Frequency of Celiac Disease among the Children with Type I Diabetes Mellitus

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ABSTRACT
Aim: To determine the frequency of celiac disease in pediatric age group patients of type 1 diabetes mellitus.
Material: This cross-sectional descriptive study including 100 children with type-I diabetes mellitus, both genders and aged between 1 to 12 years, was done at Department of Pediatric Medicine, DHQ Teaching Hospital, Sargodha from 20th February 2017 to 19th September 2017. Tissue transglutaminase antibody level was estimated in blood samples for diagnosis of celiac disease.
Results: The mean age of children was 7.8±2.7 years. In the whole sample, there were 45 (45.0%) male and 55 (55.0%) female patients. The mean duration of T1D was 3.4±1.4 years. Diabetes was controlled in 83 (83.0%) patients while 17 (17.0%) patients had uncontrolled diabetes. Celiac disease was diagnosed in 11 (11.0%) children with T1D. There was no significant difference of celiac disease between children of different ages (p-value=0.983), any gender (p-value=0.974), duration (p-value=0.655) and control of diabetes (p-value=0.912).
Conclusions: A substantial proportion of children with T1D had celiac disease which warrants routine screening of such children in future practice to enable timely identification and management of celiac disease and hence improve the outcome.
Keywords: Celiac Disease, Type-I Diabetes, Gluten Intolerance

INTRODUCTION
Celiac disease is the systemic immune mediated disorder initiated due to gluten intake in genetically vulnerable individuals.1 It effects 0.6 to 1% of population worldwide. The risk of celiac disease would be higher for those who have family history of celiac disease in 1st degree relatives (10-15%), T1D (3-16%), and Hashimoto’s thyroiditis (5%)2,3. Hereditary predisposition plays an important role in the susceptibility towards the celiac disease4. The clinical manifestations of celiac disease are diarrhea, abdominal distention, failure to thrive, short stature, osteopenia, osteoporosis and delayed puberty. Prevalence of celiac disease in patients with T1D ranges from 4.4 to 11.1%. The mechanism of association of these two diseases involves a shared genetic background.5 Prevalence of 9.1% of celiac disease in T1D children was found by a study published in 20136.

Another study conducted by Abdulrahman Al-Hussaini in middle east revealed this prevalence to be 11.3%.7 Long term complications of celiac disease are short height, recurrent stomatitis, dermatitis herpetiformis, problem in reproductive system, celiac ataxia as well as intestinal lymphoma. The basis for screening the suspects for celiac disease is to predict and initiate the treatment earlier thus reducing the hazards of prolonged complications related to the celiac disease. Tayob conducted a cohort study in 2016 in South Africa. One hundred and twenty children with T1D were enrolled. About 40.8% children had positive celiac serology, while serology of 50.8% children was negative while serology of few children was unknown. Thus the prevalence of celiac disease in children with T1D was showed as 44.5%.8

As there is variability in the prevalence of celiac disease among diabetic children and there is no such local published material, the rationale of my study is to find the exact data regarding the prevalence of celiac disease in children with T1D. This would help us to institute early diagnosis and prompt management of patients with celiac disease. The present study was conducted to determine the frequency of celiac disease in children with T1D.

MATERIAL AND METHODS
This cross-sectional descriptive study including 100 children of both genders aged between 1 to 12 years who presented with T1D, was conducted at Department of Pediatric Medicine, DHQ Teaching Hospital, Sargodha from 20th February 2017 to 19th September 2017. Children with fasting blood sugar greater than 126mg/dl and insulin dependency were included. Patients with Down syndrome and who were first or second degree relatives of patients with celiac disease were excluded from the study. Their parents were counseled and explained the details of the study and written informed consent and detailed history was taken from the parents. After approval from ethical review committee of the hospital, Blood samples of 100 children with T1D who presented in the outpatient department were taken and sent to lab for estimation of tissue transglutaminase antibody level. A cut off value of ≥300 IU/L was taken as diagnostic of celiac disease. The data was entered into SPSS version 20, computer program and analyzed accordingly. Quantitative variables e.g. age
and duration of diabetes were presented by mean±SD. Categorical variables e.g. gender, celiac disease and control of diabetes were showed as frequency & percentage. Data was stratified for age, gender, duration and control of diabetes to control the effect modifiers. Post-stratification chi-square test was applied keeping p≤0.05 as significant.

**RESULTS**

The mean age of children was 7.8±2.7 years. Mostly children were aged ≥10 years 52(52%), followed by 38(38%) patients aged between 5-10 years and 10(10%) patients aged under 5 years. There were 45(45%) male children while 55(55%) were female children. The male-to-female ratio was 1:1.2. Characteristic of patients are shown in Table I.

Celiac disease was diagnosed in 11(11%) children with T1D. There was insignificant difference observed regarding celiac disease frequency in different age groups (p-value=0.983), both genders (p-value=0.974), duration of T1D (p-value=0.655) and control of diabetes (p-value=0.912).

Table I: Characteristics of patients (n=100)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N (%)</th>
<th>Age (mean±SD) 7.8±2.7 years</th>
<th>Gender</th>
<th>Male (45(45%))</th>
<th>Female (55(55%))</th>
<th>Duration of Diabetes (Mean±SD) 3.4±1.4 years</th>
<th>Control of Diabetes Controlled (83(83%))</th>
<th>Uncontrolled (17(17%))</th>
</tr>
</thead>
</table>

Table II: Frequency of Celiac Disease in Children with T1D (n=100)

<table>
<thead>
<tr>
<th>Celiac Disease</th>
<th>Frequency</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>89</td>
<td>89.0</td>
</tr>
<tr>
<td>No</td>
<td>11</td>
<td>11.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Table III: Stratification of Celiac Disease in Children with T1D (n=100)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>n</th>
<th>Celiac Disease</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td>10</td>
<td>1 (10.0%)</td>
<td>0.983*</td>
</tr>
<tr>
<td>5-10 years</td>
<td>38</td>
<td>4 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>≥10 years</td>
<td>52</td>
<td>6 (11.5%)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>45</td>
<td>5 (11.1%)</td>
<td>0.974*</td>
</tr>
<tr>
<td>Female</td>
<td>55</td>
<td>6 (10.9%)</td>
<td></td>
</tr>
<tr>
<td>Duration of Diabetes (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td>78</td>
<td>8 (10.3%)</td>
<td>0.655*</td>
</tr>
<tr>
<td>≥5 years</td>
<td>22</td>
<td>3 (13.6%)</td>
<td></td>
</tr>
<tr>
<td>Control of Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controlled</td>
<td>83</td>
<td>9 (10.8%)</td>
<td>0.912*</td>
</tr>
<tr>
<td>Uncontrolled</td>
<td>17</td>
<td>2 (11.8%)</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

In the present study, the mean age of the patients was 7.8±2.7 years. An almost similar mean age of children was reported by Qayyum et al., i.e. 9.9±6.5 years compared to other studies. Honar et al. who reported similar frequency of 11.1% in Indian children with T1D. Singh et al also reported similar female predominance with male to female ratio of 1:1.1 in Indian children with T1D. A male-to-female ratio of 1:1.7 was presented by Laitinen et al in Finland while Honar et al. also observed ratio of 1:1.4 in Iran. This can be observed that female are more affected with celiac disease.

In the present study, the mean duration of T1D was 3.4±1.4 years. These findings were in-line with findings of a study conducted by Honar et al., who also noticed similar mean duration of diabetes upon presentation and reported it to be 3.4±0.8 years while previously Moayeria et al. reported it to be 3.5±1.8 years in Iranian such children. On further stratification of data, we did not find any significant difference between duration of diabetes more than 5 years or less than 5 years. So, screening is recommended at any age before 10 years at least for one time in life. It is very difficult to comment that children beyond 10 years of age need to be screened or not.

We observed that 11(11%) children with T1D were positive for celiac disease on serology. Our results are similar to those of Frolich-Reiterer et al who reported similar frequency of 11.1% in Germany and Larsson et al. who reported similar frequency of 11.1% in Sweden. Bhadada et al. in India and Al-Hussaini et al. in Saudi Arabia reported similar frequency of 11.1% and 11.3% respectively for celiac disease in children presenting with T1D. We relied upon estimation of tissue transglutaminase antibody level which is a single step diagnostic test. It is highly sensitive and specific as compared to other serologic test like antigladian antibodies, etc.

This study was conducted first in children with T1D belonged to local population and we observed a substantial proportion of children with T1D suffer celiac disease which warrants routine screening of such children in future practice to enable timely identification and management of celiac disease and hence improve the outcome. A very strong limitation of this study was that we could not reflect the response of treatment against celiac disease in patients with and without diabetes which could have helped in the risk stratification and management
planning of these patients. So for further studies, these recommendation should be considered.

One of the strength of the study was that we relied upon serological criteria. In many of the previous studies, histopatholgic criteria has been used. But that is invasive and need to do repeat biopsies after gluten free diet. So, this simple serologic test can be used for screening purpose in a developing country like Pakistan, where the patients do not keep follow up and invasive procedures are not easily complied by parents due to affordability issues.

CONCLUSION

It is concluded that a substantial proportion of children with T1D had celiac disease which warrants routine screening of such children in future practice to enable timely identification and management of celiac disease and hence improve the outcome.

REFERENCES

1. Khan A, Ahmad W, Kamran M. Celiac Disease in Different Age Groups and Gender in Pakistan. JRMC 2018;22(3):244-7.