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Frequency of Celiac Disease among Children with Type I Diabetes Mellitus

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ABSTRACT

Background: Type 1 diabetes mellitus (T1DM) is a metabolic condition of chronic hyperglycemia due to a lack of insulin resulting from the autoimmune destruction of pancreatic beta cells. T1DM is associated with many autoimmune conditions, especially hypothyroidism and celiac disease (CD). **Objective:** To determine the frequency of celiac disease among children and adolescents with type 1 diabetes mellitus. **Study Design:** Prospective cross-sectional study. **Settings:** Department of Pediatric Gastroenterology, Hepatology, and Nutrition, University of Child Health Sciences, The Children's Hospital, Lahore Pakistan. **Duration:** October 2019 to January 2022. **Methods:** A total of 150 children and adolescents with T1DM were included in this study. Patients already diagnosed with CD, patients with concomitant autoimmune disease, patients with Down syndrome, and patients who refused to participate and who lost follow-up were excluded from the study. All patients underwent a celiac screen, and those with positive or borderline serology had an endoscopic biopsy of the distal duodenum. Biopsy reporting was done as per Modified Marsh Classification. The patient's data and laboratory findings were recorded through a predesigned proforma and analyzed using SPSS version 20. **Results:** The mean age of participants was 8.08 ± 2.95 years, including 79 (52.7%) male and 71 (47.3%) female patients. A total of 19 (12.7%) had positive serology for celiac disease, and 8 (5.3%) had biopsy findings confirming celiac disease. **Conclusion:** Children and adolescents with T1DM have an increased tendency for CD, warranting earlier screening for timely detection and management.

Keywords: *Celiac disease, Type 1 diabetes mellitus, Children.*

INTRODUCTION

Celiac disease (CD) is an autoimmune condition leading to gluten sensitivity.[1] It is a chronic disorder that occur in genetically susceptible population having HLA-DQ2/DQ8 as a biological risk factor.[2] An abnormal immune response is triggered by gluten and related prolamines present in wheat, barley and rye. Ingestion of gluten caused enteropathy resulting in compromised small intestinal mucosal surface for absorption of nutrients. This leads to malabsorption and diarrhea.[3] Untreated CD leads to growth failure, stunting, iron deficiency, bone fractures, fertility problems and even malignancy.[4]

Type 1 diabetes mellitus (T1DM) also results as autoimmune destruction of the beta cells of pancreas leading to decreased insulin production, resulting in hyperglycemia, and associated metabolic abnormalities. [5] Both environmental and genetic factors are responsible in etiology of T1DM. The control of glucose is affected by dozen of factors among which food, body stress, exercise, and insulin doses are important. Children need proper support and care while family education also plays a key role in management of disease. [6]

The occurrence of CD is higher among children with type T1DM than in the general population (1.6–16.4% vs 0.7%), because of the autoimmune nature of both conditions.[7] Irrespective of initial diagnosis, both diseases exhibit

strong comorbidity with each other.[8] Both diseases have strong associations as they share the same genetic basic expression from the major histocompatibility complex class II antigen DQ2 encoded by the alleles DQA*501 and DQB1*201 and seven shared non-human leucocyte antigen loci.[9] Therefore, screening children with TIDM for CD is critical for timely diagnosis and prompt management. Thus, we aimed to determine the frequency of CD among our children diagnosed with T1DM.

METHODS

This was a prospective cross-sectional study conducted after approval from the Institutional Review Board with approval date of 05/10/2019 and number 56188 at the Department of Pediatric Gastroenterology, Hepatology, and Nutrition, University of Child Health Sciences, The Children's Hospital, Lahore, from October 2019 to January 2022. A total of 150 patients between ages 2 and 18 of both genders, diagnosed with T1DM, were sent for celiac screening after giving informed consent. Patients already diagnosed with CD, patients with concomitant autoimmune disease, patients with Down syndrome, and patients who refused to participate and lost follow-up were excluded from the study.

Screening of CD was done by using serum anti-tissue transglutaminase IgA antibodies (TTG IgA) via enzyme-linked immunosorbent assay (ELISA) in patients who had normal total serum IgA levels. Tissue transglutaminase IgG antibody was analyzed in patients who had IgA deficiency. Patients with positive TTG IgA levels underwent an endoscopic biopsy of the distal duodenum by a consultant pediatric gastroenterologist. Histopathological evaluation was performed according to the Modified Marsh Classification.[10] Patients' demographic data and laboratory findings were recorded through a predesigned proforma. The data was entered and analyzed using SPSS version 20.

RESULTS

The mean age of patients at presentation was 8.08 ± 2.95 years. IgA deficiency was not noted in any patient with negative serology. Various characteristics of the included patients are shown in Table 1.

Table 1: Demographic and laboratory characteristics of patients

Variables		Patients
Age (Years)		8.08 ± 2.95
Gender	**Male n (%)**	79 (52.7%)
	Female n (%)	71 (47.3%)
Positive Serology n (%)		19 (12.7%)
Biopsy Confirmed Diagnosis n (%)		8 (5.3%)

Endoscopy and duodenal biopsy were performed in all 19 seropositive patients. The characteristics of those with positive biopsies are described in Table 2.

Table 2: Clinical characteristics of CD Patients

Age (Years)	Gender	TTG IgA Ab (U/ml)	Histopathology
6	Female	49	3a
8	Male	72	3a
5.6	Female	13.76	3c
7	Female	77	3a
5	Male	200	3c
6	Male	76	3a
12	Female	19.77	2
4.3	Female	94	3a

In our study, the frequency of celiac disease among children with T1DM was found to be 5.3%.

DISCUSSION

Antibodies can appear in any patient with an autoimmune disease at any time of life, so screening for CD is recommended at the time of diagnosis of T1DM.[11] The epidemiological picture of CD is changing worldwide owing to several factors. Increased knowledge of the variability of clinical manifestations of CD, the discovery of new serological markers, and the easier and more affordable availability of screening tests have resulted in a rise in the overall incidence of CD.[12]

In our study, the mean age of the cohort was 8.08 ± 2.95 years. Singh et al. documented the ages of boys and girls as 8.2 ± 4 and 8.1 ± 3.8 years, quite comparable to ours.[13] Though a mean age ranging from as little as 6.5 ± 4.1 years to as much as 15.58 ± 5.7 years has been documented by researchers.[14,15] We had 52.7% males and 47.3% female patients. Other studies show a female preponderance of 51.5% as compared to males at 48.5%, a finding in contrast to ours.[16] Similarly, an increased ratio of female participants (59%) was documented when compared with male participants (41%), according to Honar et al.[17]

We reported the positive serology for celiac disease as 12.7% among our patients with T1DM, based on an estimation of TTG IgA Ab levels. It yields better sensitivity and specificity in comparison to other serological tests for CD. Like our findings, Joshi et al.[18] documented a prevalence of 15.49%, employing the same test. However, Jalilian et al. have documented a range of 1.4% to 24.5% for the serological prevalence of CD in T1DM patients.[19] Among the serologically positive patients, endoscopy and biopsy revealed 5.3% of our patients had confirmed celiac disease on histopathology. Al-Sinani and colleagues too documented 5.5% biopsy-positive cases among 17% seropositive Omani children for CD, a finding similar to ours.[20] Similarly, Sahin et al.

documented the prevalence of biopsy-confirmed CD among T1DM at 4.4%.[21] However, a range of 1.1% to 16.6% has been documented in the literature for biopsy-positive cases of CD with positive serology.[19]

The prevalence of celiac disease is reported to be 0.5–1% in various regions of the world. Our study documents an increased frequency of positive serology and biopsy for celiac disease among children with T1DM when compared to the general population. Periodic screening for celiac disease in children with TIDM is not meticulously practiced in developing countries like ours. This higher frequency of CD in our cohort of T1DM emphasizes earlier screening and prompt management to prevent malnutrition and calorie loss in already challenged patients with T1DM. Larger cohort, multicentric studies with prolonged follow-up are needed for drawing firm conclusions. Employing a serological test with high sensitivity and specificity and confirmation of histopathological diagnosis with duodenal biopsies were strengths of our study.

CONCLUSION

A substantial number of children and adolescents with T1DM have CD, warranting earlier screening for timely detection and management.

LIMITATIONS

Small sample size and single center study were limitations of the study.

SUGGESTIONS / RECOMMENDATIONS

Periodic screening for CD in children with T1DM needs to be meticulously practiced.

CONFLICT OF INTEREST / DISCLOSURE

There is no conflict of interest to be declared by the authors.

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