Frequency of Celiac Disease and Spontaneous Normalization Rate of Celiac Serology in Children and Adolescent Patients with Type 1 Diabetes

1Edip Unal, 1Meliha Demiral, 2Birsen Baysal 3Mehmet Agın, 4Elif Gökçe Devecioğlu, 5Hüseyin Demirbilek, 1Mehmet Nuri Özbek
1Gazi Yaşargil Training and Research Hospital, Department of Pediatric Endocrinology, Diyarbakır, Turkey
2Gazi Yaşargil Training and Research Hospital, Department of Paediatrics, Diyarbakir, Turkey
3Gazi Yaşargil Training and Research Hospital, Department of Pediatric Gastroenterology, Diyarbakır, Turkey
4Gazi Yaşargil Training and Research Hospital, Department of Pathology, Diyarbakir, Turkey
5Hacettepe University, Faculty of Medicine, Department of Pediatric Endocrinology, Ankara, Turkey

What is already known on this topic?
Celiac disease prevalence varies between 1% and 10% in children and adolescents with T1DM. In previous reports about half of the cases, CD was detected at the time of the diagnosis of T1DM. Recently, few studies have shown normalization of celiac serology in patients with T1DM, even with no gluten-free dietary intervention.

What does this study add?
In our study, the majority (97.8%) of cases were diagnosed within the first five years of T1DM. In 23.3% of cases, positive celiac serology spontaneously resolved without a gluten-free diet. Therefore, considering all of the serologically positive individuals as CD and giving a gluten-free diet imposes an additional psychological burden for children and families. This implication would negatively affect the compliance to the T1DM management. The presence of symptoms and high anti-TTG IgA levels were shown to be highly predictive for BPCD.

Abstract
Purpose: The prevalence of celiac disease (CD) varies between 1% and 10% in patients with type 1 diabetes mellitus (T1DM). This study aims to determine the frequency of spontaneous recovery of celiac serology and the biopsy-proven CD frequency (BPCD) in patients with T1DM.
Methods: The data of 668 patients with celiac serology from 779 patients who were followed for the last 10 years with the diagnosis of T1DM were retrospectively evaluated.
Results: Positive serology was detected in 103 out of 668 (15.4%) patients. There was spontaneous normalization in 24(23.3%), fluctuation in 11(10.7%) and permanently positive serology in 68(66%) of these patients. In 46 out of 53(86.8%) patients with positive serology diagnosis of CD was confirmed with a biopsy (BPCD). The frequency of BPCD was 6.9%, and the serology in 76.1% of them was positive at the time of the diagnosis of T1DM. The weight, height and BMI-SDS at the time of diagnosis were lower in patients with BPCD compared to the group without CD. The anti-tissue transglutaminase-IgA level of 11.8 times higher than the upper limit of normal revealed the best sensitivity (93%) and specificity (90%) for BPCD (AUC:0.95; 95% CI: 0.912-1; p<0.001).
Conclusion: In our cohort, the frequency of positive serology for CD was 15.4%, while the rate of BPCD was 6.9%. The majority (97.8%) of cases were diagnosed within the first five years of T1DM. In 23.3% of cases, positive anti-TTG IgA spontaneously resolved without a gluten-free diet. Therefore, serological follow-up instead of immediate duodenal biopsy or gluten-free diet therapy, particularly for patients with asymptomatic and mild anti-TTG IgA level, is warranted.

Keywords: Celiac disease, children, spontaneous normalization, type 1 diabetes,
and giving a gluten-free diet imposes an additional psychological burden for children and families. This implication would also negatively affect the compliance to the T1DM management.

The aim of present study is to determine the frequency of BPCD and spontaneous recovery of high anti-TTG IgA levels in patients with T1DM. We also investigate the predictive factors for BPCD and spontaneous normalization of celiac serology.

Materials and Methods

The hospital files of 779 patients who have been followed for the last 10 years (2009-2019) with the diagnosis of T1DM at the Pediatric Endocrinology Clinic of Gazi Yaşargil Training and Research Hospital, University of Health Sciences were retrospectively analyzed. The age, gender, mean HbA1c level, anti-TTG IgA level status of patients with T1DM were recorded. Patients who anti-TTG IgA levels were not available were excluded. Anti-TTG IgA level was measured by enzyme-linked immunosorbent assay (Euroimmun kit, Euroimmun Analyzer I, Germany). Samples were analyzed in a central laboratory where the same method was used for analysis of Celiac serology. According to the method used in our laboratory; anti-TTG IgA level <12 IU/mL was considered as negative, 12-18 IU/mL as borderline, and >18 IU/mL as positive celiac serology. Positive anti-TTG IgA level that persistently remain negative for 6 months was considered as spontaneous normalization of celiac serology (group 1). If anti-TTG IgA level was initially positive, disappeared temporarily and finally re-appear, this situation was defined as fluctuation of the celiac serology. Pathology reports of all cases underwent endoscopic biopsy were examined. According to the biopsy results of the patients, those with Marsh scores 2 and 3 were accepted as biopsy-proven celiac disease (BPCD) (group 2). Those with anti-TTG IgA positive while Marsh score 0 and 1 were considered as potential CD (12).

Serological autoantibody titers were recorded as multiples of the upper limit of normal (ULN). Bodyweight standard deviation score (SDS), height SDS and body mass index (BMI) SDS values were extracted from the patients medical files. Besides, anthropometric measurements of patients with BPCD were assessed as before and after a gluten-free diet (GFD). The study was performed in accordance with the rules of the Declaration of Helsinki and approved by the Institutional Ethics Committee of Gazi Yaşargil Training and Research Hospital (Document number: 17.01.2020/011). Since the study was retrospective, informed consent was not available from the parents of the patients.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 21 (IBM Corp., Armonk, NY, USA). Numerical variables were expressed as mean ± standard deviation (SD) or median and interquartile range (IQR), categorical variables were expressed as number and per cent (%). For evaluation of the normality distribution of the data, the Shapiro-Wilk test was used. For numerical comparisons, independent sample t-test or Mann-Whitney U-tests were used subject to the normality distribution of data. Chi-square test was used to compare categorical variables. The repeated measure of weight-SDS, height-SDS and BMI-SDS values of the patients with BPCD at the time of the diagnosis and the last follow-up visit were compared with a paired-sample t-test. In the diagnosis of BPCD, receiver operating characteristics (ROC) curve analysis was performed for the anti-TTG IgA level recorded as the multiples of the upper limit of normal. A p < 0.05 value was considered statistically significant.

Results

The study included 779 patients, 367 (47.1%) male and 412 (52.9%) female with T1DM. Of those 668 out of 779 patients had at least one anti-TTG IgA test result (Figure 1). The mean age of the diagnosis for T1DM was 8.75 ± 6.75 (range: 0.5-17.92) with a mean follow-up duration of 3.91 ± 4.47 (range: 0.17-16.92).

To exclude the false-negative anti-TTG IgA serology due to concomitant IgA deficiency, we examined serum IgA in all patients which were within normal limits in all cases. Positive Anti-TTG IgA was detected in 103 out of 668 (15.4%) patients, whose celiac serology was available. Spontaneous normalization was detected in 24 out of 103 (23.3%) patients within a median duration of 9 (range: 2-24 months) months. In the spontaneous normalization group, median follow-up time after the disappearance of anti-TTG IgA antibody was 25.5 months (range: 6-105). There was a statistically significant difference between serum anti-TTG IgA levels of groups 1 and 2 at diagnosis (group 1, median 2 X ULN (range 1.1–11.5); group 2, median 16.6 X ULN (range 4.1–123) (P < 0.05) (Table 1). In one of 24 patients who had spontaneous normalization, the anti-TTG IgA level was above 11 times ULN. In two of 46 patients who had persistent antibody positivity, the anti-TTG IgA level was below 11 times the ULN. In 103 patients with positive celiac serology, fluctuating celiac serology was detected in 11 (10.7%) while celiac serology remains positive in 68 (66%). Autoantibodies became positive again after a median duration of 5 months (25th-75th quartiles: 4-6 months) in the fluctuation group. The antibody levels of the groups showing anti-TTG IgA levels of persistent, fluctuation and spontaneous normalization are summarized (Figure 2). An endoscopic biopsy was performed in 53 out of 68 (77.9%) patients who had permanently positive serology. The biopsy was not performed in 15 (22.1%) cases due to family refusal. Forty-nine out of 53 (84.8%) patients who underwent biopsy were diagnosed with BPCD suggesting a frequency of BPCD as 6.9% (46/668).

Thirty-five out of 46 (76.1%) patients with BPCD were diagnosed at the time of the diagnosis of T1DM, 11 (21.7%) within following five years and one patient (2.2%) at the 8.5 years of T1DM diagnosis. In BPCD patients, weight, height and BMI-SDS at the time of the diagnosis and height-SDS at the final follow-up visit were found lower than the patients who had not CD (p<0.001, p=0.02, p=0.01, p<0.001, respectively). There was no statistically significant difference between the mean HbA1c levels of those with BPCD and celiac negative patients (Table 2). In the ROC analysis, the anti-TTG IgA level that is 11.8 times higher than the ULN had the best sensitivity (93%) and specificity (90%) for BPCD (AUC: 0.95, 95% CI: 0.912-1, p < 0.001) (Figure 3).

Anti-thyroid peroxidase and anti-thyroglobulin was examined in 562 of the patients with celiac serology and were positive in 69 cases. While BPCD was detected in 8 out of 69 (11.6%) patients with T1DM and positive thyroid autoantibody, it was present in 30 out of 493 (6.1%) patients with negative thyroid autoantibody (p: 0.054) (Table 3). The BPCD was detected in 13 out of 146 (8.7%) patients diagnosed with T1DM under the age of five, and in 33 out of 489 (6.7%) patients over the age of five (p: 0.38) (Table 3).
The rate of BPCD was 6.4% in girls and 8.2% in boys (p: 0.39) (Table 3). There was no statistically significant difference between the weight, height and BMI-SDS values at the time of the diagnosis and the final follow-up visit of patients with BPCD (Table 4).

**Discussion**

In the present study, serological CD prevalence was 15.4%, and BPCD prevalence was 6.9%. In patients with T1DM, due to genetic predisposition, the frequency of CD and other autoimmune diseases is higher than the normal population (2). The overall prevalence of CD varies between 1% and 10% in children and adolescents with T1DM (3-6). In an international comparative study, 52,721 children and adolescents with T1DM, the overall CD prevalence has been reported as 3.5% with a frequency of 1.9% in the USA and 7.7% in Australia (13). In similar to our study, previous studies conducted in our country, CD prevalence in children with T1DM has been reported between 3.5% and 7.8% (14-17).

Recently, some studies evaluating CD prevalence in patients with T1DM, have reported a spontaneously normalized celiac serology up to 20-35% (9-11, 18). The duration for a positive serology recovered to negative is about 1-2 years after diagnosis (10, 11). Similarly, in our study, 24 out of 103 (23.3%) patients, positive celiac serology spontaneously recovered within a median duration of 9 months (3-24 months), without a gluten-free dietary intervention. In a study involving 446 pediatric T1DM patients, the rate of spontaneous recovery of celiac serology was reported as 27.6%. Having a negative anti-endomysial antibody, and low anti-TTG IgA levels (2.3 ± 2.1 ULN) have been reported as predictive factors (10). In our study, all patients with spontaneously recovered celiac serology were asymptomatic, and median anti-TTG IgA levels were low. In only one case, the anti-TTG IgA level was 11.5 times of ULN. In previous studies, spontaneous recovery of celiac serology in very high anti-TTG IgA levels has not been reported (9-11). Therefore, we do suggest that serological follow-up might be a more appropriate strategy in patients with asymptomatic and mildly elevated anti-TTG IgA levels instead of performing an intestinal biopsy immediately (9-11, 18).

In previous studies evaluating spontaneous normalization of celiac serology, there is limited data on re-appearance of celiac serology in patients with spontaneous normalization (9-11). In only one study, it has been reported that autoantibodies reappeared in three of 18 patients with spontaneous normalization (10). However, there is no data about the duration for re-appearance (10). In our study, the median follow-up time after anti-TTG IGA level was negative in the spontaneous normalization group was 25.5 months. In 3 of the 24 patients who developed spontaneous normalization, the follow-up period of remaining negative was less than 1 year, while in 21 patients the follow-up period was at least 15 months. Enenso, the duration of remaining negative was not short, this does not eliminate the possibility of reappearance of autoantibodies.

Therefore, regular follow-up of celiac serology in patients with spontaneous normalization is warranted. In the latest European Society Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines, it was emphasized that the level of anti-TTG Iga should be at least 10 times higher than the ULN for the diagnosis of CD without duodenal biopsy (12). Also, for a serology-based diagnosis without biopsy, the ELSA testing and the presence of symptoms are not mandatory criteria (12). In our study, the cut-off value of anti-TTG IgA was 11.8 XULN and shown to have high sensitivity and specificity in predicting BPCD.

Most patients with T1DM and CD have little or no symptoms of malabsorption, and gastrointestinal complaints are usually mild. Therefore, it is challenging to consider a diagnosis of CD in patients with T1DM based on clinical findings or routine laboratory tests. Serological examinations would help to detect subclinical disease (19). In our study, 25 out of 46 (54.3%) patients with BPCD had symptoms of gastrointestinal (abdominal pain, diarrhea, constipation, distention) or non-gastrointestinal symptom (short stature, weight loss, recurrent episodes of hypoglycemia). In a previous study, the presence of CD symptoms, younger age for onset of T1DM, anti-TTG IgA level higher than 7-8 ULN, and positive anti-endomysial antibody were suggested predictive for BPCD (11). Similarly, in another study, the presence of gastrointestinal symptoms and high anti-TTG IgA levels have shown reliable predictor for CD (20). In our study, the presence of symptoms and high anti-TTG IgA levels were showed highly predictive for BPCD. Only in one asymptomatic patient with high anti-TTG IgA level (> 10 times the upper limit of normal), a biopsy was negative, which further emphasized the impact of having CD symptoms.

The overall prevalence of CD is higher in female (21). Various studies in children and adolescents with T1DM reported variable sex distribution as a higher prevalence in girls (10, 13, 22, 23), in male (3, 24) or no difference in boys and girls (9, 18, 25). In our study, there was no predominance of CD prevalence in boys and girls.

The frequency of CD is reported higher in patients with an earlier age of T1DM diagnosis (especially <5 years) (5, 13, 18, 21). However, the results of some other studies revealed no relationship between the age for diagnosis of T1DM and the frequency of CD (3, 19, 24, 26, 27). In our study, there was no statistically significant difference in the frequency of CD between the patients with age for diagnosis of T1DM <5 years and >5 years. In previous reports about half of the cases, the CD was detected at the time of the diagnosis of T1DM (9, 19), and most of the remaining cases were identified within the last five years following diagnosis of T1DM (9, 18). In a review of 9 longitudinal cohort studies with celiac screening between 5 and 18 years, in patients with T1DM; it has been reported that 79% of celiac cases were diagnosed within the first five years following the diagnosis of T1DM. Therefore, screening for CD is recommended at the diagnosis of T1DM and subsequent 2 and 5 years in case of asymptomatic and negative family history of CD. In the same review, it was mentioned that determination of the frequency of CD after five years of diabetes period is challenged due to lack of data obtained from long-term follow-up. Some studies with long-term follow-up, 16% of CD cases were reported diagnosed between 5 and 10 years, and 5% after >10 years (28). Thereby, the CD should be considered at any time in patients with symptoms of CD (28). In our study, the CD was detected in 76.1% of cases at the time of the diagnosis of T1DM, in 21.7% within 5 years and in 2.2% of the cases 8.5 years following the diagnosis of the T1DM. To the best of our knowledge, the rate of detection CD at the time of the diagnosis of T1DM (76.1%) is the highest ever reported in the literature.

The comorbidity of CD and T1DM in children has been reported associated with increased risk of autoimmune thyroid disease (AITD) (29-31). However, although the study evaluating the CD prevalence in patients with both T1DM and AITD are scarce, a few studies conducted on this association revealed no difference (32, 33). In our study, CD prevalence in patients...
with T1DM andAITD (11.6%) was higher than patients with T1DM alone (6.1%), but the difference did not reach statistical significance.

There are controversial data regarding metabolic control and its association with T1DM and CD comorbidity. Some studies have reported no difference in metabolic control between the children with only T1DM and children with both T1DM and CD (34-36), while in some studies, HbA1c was lower in patients with T1DM and CD comorbidity (37). In the present study, we did not find a difference in HbA1c levels of T1DM patients with and without CD. However, it should be kept in mind that having similar HbA1c result does not eliminate the increased risk of developing diabetes complications. Because, CD may increase glycemic variability and frequent hypoglycemia due to malabsorption which may result in a low HbA1c, thereby lead underestimation of poor glycemic control.

It has been shown that there was no difference in height and BMI SDS scores between children with the diagnosis of T1DM and children with both T1DM and CD (19, 37, 38). However, some studies reported a lower height SDS in the T1DM patients with CD (13, 39). There are also studies indicating that gluten-free diet therapy does not change the height and BMI SDS (37, 38, 40), while some others reported a better height SDS after gluten-free diet (41). In our study, the height, weight and BMI SDS values of T1DM patients with CD were lower than those without CD. In addition, we did not find any difference between the weight, BMI and height SDS of the patients with CD before and after the gluten-free diet. This finding was in line with previous reports (37,38). However, the lack of improvement in growth parameters can be attributed to incompliance to gluten-free diet due to the low socioeconomic and cultural level of the region where our study was conducted.

Study Limitations

The main limitation of our study was that some individuals with positive TTG-IgA antibodies (n = 15) did not undergo duodenal biopsy. Another major limitation of the study is the retrospective nature of design.

Conclusion

In conclusion; we found the frequency of BPCD in our patients with T1DM as 6.9%. Approximately ¾ of the cases were diagnosed at the diagnosis of T1DM, 97.8% of them were diagnosed within the first five years. High anti-TTG IgA titers, particularly in patients with CD symptoms, can be used as a valuable parameter to predict CD. However, spontaneous normalization of celiac serology suggested performing serological follow-up instead of immediate duodenal biopsy or gluten-free diet therapy, especially in patients with asymptomatic and mild anti-TTG IgA antibody levels. Having CD at the diagnosis of T1DM did not affect the metabolic control whilst associated with poor growth parameters. Nevertheless, no improvement was seen in growth parameters which were attributed to incompliance to the gluten-free diet.

Ethics

Ethics Committee Approval: It was taken

Informed Consent: It was taken

Authorship Contributions

Surgical and Medical Practices: Edip Unal, Mehmet Nuri Özbebek, Meliha Demiral, Hüseyin Demirbilek
Concept: Edip Unal, Meliha Demiral, Birsen Baysal, Mehmet Agin, Mehmet Nuri Özbebek
Design: Edip Unal, Birsen Baysal, Mehmet Nuri Özbebek, Hüseyin Demirbilek
Data Collection or Processing: Edip Unal, Birsen Baysal, Elif Gökle Devecioğlu, Mehmet Agin
Analysis or Interpretation: Meliha Demiral, Mehmet Nuri Özbebek, Hüseyin Demirbilek, Mehmet Agin, Elif Gökle Devecioğlu
Literature Search: Edip Unal, Birsen Baysal, Hüseyin Demirbilek, Meliha Demiral, Elif Gökle Devecioğlu
Writing: Edip Unal, Meliha Demiral, Mehmet Nuri Özbebek, Hüseyin Demirbilek

Conflict of Interest: No conflict of interest

Financial Disclosure: No financial disclosure

References


Figure 1: A flow diagram of the study participants.
Figure 2: Trend of the anti-TTG IgA levels in patients with persistent, fluctuation and spontaneous normalization group.
Figure 3: ROC analysis of anti-TTG-IgA level for prediction of BPCD (Sensitivity: 93%, specificity: 90%, AUC: 0.95, p < 0.001)

Table 1. Comparison of anthropometric and laboratory features of T1DM patients with BPCD and spontaneously recovered positive celiac serology

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n: 24)</th>
<th>Group 2 (n: 46)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of diagnosis (year)</td>
<td>9.07 ± 4.16</td>
<td>8.12 ± 4.58</td>
<td>0.40†</td>
</tr>
<tr>
<td>Latest age (year)</td>
<td>13.33 (2.25-22)</td>
<td>14.04 (4.25-19.5)</td>
<td>0.683 *</td>
</tr>
<tr>
<td>Duration of T1DM (year)</td>
<td>2.83 (0.92-9.75)</td>
<td>3.12 (0.25-16.33)</td>
<td>0.569 *</td>
</tr>
<tr>
<td>Anti-TTG–IgA*** (ULN)</td>
<td>2.11-11.5</td>
<td>16.6 (4.1-123)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean HbA1c (%)</td>
<td>8.8 ± 1.78</td>
<td>9.45 ± 2.06</td>
<td>0.24 †</td>
</tr>
<tr>
<td>Height at diagnosis SDS</td>
<td>-1.04 ± 0.91</td>
<td>-1.21 ± 1.37</td>
<td>0.63 †</td>
</tr>
<tr>
<td>Latest weight (SDS)</td>
<td>-0.58 ± 1.00</td>
<td>-0.98 ± 1.29</td>
<td>0.29 †</td>
</tr>
<tr>
<td>BMI at diagnosis SDS</td>
<td>-1.11 ± 1.03</td>
<td>-0.85 ± 1.37</td>
<td>0.50 †</td>
</tr>
<tr>
<td>Latest weight (SDS)</td>
<td>-0.50 ± 1.14</td>
<td>-1.11 ± 1.40</td>
<td>0.10 †</td>
</tr>
<tr>
<td>Latest height (SDS)</td>
<td>-0.55 ± 1.23</td>
<td>-1.46 ± 1.27</td>
<td>0.01 †</td>
</tr>
<tr>
<td>Latest BMI (SDS)</td>
<td>-0.17 ± 0.87</td>
<td>-0.37 ± 1.27</td>
<td>0.53 †</td>
</tr>
</tbody>
</table>

* Mann-Whitney U test, † Student’s t-test; data are given as mean ± SD or median (IQR 25th–75th percentile). Anti-TTG–IgA antibody titer reported as times the upper limit of normal (ULN), BMI, body mass index; HbA1c, glycated haemoglobin; SDS, standard deviation score.
Table 2. Comparison of anthropometric and laboratory features of T1DM patients with and without CD

<table>
<thead>
<tr>
<th></th>
<th>CD negative (n:589)</th>
<th>CD positive (n: 46)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of diagnosis (year)</td>
<td>9 (0.5-17.92)</td>
<td>7.58 (0.67-17.92)</td>
<td>0.410*</td>
</tr>
<tr>
<td>Latest age (year)</td>
<td>13.83 (1.25-21.5)</td>
<td>14.04 (4.25-19.5)</td>
<td>0.818*</td>
</tr>
<tr>
<td>Duration of T1DM (year)</td>
<td>4 (0.17-16.92)</td>
<td>3.12 (0.25-16.33)</td>
<td>0.754*</td>
</tr>
<tr>
<td>Mean HbA1c (%)</td>
<td>8.75 (4.9-14.3)</td>
<td>9.37 (6.3-15.2)</td>
<td>0.318*</td>
</tr>
<tr>
<td>Weight at diagnosis (SDS)</td>
<td>-0.41 ± 1.11</td>
<td>-1.21 ± 1.37</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Height at diagnosis SDS</td>
<td>-0.29 ± 1.21</td>
<td>-0.98 ± 1.29</td>
<td>0.02†</td>
</tr>
<tr>
<td>BMI at diagnosis (SDS)</td>
<td>-0.35 ± 1.16</td>
<td>-0.85 ± 1.37</td>
<td>0.01†</td>
</tr>
<tr>
<td>Latest weight (SDS)</td>
<td>-0.57 ± 1.15</td>
<td>-1.11 ± 1.40</td>
<td>0.05†</td>
</tr>
<tr>
<td>Latest height (SDS)</td>
<td>-0.80 ± 1.15</td>
<td>-1.46 ± 1.27</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Latest BMI (SDS)</td>
<td>-0.17 ± 1.07</td>
<td>-0.37 ± 1.27</td>
<td>0.25†</td>
</tr>
</tbody>
</table>

*Mann–Whitney U test, †Student’s t-test; data are given as mean ± SD or median (IQR 25th–75th percentile). BMI, body mass index; HbA1c, glycated haemoglobin; SDS, standard deviation score.

Table 3. The frequency of BPCD according to age and presence of AITD accompany to T1DM

<table>
<thead>
<tr>
<th></th>
<th>BPCD n (%)</th>
<th>P* value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>22 (6.4%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Male</td>
<td>24 (8.2%)</td>
<td></td>
</tr>
<tr>
<td>AITD</td>
<td>8 (11.6%)</td>
<td>0.05</td>
</tr>
<tr>
<td>No AITD</td>
<td>30 (6.1%)</td>
<td></td>
</tr>
<tr>
<td>T1DM diagnosis age &lt;5 years</td>
<td>13 (8.9%)</td>
<td>0.38</td>
</tr>
<tr>
<td>T1DM diagnosis age &gt;5 years</td>
<td>33 (6.7%)</td>
<td></td>
</tr>
</tbody>
</table>

BPCD: Biopsy proven celiac disease, AITD: Autoimmune thyroid disease

Table 4. Comparison of anthropometric features of T1DM patients at the time of the diagnosis of CD and after gluten-free diet

<table>
<thead>
<tr>
<th></th>
<th>At diagnosis of CD</th>
<th>After gluten-free diet</th>
<th>P* value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight SDS</td>
<td>-1.18 ± 1.31</td>
<td>-1.14 ± 1.35</td>
<td>0.82</td>
</tr>
<tr>
<td>Height SDS</td>
<td>-1.17 ± 1.33</td>
<td>-1.44 ± 1.32</td>
<td>0.051</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>-0.74 ±1.41</td>
<td>-0.42 ± 1.21</td>
<td>0.14</td>
</tr>
</tbody>
</table>

CD: Celiac disease, BMI: body mass index; SDS: standard deviation score *Paired Sample Test