type 2 diabetic in patients. Failure to recognize and poor management often encountered in some treated type 2 diabetics. The thyroid hormones directly control insulin secretion and thyroid function is intrinsically linked to insulin resistance, so the DM type-2 might be due to an insulin receptor inactivation or mutation in β-cells of pancreas. Our results confirm a higher prevalence of thyroid dysfunction (especially Primary hypothyroidism) in north Indian diabetic population compared to that healthy individual.

References