Prevalence and characteristics of celiac disease in type I diabetes mellitus in Saudi Arabia

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ABSTRACT

Objective: To examine the prevalence of celiac disease in young patients in the Kingdom of Saudi Arabia with type I diabetes mellitus.

Methods: Serum gliadin immunoglobulin (Ig) A and reticulin IgA antibody determination was performed in 123 patients with type I diabetes mellitus attending the pediatric diabetic clinic at King Faisal Specialist Hospital and Research Centre, Riyadh, Kingdom of Saudi Arabia between 1995 and 1996.

Results: Elevated serum gliadin and reticulin IgA antibodies were found in the sera of 10 (8.1%) of the 123 diabetic children; none had gastrointestinal symptoms. Six of the 10 subjects had jejunal biopsy, which showed total villus atrophy. Four subjects did not undergo jejunal biopsy. The gender ratio of the biopsy positive is 5 male:1 female. All subjects with IgA positive were put on gluten free diet and normalized in a few months.

Conclusion: The maximum prevalence of celiac disease in our population was 8.1% based on immunological marker and the minimum was 4.9% based on antibodies and biopsy results.


The relationship between type I diabetes mellitus and celiac disease (CD) has been known for almost half a century,1 more reports since then have appeared in the literature.2-7 Prevalence of CD is between 1.4% and 11.1% among diabetic children, but the prevalence in the Kingdom of Saudi Arabia (KSA) has not been determined. To address this issue, gliadin and reticulin antibodies8-12 were measured in all children attending the diabetes clinic at King Faisal Specialist Hospital and Research Centre (KFSH&RC), Riyadh, KSA and where possible, positive results were confirmed by jejunal biopsy. It is noteworthy that none of our cases of type I diabetes mellitus and CD have gastrointestinal symptoms; only one child presented with growth failure.

Methods. Subjects. The subject population included all 123 patients with type I diabetes mellitus that were followed in the Pediatrics Diabetes Clinic at KFSH&RC in 1995 and 1996. There were 69 males and 54 females who ranged in age from 2-33 years (mean ± SD 10 ± 4). The age at onset of type I diabetes mellitus was between 0.4 and 12 years (7 ± 3) and the duration of type I diabetes mellitus was between 0.2 and 15 years (8 ± 3).

Procedures. Blood for determination of gliadin and reticulin antibodies were obtained during routine clinic visits on an annual basis and antibody positive patients were encouraged to undergo jejunal biopsy to confirm the diagnosis. Jejunal biopsy specimens were obtained...
Celiac disease with diabetes in Saudi Arabia ... Al-Ashwal et al

using pediatric size Crosby capsule and examined histologically by the local pathologist at KFSH&RC.

**Analyses.** Gliadin immunoglobulin (Ig) A antibodies were determined by the gluten IgA enzyme immunoassay test (Pharmacia Diagnostics AB, Uppsal, Sweden) which is a solid phase enzyme immunoassay. Estimation of gliadin antibody was carried out according to the manufacturers instruction, as directed by Ascher et al. The test has high sensitivity (91-97%) and specificity (92-98%) for villous atrophy. Reticulin antibodies (Type R1) were measured using an indirect immunofluorescent method according to Maki et al. Serum titers diluted equal to or more than 1:40 were considered positive. The method also has high sensitivity (97%) and specificity (98%) for villous atrophy.

**Results.** Elevated gliadin IgA levels were found in the sera of 10 (8.1%) of 123 diabetic children in our clinic. Clinical description and test results in the 8 males and 2 females are shown in Table 1. None had any gastrointestinal symptoms. Six of the 10 subjects had jejunal biopsies and all biopsies showed total villous atrophy, biopsy was not carried out in the other 4 subjects. All 10 patients who were gliadin IgA positive were put on a gluten-free diet; all normalized their gliadin IgA levels within a few months. Figure 1 shows the growth curve of one of the patients in our group (patient 4). She was diagnosed with type I diabetes mellitus at 5 years of age and already had severely stunted growth, but no gastrointestinal symptoms. Physical examination was, otherwise, normal and laboratory studies failed to reveal an underlying cause for short stature. Although her diabetes was controlled, as indicated by normal hemoglobin A1C levels, height and weight velocities remained below normal at 2-3 cm and 1-3 kg per year. Celiac disease was finally diagnosed at 10 years of age and gluten-free diet initiated. Diagnosis and treatment of CD in this patient led to a substantial increase in growth rate (Figure 1).

**Discussion.** Type I diabetes and CD are parts of polyglandular autoimmune disease, Type II cluster that includes thyroid, adrenal and other autoimmune disease. The association between type I diabetes mellitus and CD is not surprising, since both conditions have an increase frequency of human leukocyte antigen (HLA)-DR3 and other HLA number. Although CD occasionally precedes the onset, type I diabetes mellitus is diagnosed before CD in the great majority of patients,

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**Table 1 - Antibody level and histological finding of intestinal biopsy.**

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Sex</th>
<th>Onset of type 1 diabetes mellitus (years)</th>
<th>Age at diagnosis of celiac disease (years)</th>
<th>Gliadin immunoglobulin A</th>
<th>Reticulin immunoglobulin A</th>
<th>Biopsy Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>2</td>
<td>3.4</td>
<td>290</td>
<td>Positive</td>
<td>Total villous atrophy</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>9.5</td>
<td>13</td>
<td>49</td>
<td>Negative</td>
<td>Not done</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>1.4</td>
<td>1.8</td>
<td>106</td>
<td>Negative</td>
<td>Not done</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>5</td>
<td>10</td>
<td>230</td>
<td>Positive</td>
<td>Total villous atrophy</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>7.5</td>
<td>9</td>
<td>210</td>
<td>Positive</td>
<td>Total villous atrophy</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>3</td>
<td>12.5</td>
<td>45</td>
<td>Negative</td>
<td>Not done</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>9</td>
<td>11</td>
<td>190</td>
<td>Positive</td>
<td>Total villous atrophy</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>10</td>
<td>10.2</td>
<td>56</td>
<td>Negative</td>
<td>Not done</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>12</td>
<td>12.3</td>
<td>175</td>
<td>Positive</td>
<td>Total villous atrophy</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>2.3</td>
<td>2.4</td>
<td>170</td>
<td>Positive</td>
<td>Total villous atrophy</td>
</tr>
</tbody>
</table>
as was the case in all our patients. The reported prevalence of CD in patients with type I diabetes mellitus has varied widely in different populations, ranging from 1.2% in Finland to 11.1% in Italy.

In our survey of Saudi children attending the Pediatrics Diabetes Clinic at KFSH&RC, we found 10 of the 123 patients positive for gliadin antibodies. Four of our gliadin antibody positive patients did not undergo biopsy; whereas total villous atrophy was confirmed in all 6 who underwent jejunal biopsy.

Although gliadin antibodies are very sensitive markers for the presence of clinical CD, it is possible that some patients were antibody positive, without having frank disease. These patients could have latent diseases and need to be closely followed up. The maximum prevalence of CD in our population was 8.1%, based on immunologic findings and the minimum prevalence was 4.8%, based on antibody and biopsy results.

The usefulness of screening for CD in diabetic children, even without gastrointestinal symptoms is illustrated by the impaired growth demonstrated by patient 4 in our study. Celiac disease is an important cause of short stature in children with, and without, diabetes. While delayed growth is likely to be related to malabsorption, low growth hormone, and insulin-like growth factor levels have been reported. It is also important to repeat gluten antibody determination over time, because a single negative result does not exclude the development of the disease later. It is highly recommended based on our experience and others that all patients with type I diabetes should be screened routinely even if they do not have any gastrointestinal symptoms.

References