LETTER TO THE EDITOR

Increased frequency of subclinical hypothyroidism and thyroid-associated antibodies in siblings of children and adolescents with type 1 diabetes mellitus

A Mohn, S Di Michele, R Faricelli, S Martinotti and F Chiarelli
Department of Paediatrics and 1Department of Clinical Pathology, University of Chieti, Chieti, Italy

(Correspondence should be addressed to A Mohn; Email: amohn@unich.it)

In recent years, it has been well established that early detection of thyroid autoimmunity or disease in children is important, leading to the idea of treating patients with subclinical hypothyroidism in the presence of high serum thyroid antibody, as progression to overt hypothyroidism is common (1). Furthermore, thyroxine replacement therapy started early in patients with subclinical hypothyroidism reduces the risk of hyperlipidemia and atherosclerotic heart disease (2). Disease-associated autoantibodies can be easily used as a tool to identify patients at increased risk of progression to clinical thyroid dysfunction. Because siblings of patients with type 1 diabetes mellitus (T1DM) share the HLA-risk alleles, we asked whether they might be at increased risk of thyroid autoimmunity and disease.

Therefore, screening for thyroid-correlated antibodies, together with thyroid function testing, was offered to siblings of children and adolescents with T1DM. We excluded siblings of diabetic patients with thyroid autoimmunity or disease. As a control group, we also analyzed sera from healthy children and adolescents matched for age and sex without a family history of autoimmune disease. All children were Caucasian from the Abruzzo region of Italy. Written, informed consent was obtained from the parents of all children and adolescents before entry to the study.

A single blood sample was taken for thyroid function testing (thyroid-stimulating hormone (TSH) and free thyroxine (FT4)) and antibodies to thyroglobulin (TG) and to thyroid peroxidase (TPO).

Thyroid hormone levels were determined by double-antibody radioimmunoassay. Normal basal values for our laboratory were 6–18 pg/ml for FT4 and 0.3–4.1 μU/ml for TSH. Antibodies to TG and TPO were quantitated by ELISA. A titer exceeding 100 IU/ml was considered positive. Patients with positive thyroid antibodies were considered to be affected by autoimmune thyroiditis with subclinical hypothyroidism when increased serum TSH (>5 μU/ml) concentration with normal FT4 values was found.

The screening was performed in 123 siblings (67 M, 56 F) out of 151 (70 M, 81 F) aged 9.2±4.5 years. These children were matched with 140 control subjects (81 M, 59 F) aged 9.2±3.8 years (Table 1). The data were evaluated statistically by Fisher’s exact probability test with SPSS, Version 10.0 (SPSS, Chicago, IL, USA).

Among the group of siblings, nine children (4 M, 5 F) tested positive for antibodies to TG (mean 358 IU/ml, range 108–761) and to TPO (mean 758 IU/ml, range 100–1982). Three of these children presented subclinical hypothyroidism: two adolescent girls (TSH, 9.5 and 7.64 μU/ml; FT, 4.7 and 12 pg/ml respectively) and a 6-year-old boy (TSH, 8.45 μU/ml; FT, 4.8 pg/ml). These three children were started on treatment with L-thyroxine. In the control group, two girls aged 8.8 and 9.8 years respectively presented antibodies to TG (mean 107 IU/ml, range 88–126) and to TPO (mean 181 IU/ml, range 150–202) (P = 0.01) with normal thyroid function.

Table 1 Frequency of autoimmune phenomena in siblings of T1DM patients compared to controls without family history of T1DM.

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<tr>
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<th>Siblings</th>
<th>Controls</th>
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<tr>
<td>Cases</td>
<td>123 (67 M, 56 F)</td>
<td>140 (81 M, 59 F)</td>
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<tr>
<td>Thyroid disease-associated antibodies</td>
<td>9 (7.3%)</td>
<td>2 (1.4%)</td>
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<tr>
<td>Subclinical hypothyroidism</td>
<td>3 (2.4%)</td>
<td>0</td>
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Despite the relatively small number of subjects, this cross-sectional study highlights that siblings of patients with T1DM present a frequency of 7% of thyroid-associated antibodies, which is significantly higher than in normal controls and is in line with previous studies (3–5). Furthermore, in our population, we detected an increased frequency of thyroid dysfunction, which is less common, as routine screening for siblings of diabetic patients is usually not performed (6). Although the adolescent girls might have been diagnosed by a thorough clinician, which reflects the occurrence within the general population, the boy was at high risk.
risk of remaining undetected for a long time. This small study demonstrates that clinicians should be highly aware of the possibility of thyroid dysfunction in this population, and early diagnostic procedures should be performed, especially in consideration of the well-documented long-term complications of undiagnosed hypothyroidism.

References


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