Prevalence of Autoimmune Diseases among Type 1 Diabetes Mellitus in Saudi Arabia

MOSLEH JABARI, M.D. 1; ABDULLAH AL-FARIS, M.D. 2; MOHAMMED AL-SAYED, M.D. 2; SULTAN A. AL-MEDHESH, M.D. 3; NASSER AL-SOBAIE, M.B.B.S. 4; ABDULLAH AL-ORAINI, M.B.B.S. 4 and HASSAN AL-SHEHRI, M.D. 1

The Department of Pediatrics, College of Medicine, Al-Imam Mohammad Ibn Saud Islamic University 1, Security Forces Hospital 2, Riyadh and College of Medicine, Najran University, Najran 3 and College of Medicine, Al-Imam Mohammad Ibn Saud Islamic University, Riyadh 4, Saudi Arabia

Abstract

Objective: To find out the prevalence of thyroid dysfunction and celiac disease among Type 1 Diabetes Mellitus (T1DM) patients in Riyadh, Saudi Arabia.

Material and Methods: A retrospective hospital-based study included 536 T1DM children at the “Security Force Hospital”, in Riyadh, Saudi Arabia during the period from September 2001 to June 2015.

Results: Out of 536 patients, 11 (2.1%) were diagnosed as “overt hypothyroidism”, and 124 (23.1%) were diagnosed as “subclinical hypothyroidism”. In addition, 101 (19%) patients had endomysial antibodies (EMA). Of these patients with positive EMA, 32.7% had histological changes in their small bowels. Presence of histological changes was significantly higher among those with high EMA serum levels than those with low levels.

Conclusions: Prevalence of autoimmune diseases, e.g., autoimmune thyroiditis and celiac disease, are relatively high among patients with T1DM in Riyadh, Saudi Arabia. This high prevalence is associated with several biochemical changes, mainly in the form of antibodies production.

Key Words: Type 1 diabetes mellitus – Hypothyroidism – Celiac disease – Thyroid peroxidase antibodies – Endomysial antibody – Thyroid function tests.

Introduction

TYPE 1 Diabetes Mellitus (T1DM), is a common autoimmune endocrine disease among children [1], with an increasing incidence worldwide [2]. Prevalence of T1DM in Saudi Arabia among children is 109.5 per 100,000 [3].

Different genetic, immunological and environmental factors contribute to activation of T-cell mediated autoimmune reaction against insulin producing β-cells in the pancreas [4]. T1DM is strongly believed to be one of the autoimmune associated diseases, which include hypothyroidism, celiac disease, addison disease, vitiligo and autoimmune hemolytic anemia [5].

The most common associated disease with T1DM is Hashimoto’s thyroiditis [6]. Prevalence of celiac disease among patients with T1DM is about 20 times higher than in the general population, with almost 60% of cases being already present at diabetes onset, but mostly undetected. An additional 40% of patients develop celiac disease after few years of T1DM diagnosis [7].

The relatively high frequency of development of autoimmune diseases in patients with T1DM may be due to multiple immunologic abnormalities. Lymphocytes and macrophages, of the organ, with impaired activity of the organ by atrophy are major characteristics of most organ-specific autoimmune diseases. The majority of organ-specific autoimmune diseases are characterized by this progressive autoimmune process [8].

Antibodies against specific antigen are detectable in blood before the clinical onset of the specific disease. Therefore, they may be considered as disease markers [9]. Thus, routine screening for T1DM patients for autoimmune diseases, especially thyroid diseases and celiac disease, has been recommended [10].

This study aimed to find out the prevalence of thyroid dysfunction and celiac disease among T1DM patients.

Correspondence to: Dr. Hassan Alshehri, E-Mail: dr.h.alshehri@hotmail.com
Patients and Methods

This is a retrospective record-based study, that included children who were diagnosed as T1DM during the period from September 2001 till June 2015 in the "Pediatric Endocrinology" Clinic at the “Security Force Hospital” in Riyadh, Saudi Arabia.

The study sample included 536 T 1 DM patients who were diagnosed before the age of 12 years. All patients were screened to identify presence of autoimmune thyroid dysfunction and celiac disease.

All T 1 DM patients were screened for thyroid dysfunction by testing for Thyroid Peroxidase Antibody (TPOAb), serum level of Thyroid Stimulating Hormone (TSH) and Free Thyroxin index (FT4) in the blood. The diagnosis of subclinical autoimmune thyroiditis was based on high levels of TSH (more than 5 IU/L), associated with normal FT4, while clinical hypothyroidism was based on high levels of TSH (more than 5mU/L) associated with low FT4 levels (<1 1pmol/L) [11].

Serological screening for celiac disease included Endomysial Antibodies (EMA). If EMA were detected, the diabetic child was referred for endoscopy, where biopsy specimens were taken through upper gastrointestinal endoscopy to detect small bowel mucosal damage.

This study was approved by the Ethical and Research Committee at the “Security Force” Hospital and the College of Medicine in “Imam Mohammed Ibn Saud” University, Riyadh, Kingdom of Saudi Arabia.

Results

Table (1) shows that 53.5% of our T1DM patients were females. At the time of admission, 20 patients (3.7%) were less than 2 years of age, 168 patients (31.3%) aged 2-5 years; 257 patients (47.9%) aged 6-10 years; and 91 patients (17%) aged more than 10 years.

Table (2) shows that 135 T1DM patients (25.2%) had high TSH serum levels (>5 IU/L), 15 patients (2.8%) had low FT4 serum levels (<1 1 pmol/L), while 19 patients (3.5%) had high FT4 serum levels (>22 pmol/L). TPOAb were detected in 226 patients (42.2%).

Table (3) shows that 11 patients (2.1%) had “overt hypothyroidism” (i.e., low FT4 and high TSH serum levels), while 124 patients (23.1%) had “subclinical hypothyroidism” (i.e., normal FT4 and high TSH serum levels). FT4 serum levels differed significantly according to TSH serum levels (p<0.001). TPOAb were significantly more prevalent among T 1 DM patients with higher TSH serum levels than those with normal TSH serum levels (13.6% and 11.6%, respectively, p=0.002).

Table (1): Personal characteristics of study sample.

<table>
<thead>
<tr>
<th>Personal characteristics</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: Male</td>
<td>249</td>
<td>44.2</td>
</tr>
<tr>
<td>Female</td>
<td>287</td>
<td>53.5</td>
</tr>
</tbody>
</table>

Table (2): Laboratory investigations performed to type 1 diabetes mellitus patients.

<table>
<thead>
<tr>
<th>Laboratory investigations</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH serum level:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (up to 5 IU/L)</td>
<td>401</td>
<td>74.8</td>
</tr>
<tr>
<td>High (&gt;5 IU/L)</td>
<td>135</td>
<td>25.2</td>
</tr>
<tr>
<td>FT4 serum level:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (&lt;11pmol/L)</td>
<td>15</td>
<td>2.8</td>
</tr>
<tr>
<td>Normal (11-22pmol/L)</td>
<td>502</td>
<td>93.7</td>
</tr>
<tr>
<td>High (&gt;22pmol/L)</td>
<td>19</td>
<td>3.5</td>
</tr>
<tr>
<td>Thyroid peroxidase antibody (TPOAb):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>310</td>
<td>57.8</td>
</tr>
<tr>
<td>Positive</td>
<td>226</td>
<td>42.2</td>
</tr>
</tbody>
</table>

Table (3): Levels of serum FT4 and Thyroid Peroxidase Antibodies (TPOAb) according to TSH serum levels among type 1 diabetes mellitus patients.

<table>
<thead>
<tr>
<th>Laboratory findings</th>
<th>Normal</th>
<th>High</th>
<th>Total</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>FT4 levels:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>4</td>
<td>0.7</td>
<td>11</td>
<td>2.1</td>
</tr>
<tr>
<td>Normal</td>
<td>378</td>
<td>70.5</td>
<td>124</td>
<td>23.1</td>
</tr>
<tr>
<td>High</td>
<td>19</td>
<td>3.5</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>TPOAb:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>248</td>
<td>46.3</td>
<td>62</td>
<td>11.6</td>
</tr>
<tr>
<td>Positive</td>
<td>153</td>
<td>28.5</td>
<td>73</td>
<td>13.6</td>
</tr>
</tbody>
</table>
Table (4): Presence of histological changes according to Endomysial Antibodies (EMA) serum levels among type 1 diabetes mellitus patients.

<table>
<thead>
<tr>
<th>EMA Serum levels</th>
<th>No histological changes</th>
<th>Histological changes</th>
<th>Total (n=536)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>70U/mL</td>
<td>46</td>
<td>92.0</td>
<td>4</td>
</tr>
<tr>
<td>&gt;70U/mL</td>
<td>22</td>
<td>43.1</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>66.3</td>
<td>33</td>
</tr>
</tbody>
</table>

p<0.001.

Discussion

This study showed that more than half of our patients (53.5%) were females. This finding is in agreement with that of [12], who stated that a female excess of diabetic children is present in populations of African or Asian origin [12].

This study showed that Thyroid Peroxidase Antibodies (TPOAb) were detected in 226 patients (42.2%). TPOAb were significantly more prevalent among patients with higher TSH levels than those with normal levels. Moreover, prevalence of thyroid dysfunction among our T1 DM children was relatively high, where 11 (2.1%) had overt hypothyroidism and 124 patients (23.1%) patients had subclinical hypothyroidism.

These findings are in agreement with those of several studies. Hanukoglu et al., [13], reported that T1DM patients have higher risk for the development of autoimmune diseases, as compared with the general population. Silent and latent forms of these autoimmune-associated diseases, are characterized by the presence of circulating autoantibodies with mild or no symptoms with or without morphological abnormalities. Al-Jurayyan [8] added that thyroid dysfunction has been noted as the most common associated disease in T 1 DM patients. Holl et al., [14] reported that subclinical hypothyroidism has been reported in up to 58% of patients with thyroid autoantibodies.

Aljabri et al., [15] explained that the high frequency of development of autoimmune disease in T 1 DM patients may be due to multiple immunologic abnormalities. More than 30% of T1DM patients have other antibodies that attack other organs, such as small bowel that may cause celiac disease and the thyroid glands that may cause hypothyroidism.

Results of the present study showed that 19% of our patients had anti-Endymesial Antibodies (EMA), with manifest histological changes in the small bowel only among 32.7% of those with EMA. Presence of histological changes was significantly higher among those with high EMA serum levels.

These findings are in accordance with those of Saada et al., [16], in Saudi Arabia, who reported that, with biopsy of the small bowel as the gold standard for diagnosis, up to 12% of their T1DM patients had celiac disease.

In conclusion, prevalence of autoimmune diseases, e.g., autoimmune thyroiditis and celiac disease, are relatively high among patients with T 1 DM in Riyadh, Saudi Arabia. This high prevalence is associated with several biochemical changes, mainly in the form of antibodies production. Regular screening of children with T1DM for autoimmune diseases is recommended. Further studies are needed to investigate prevalence of other autoimmune disorders among T1DM patients.

References

7- BARERA G., BONFANTI R., VISCARDI M., et al.: Occurrence of Celiac Disease after onset of type 1 diabetes:
الملخص العربي

هدف البحث: معرفة مدى انتشار خلل وظائف الغدة الدرقية ومرض الاضطرابات الهمضية (مرض سيلياك) بين مرضى النوع الأول من داء السكري في مدينة الرياض بالمملكة العربية السعودية.

منهجية البحث: تم عمل دراسة بطرقية من خلال مراجعة بيانات 386 مريضاً مصاباً بالنوع الأول من داء السكري خلال الفترة من سبتمبر 2000 إلى يونيو 2015، في مستشفى قرى الآمن في الرياض بالمملكة العربية السعودية.

النتائج: تم تشخيص 11 مريضاً (2.1%) بقصور الغدة الدرقية دون السريرية، بالإضافة إلى ذلك كان لدى 101 مريضاً (19%) أجسام مضادة (EMA) لتيتريتاس النسيجية في الأمعاء الدقيقة. وقد لوحظ وجود تغيرات نسيجية بشكل أكبر بين المرضى الذين لديهم مستويات مترتفعة من المصل. شنнии مقارنة بنم ديهم مستوى منخفضة.

الاستنتاج: إن معدلات انتشار أمراض المناعة الذاتية، ومنها على سبيل المثال التهاب الغدة الدرقية المناعية ومرض الاضطرابات الهمضية (مرض سيلياك)، مرتفعة نسبياً بين مرضى النوع الأول من داء السكري، وترتبط نسبة الانتشار هذه مع العديد من التغيرات البيوكيميائية التي غالباً ما تكون مصحوبة بزيادة في إنتاج الأجسام المضادة.