OBJECTIVE — To evaluate the prevalence of \( \beta \)-cell autoimmunity and the usefulness of a type 1 diabetes screening in patients with celiac disease.

RESEARCH DESIGN AND METHODS — We measured GAD antibodies (GADAs), insulinoma-associated protein 2 antigens (IA-2As), and insulin autoantibodies (IAAs) in 188 young Italian patients with celiac disease (66 male [35.1%]). Mean age at celiac disease diagnosis was 5.4 years (0.5–17.1), and mean celiac disease duration was 4.2 years (0–28.8). Celiac disease was diagnosed by jejunal biopsy after positivity for endomysial and tissue transglutaminase antibody was confirmed.

RESULTS — GADAs were positive in seven patients (3.7%), and IA-2As were positive in two patients. IAAs were negative in all cases. Metabolic evaluation was normal, and no patients developed diabetes during follow-up. There was no significant association among \( \beta \)-cell autoimmunity and sex, age, pubertal stage, family history, or coexistence of other autoimmune disorders, compliance to a gluten-free diet was confirmed.

CONCLUSIONS — Our results showed a low prevalence of \( \beta \)-cell autoimmunity and do not support a precocious screening for \( \beta \)-cell autoimmunity in young celiac disease patients.

\( \beta \)-Cell Autoimmunity in Pediatric Celiac Disease: The Case for Routine Screening?

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found HLA-DQ2 in six cases, HLA-DQ8 in one case, and HLA-DQ2/DQ8 in one case. Among the remaining 72 patients without β-cell autoantibodies, we found HLA-DQ2 in 69 cases, HLA-DQ8 in two cases, and HLA-DQ2/DQ8 in one case.

**CONCLUSIONS** — A low prevalence of diabetes-related antibodies in celiac disease patients was observed, as well as no association with other autoimmune disorders. In adults, celiac disease is associated with several autoimmune disorders (mostly type 1 diabetes and thyroid diseases). Otherwise, in pediatric celiac disease patients, the rate and significance of diabetes-related antibodies yielded conflicting results (7).

Di Mario et al. (8) evaluated IAAs and islet cell antibodies (ICAs) in children with newly diagnosed celiac disease on a gluten-containing diet, in those with long-standing celiac disease following GFD, and in control groups and raised the question as to whether they are predictive of subclinical diabetes or whether they are indicators of a general autoimmune disease. Karagiozoglou-Lampoudi et al. (9) reported no positivity for ICA in pediatric celiac disease patients. Galli-Tsinopoulou et al. (10) showed GADA and IA-2A in 23% of celiac disease patients and recommended screening for β-cell autoimmunity.

In a retrospective study of 90 young Italian patients with celiac disease, the prevalence of diabetes-related autoantibodies was 11.1% and related to gluten exposure (7). Similarly, in an Italian large case series of adult celiac disease patients, a high prevalence (9%) of one diabetes-related autoantibody (ICA, IA-2A, or GADA) was observed independently of GFD compliance (11). Despite this high rate of diabetes-related autoimmunity, no incident cases of diabetes were reported, supporting the role of common genetic susceptibility to both diseases and factors involved in gut permeability (7).

Conflicting data about prevalence of diabetes-related autoantibodies in celiac disease patients could be due to the improvement of laboratory methods, which excluded false-positive data. In young celiac disease patients, the length of gluten exposure could influence the development of other autoimmune disorders (7). Bonamico et al. (12) reported at least one endocrine-related serum autoantibody (either ICA or anti-thyroid microsomal antibody) in 50% of adolescents with undiagnosed celiac disease but in only 12% of celiac disease patients on GFD, suggesting that these autoantibodies could be partly gluten dependent.

Abnormal regulation of intestinal permeability and increased autoantibody production in the setting of chronic gut inflammation are trigger factors for the development of autoimmune response (12). Recent evidence suggests that gluten-induced upregulation of zonulin, an intestinal peptide involved in the regulation of gut tight junctions, could be responsible for the aberrant increase in gut permeability otherwise found in type 1 diabetes (13). The gut immune system includes the majority of the total lymphoid tissue in humans; therefore, a detrimental response to dietary components would have repercussions throughout the organism, carried either by immune cells or immune mediators released from the gut (14).

Laadhar et al. (4) did not find differences in prevalence of β-cell autoantibodies between children with newly diagnosed celiac disease and control groups and concluded that screening for diabetes-related autoantibodies is not justified. This opinion has been shared by Fanciulli et al. (5), who did not recommend regular screening for β-cell autoimmunity in all celiac disease patients because of low prevalence of diabetes-related autoimmunity in young celiac disease patients.

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**References**


**Table 1—Clinical characteristics of celiac disease patients (n = 188)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>66</td>
<td>35.1%</td>
</tr>
<tr>
<td>Female</td>
<td>122</td>
<td>64.9%</td>
</tr>
<tr>
<td><strong>Tanner pubertal stage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>103</td>
<td>54.8%</td>
</tr>
<tr>
<td>II</td>
<td>26</td>
<td>13.8%</td>
</tr>
<tr>
<td>III</td>
<td>18</td>
<td>9.6%</td>
</tr>
<tr>
<td>IV</td>
<td>10</td>
<td>5.3%</td>
</tr>
<tr>
<td>V</td>
<td>31</td>
<td>16.5%</td>
</tr>
<tr>
<td><strong>Age at celiac disease diagnosis (years)</strong></td>
<td>5.4 ± 4.2</td>
<td>0.5–17.1</td>
</tr>
<tr>
<td><strong>Age at study visit (years)</strong></td>
<td>10.4 ± 6.8</td>
<td>1.5–48.2</td>
</tr>
<tr>
<td><strong>Celiac disease duration (years)</strong></td>
<td>4.2 ± 5.9</td>
<td>0.2–28.8</td>
</tr>
</tbody>
</table>

Data are n (%), means ± SD, or median (minimum–maximum) unless otherwise indicated.

