THYROID DYSFUNCTION IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS IN NORTHWEST RAJASTHAN, INDIA

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ABSTRACT

Objective: The prevalence of thyroid dysfunction in patients with type 1 diabetes is two to threefold higher than in the general population and occurrence of thyroid dysfunction is often diagnosed late in type 1 diabetic population. Our aim is to determine the natural history of thyroid dysfunction in Indian patients with type 1 diabetes.

Methods: Sixty type 1 diabetic patients were recruited in the study from the diabetic clinic attached with S.P. Medical College, Bikaner. In addition to clinical assessment of all patients, determinations were made of thyroid function tests (thyroid stimulating hormone [TSH], thyroxine [T4] and triiodothyronine [T3]) and thyroid peroxidase (TPO) antibodies.

Results: Out of 60 type 1 diabetic patients, a total of 8 patients had hypothyroidism and 1 patient had hyperthyroidism. 1 patient having hypothyroidism before the onset of diabetes was excluded from the study. The mean age at diagnosis was 13±7.5 yrs for type 1 diabetes and 15±9.4 yrs for hypothyroidism. Hypothyroidism was more common in female 6/59 (10.2%) than in male subjects 2/59 (3.39%) and in patients with positive TPO antibodies. There was no difference in BMI, HbA1c, lipid profile, insulin level and c-peptide between patients with/without thyroid dysfunction.

Conclusions: The present study indicates that each child with type 1 diabetes, apart form diabetes control, should undergo regular screening of serum TSH measurements to detect asymptomatic thyroid dysfunction, particularly those with positive TPO antibodies.

INTRODUCTION

Type 1 diabetes is a heterogeneous autoimmune disease and is frequently associated with other organ-specific autoimmune diseases, including thyroid disease. Thyroid disorders are highly prevalent in the general population (Wang et al., 1997). Thyroid function tests might be affected by diabetes and obesity. Cross-sectional study has reported that 7.5% of women and 2.8% of men of all ages have abnormal serum thyroid-stimulating hormone (TSH) levels (Tunbridge et al., 1977). The Colorado Thyroid Disease Prevalence Study reported that among 25,862 subjects attending a state-wide health fair, 11.7% of subjects had an abnormal serum TSH concentration. Primary hypothyroidism (TSH >5.1 mU/l) was detected in 9.5% and hyperthyroidism in 2.2% of subjects, most of whom were asymptomatic (Canaris et al., 2000). The prevalence of thyroid dysfunction increases with advancing age and in subjects with thyroid antibodies (Parle et al., 1991). The Third National Health and Nutrition Examination Survey (NHANES III), from a sample of 17,353 people aged ≥12 years representing the geographic and ethnic distribution of the United States population, reported a prevalence of hypothyroidism in 4.6% (0.3% clinical and 4.3% subclinical) and hyperthyroidism in 1.2% (0.5% clinical and 0.7% sub clinical) (Hollowell et al., 2002). The prevalence of thyroid dysfunction increased from 5-8% during the 3 years follow up period (Hansen, 2003).

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as evidence by deficient C-peptide secretion <$0.6ng/ml, age <30 years and the absence of hypertension, hypercholesterolemia and diabetic ketoacidosis. Out of screened 60 type 1 diabetic patient, 1 patient having hypothyroidism before the onset of diabetes was excluded from the study. In addition to monitoring their glycemic control and diabetic complications, all patients had thyroid function test (TSH, thyroxine (T4) and triiodothyronine (T3)). The presence of TPO antibodies was also determined.

**Table 1. Clinical, biochemical and immunological characteristics of patients with type 1 diabetes with or without hypothyroidism**

<table>
<thead>
<tr>
<th></th>
<th>With Hypothyroidism</th>
<th>Without Hypothyroidism</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>8</td>
<td>51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>2/6</td>
<td>31/20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>17±5.2</td>
<td>17±4.4</td>
<td></td>
<td></td>
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<tr>
<td>Glycemia (mg%)</td>
<td>198±36.4</td>
<td>212±40.3</td>
<td>0.28</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.8±1.3</td>
<td>8.1±0.9</td>
<td>0.19</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>C-peptide levels (ng/ml)</td>
<td>0.18±0.13</td>
<td>0.21±0.17</td>
<td>0.14</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>Insulin dose (U/kg)</td>
<td>0.68±0.20</td>
<td>0.61±0.24</td>
<td>0.29</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>TSH mu/l</td>
<td>8±2.6</td>
<td>1.6±0.4</td>
<td>2.45</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>TPO antibodies in (n%)</td>
<td>5(62.5)</td>
<td>3(37.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, diabetes onset (yrs)</td>
<td>13±7.5</td>
<td>14±8.4</td>
<td>0.8</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>Age, Hypothyroidism yrs</td>
<td>15±9.4</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time between onset of diabetes and hypothyroidism</td>
<td>3±2.1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Data are mean ± SE

**DISCUSSION**

The present study shows that 13.5% patients had thyroid dysfunction in type 1 diabetes. An association between diabetes and thyroid disease has long been recognized, although the reported prevalence of thyroid dysfunction in diabetic populations varies widely between studies (Gray et al., 1973; Perros et al., 1995; and Radetti et al., 1995). Cross-sectional studies have reported a prevalence of hypothyroidism in 12-24% of female and <6% of male patients with type 1 diabetes, as well as in 3-6% of type 2 diabetic patients (Perros et al., 1995; Gray et al., 1979). The NHANES III reported a prevalence of hypothyroidism in 4.6% (0.3% clinical and 4.3% subclinical) and hyperthyroidism in 1.2% (0.5% clinical and 0.7% subclinical) and positive TPO antibodies in 13% of the United States population (Hollowell, 2002). Age, sex, time of evolution of diabetes, genetic back ground and period of follow up can explain the difference across studies. This prospective study also provides good evidence of the association between autoimmune hypothyroidism and type 1 diabetes.

Population screening for thyroid dysfunction may prevent the development of overt thyroid dysfunction and may allow early treatment of hyperlipidemia (Hollowell, 2002), prevention of associated cardiovascular complications (Geul et al., 1993 and Hak et al., 2000) and metabolic bone disorders (Greenspan, 1999). The American College of Physicians recently published guidelines on screening for thyroid disease with a sensitive TSH test in the primary care setting (Helfand and Redfern, 1998). Dietary carbohydrates content had an influence on the magnitude of fall in serum T3 (Mathieson et al., 1986). A confounding effect of some of these factors is difficult to be excluded as there were some differences in sex distribution, age and clinical presentations. Some effects of the study method deserve further comments. TPO can be assessed by agglutination and radio immunoassay.
It is generally accepted that both are sensitive, specific and well connected (Hay and Klee, 1988). In the present study, we observed 1.6% prevalence of hyperthyroidism. The prevalence of hyperthyroidism varied from 0.5% to 3% in patients with type 1 diabetes (Perros et al., 1995 and Araujo et al., 2008). The reason for the different prevalence of hyperthyroidism case in our study is not known but may relate to the relatively small number of subjects and/or to the more defined population of patients with type 1 diabetes included in this study.

The presence of TPO antibodies was associated with an increased risk of hypothyroidism. Out of 8 TPO antibodies positive subjects (62.5%) were found with hypothyroidism. In a survey, the use of TPO to predict hypothyroidism was found to have a 67% positive predictive value (Hay and Klee, 1988). TPO positive patients were 17.91 times as likely to develop hypothyroidism as TPO negative patients (Guillermo E. Umpierrez, 2003). A total of 18 (33%) patients had positive TPO antibodies (8 men and 10 women). In one recent study, 72% TPO antibodies positive patients developed thyroid dysfunction indicating strong association of TPO antibodies with increased risk of hypothyroidism (Gemma C Gonzalez, 2007). Biochemical thyroid dysfunction and thyroid autoimmunity were evident in type 1 diabetics who were apparently euthyroid hence thyroid function tests are recommended in order to minimize the risk of undiagnosed hypothyroidism in these patients.

REFERENCES


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