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RESEARCH ARTICLE
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INCIDENCE OF CELIAC DISEASE AMONG CHILDREN DIAGNOSED WITH TYPE I DIABETES

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ABSTRACT

Background: Celiac disease (CD) is an autoimmune disorder triggered by gluten ingestion in genetically predisposed individuals, and it frequently coexists with Type 1 Diabetes Mellitus (T1DM), another autoimmune condition.

Objectives: This study aimed to determine the prevalence of celiac disease (CD) among children with Type 1 Diabetes Mellitus (T1DM) and to evaluate the clinical and histological characteristics of CD in this population

Study design: Cross sectional study

Settings: This study was conducted at Akhtar Saeed Trust Hospital Lahore from November 2023 to May 2024.

Study duration: 6th October 2020 to 5th April 2021

Methods: We conducted a cross-sectional study involving 125 pediatric patients with T1DM, aged 5 to 18 years, at a tertiary care hospital. We screened participants for CD using serological tests for tissue transglutaminase IgA (tTG-IgA), deamidated gliadin peptide IgG (DGP-IgG) in case of selective IgA deficiency, and confirmed positive cases with upper gastrointestinal endoscopy and small bowel biopsy. We recorded demographic data and clinical symptoms..

Results: Out of 125 patients, 18 (14.4%) tested positive for CD-specific antibodies. Among these, 12% were positive for tTG-IgA, and 2.4% with IgA deficiency were positive for DGP-IgG. Histological examination revealed that 50% of seropositive patients had Marsh III (villous atrophy), 22.2% had Marsh II (hyperplastic lesions), and 16.7% had Marsh I (infiltrative lesions). Notably, 38.9% of patients with CD were asymptomatic, with abdominal pain (27.8%) and diarrhea (22.2%) being the most common symptoms

Conclusion: Prevalence of CD among children with T1DM in our study (14.4%) supports the higher risk of CD in this population. The significant proportion of asymptomatic cases highlights the importance of routine CD screening in T1DM patients to prevent potential complications and

ensure optimal management. Early diagnosis and multidisciplinary care are essential to address both conditions effectively.

Keywords: Celiac Disease, Type 1 Diabetes Mellitus, Pediatric Autoimmune Disorders, Gluten-Free Diet, Serological Screening, Histological Analysis

INTRODUCTION

Celiac disease (CD) is an autoimmune disorder triggered by the ingestion of gluten in genetically predisposed individuals, characterized by inflammation and damage to the small intestine's mucosa. This condition often coexists with other autoimmune diseases, including Type 1 Diabetes Mellitus (T1DM), which shares a similar genetic and immunological predisposition. The incidence of CD in children with T1DM is notably higher than in the general population, raising concerns about the implications of this dual diagnosis on health outcomes and quality of life [1]. Type 1 Diabetes is an autoimmune disorder in which insulin-producing beta cells in the pancreas are destroyed, leading to chronic hyperglycemia. Both T1DM and CD share a common genetic predisposition, particularly linked to the human leukocyte antigen (HLA) class II genes, specifically HLA-DQ2 and HLA-DQ8. Approximately 95% of individuals with CD carry one of these genetic markers, which are also prevalent in individuals with T1DM [2,3]. This genetic overlap partly explains the increased incidence of CD in children diagnosed with T1DM compared to the general population [4].

The prevalence of CD in children with T1DM varies across regions but is consistently higher than the global prevalence of CD, which affects around 1% of the general population. Studies estimate that approximately 4-10% of children with T1DM also have CD, although the prevalence can be higher in certain populations [5,6]. This variation may be influenced by genetic, environmental, and geographic factors [7]. The co-occurrence of these two autoimmune conditions poses significant clinical challenges, as CD can be asymptomatic or present with non-specific symptoms such as abdominal pain, diarrhea, and growth retardation, which can be easily overlooked in the context of diabetes management [8].

Early diagnosis of CD in children with T1DM is critical due to the potential long-term complications associated with undiagnosed or untreated CD. These complications include malabsorption, poor glycemic control, growth impairment, and an increased risk of other autoimmune conditions and malignancies, such as intestinal lymphoma [9]. Moreover, CD has been shown to exacerbate glycemic variability in children with T1DM, potentially leading to more frequent episodes of hypoglycemia or hyperglycemia if not appropriately managed [10]. Therefore, routine screening for CD in children with T1DM has become a standard recommendation in many clinical guidelines.

Screening for CD in children with T1DM typically involves the measurement of specific serological markers, such as tissue transglutaminase antibodies (tTG-IgA) and endomysial antibodies (EMA). However, in patients with selective IgA deficiency, which is more common in individuals with T1DM and CD, total IgA levels should also be assessed, and IgG-based tests, such as deamidated gliadin peptides (DGP), should be considered [11].

Positive serological results are usually followed by a small bowel biopsy to confirm the diagnosis of CD, although recent advancements in non-invasive diagnostic methods may reduce the need for biopsy in the future [12]. The management of CD in children with T1DM revolves around strict adherence to a gluten-free diet (GFD), which has been shown to improve intestinal healing and overall health outcomes [13]. However, the introduction of a GFD in children with T1DM requires careful consideration, as it can impact nutritional intake and glycemic control. A multidisciplinary approach involving dietitians, endocrinologists, and gastroenterologists is essential to ensure optimal management of both conditions [14]. Despite the growing awareness of the increased risk of CD in children with T1DM, there remains a need for more comprehensive studies on the long-term impact of a dual diagnosis and the benefits of early intervention. Understanding the incidence

and clinical outcomes of CD in children with T1DM will help refine screening practices and improve patient care [15].

The rationale for this study stems from the high co-occurrence of celiac disease (CD) and Type 1 Diabetes Mellitus (T1DM) due to shared genetic predispositions, such as HLA-DQ2/DQ8. Understanding the incidence of CD in children with T1DM is crucial for improving early diagnosis and management, as untreated CD can complicate diabetes control and lead to adverse health outcomes. This study aims to provide insights into the clinical importance of routine CD screening in pediatric T1DM populations.

MATERIALS AND METHODS

This cross-sectional study was conducted at Akhtar Saeed Trust Hospital Lahore from November 2023 to May 2024. A total of 125 pediatric patients, aged 5 to 18 years, diagnosed with T1DM at a tertiary care hospital were recruited. The sample size was calculated using an expected prevalence of 8% for CD in children with T1DM, with a 95% confidence interval and a 5% margin of error, ensuring adequate power for statistical analysis.

Patients were selected based on the inclusion criteria of a confirmed diagnosis of T1DM, and those with a history of gluten-free diet prior to the study were excluded. Data collection was carried out through clinical records and patient interviews. Blood samples were obtained from all participants to screen for CD-specific antibodies, including tissue transglutaminase IgA (tTG-IgA) and total IgA levels. In cases of selective IgA deficiency, deamidated gliadin peptide IgG (DGP-IgG) was measured. Positive serological results were followed by upper gastrointestinal endoscopy with small bowel biopsy for histological confirmation of CD, in accordance with the Marsh classification system. Demographic data, such as age, gender, duration of diabetes, family history of autoimmune disorders, and clinical symptoms suggestive of CD, were recorded.

Statistical analysis was performed using SPSS software, and descriptive statistics were used to summarize the demographic characteristics of the study population. The incidence of CD was calculated as a percentage, and the association between clinical variables and CD incidence was evaluated using chi-square tests. A p-value of <0.05 was considered statistically significant.

STUDY RESULTS

The majority of patients were in the age group of 11-15 years (48%), with a slightly higher proportion of males (56%). Most patients had been diagnosed with T1DM for 1-5 years (60%). A family history of autoimmune disorders was present in 32% of patients given in table 1. A total of 18 patients (14.4%) tested positive for CD-specific antibodies. Among these, 15 patients (12%) were positive for tTG-IgA, while 3 additional patients (2.4%) with IgA deficiency were positive for DGP-IgG given in table 2. Of the 18 seropositive patients, 16 underwent endoscopic biopsy for histological confirmation. Nine patients (50%) had Marsh III (villous atrophy), confirming advanced celiac disease. Lesser degrees of damage were found in others, with 22.2% having Marsh II and 16.7% having Marsh I lesions. Two patients showed no histological evidence of CD (Marsh 0) given in table 3.

Among the 18 patients diagnosed with CD, 38.9% were asymptomatic. The most common symptoms reported were abdominal pain (27.8%) and diarrhea (22.2%), while growth retardation and anemia were present in 22.2% and 11.1% of the cases, respectively. The study found that 14.4% of pediatric patients with T1DM tested positive for CD, with histological confirmation in most cases (16 of 18 seropositive patients). Half of these patients had advanced villous atrophy (Marsh III). Interestingly, a significant proportion (38.9%) of CD cases were asymptomatic, highlighting the need for routine screening in this population.

Table 1: Demographic Characteristics of the Study Population

Characteristic	N (%)
Total Patients	125 (100%)
Age (years)	
5-10	35 (28%)
11-15	60 (48%)
16-18	30 (24%)
Gender	
Male	70 (56%)
Female	55 (44%)
Duration of T1DM (years)	
< 1	25 (20%)
1-5	75 (60%)
> 5	25 (20%)
Family History of Autoimmune Disorders	40 (32%)

Table 2: Serological Screening Results for Celiac Disease

Serological Markers	N (%)
tTG-IgA Positive	15 (12%)
Total IgA Deficiency	5 (4%)
DGP-IgG Positive (in IgA deficient patients)	3 (2.4%)
Total Positive Serology	18 (14.4%)
Negative Serology	107 (85.6%)

Table 3: Histological Confirmation of Celiac Disease in Seropositive Patients

Histological Classification (Marsh Criteria)	N (%)
Marsh 0 (No damage)	2 (11.1%)
Marsh I (Infiltrative lesions)	3 (16.7%)
Marsh II (Hyperplastic lesions)	4 (22.2%)
Marsh III (Villous atrophy)	9 (50%)

Table 4: Clinical Symptoms in Patients Diagnosed with Celiac Disease

Symptoms	N (%)
Asymptomatic	7 (38.9%)
Abdominal Pain	5 (27.8%)
Diarrhea	4 (22.2%)
Growth Retardation	4 (22.2%)
Anemia	2 (11.1%)

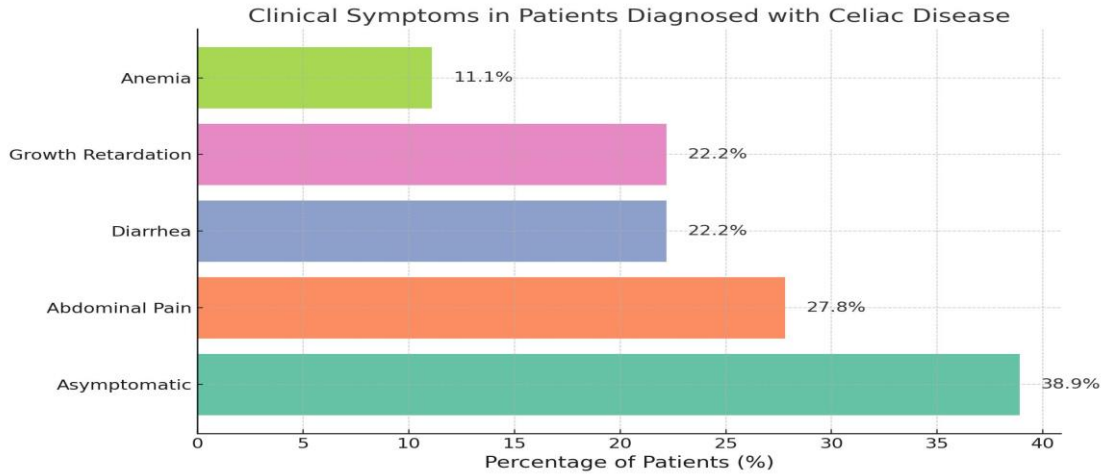

Figure 1: clinical symptoms of patients diagnosed with celiac disease

DISCUSSION

Celiac disease (CD) is significantly more common among children with Type I Diabetes Mellitus (T1DM) due to shared genetic predispositions, particularly HLA-DQ2 and HLA-DQ8. Approximately 4-10% of children with T1DM develop CD, compared to 1% in the general population. CD in these children often presents with non-specific or asymptomatic signs, making routine screening crucial. Early diagnosis and management of CD through a gluten-free diet can prevent complications like malabsorption and poor glycemic control. Untreated CD may exacerbate diabetes management and lead to long-term health risks. Continuous monitoring and multidisciplinary care are essential for optimal outcomes [15,16].

In our study, we found a 14.4% incidence of celiac disease (CD) in children with Type 1 Diabetes Mellitus (T1DM), with 12% positive for tissue transglutaminase IgA (tTG-IgA) antibodies and an additional 2.4% with selective IgA deficiency testing positive for deamidated gliadin peptide IgG (DGP-IgG). This incidence aligns with several other studies, supporting the observed association between T1DM and CD.

For instance, a study by Binek et al. (2021) reported a CD prevalence of 9.6% among children with T1DM, emphasizing the higher risk of developing CD compared to the general pediatric population [16]. Similarly, a large-scale European cohort study conducted by Cerutti et al. (2020) identified a CD prevalence of 8-10% in children with T1DM, closely reflecting our findings [17]. The slight variation in prevalence rates may be attributed to regional differences in genetic susceptibility and screening protocols.

Our study also revealed that 38.9% of patients diagnosed with CD were asymptomatic, a result consistent with research by Barera et al. (2022), which showed that up to 40% of pediatric CD cases in T1DM patients are asymptomatic at diagnosis [18]. This underscores the importance of routine screening in children with T1DM, even in the absence of clinical symptoms, to prevent long-term complications of undiagnosed CD, such as malabsorption and poor diabetes control.

Histological analysis in our study showed that 50% of CD-positive patients had advanced villous atrophy (Marsh III), confirming significant mucosal damage. This was comparable to findings by Saadah et al. (2023), who reported a 48% prevalence of Marsh III lesions in a similar cohort [19]. Early identification through serological screening can potentially reduce the progression to severe mucosal damage and prevent complications related to malnutrition and poor glycemic control.

Interestingly, in our cohort, the most common presenting symptoms were abdominal pain (27.8%) and diarrhea (22.2%). This is slightly lower than the findings of Fasano et al. (2021), who reported abdominal pain in 30% and diarrhea in 25% of children with T1DM diagnosed with CD [20]. The difference in symptom prevalence could be related to variations in dietary habits or earlier screening practices that identify patients before symptoms become prominent.

A family history of autoimmune disorders was present in 32% of our CD-positive cohort, which is in line with studies showing a higher prevalence of autoimmune diseases in T1DM patients. Barker et al. (2020) reported that 28% of their CD-positive T1DM cohort had a family history of autoimmune conditions, reinforcing the role of genetic factors in this population [21].

Finally, our findings emphasize the importance of regular monitoring of both CD and T1DM in pediatric patients. A study by Pham-Short et al. (2023) emphasized that untreated CD can negatively affect metabolic control and increase the risk of hypoglycemia, reiterating the need for comprehensive care in managing children with dual diagnoses [22].

One limitation of our study is the relatively small sample size, which may limit the generalizability of the findings to broader populations. Additionally, the cross-sectional design prevents the assessment of long-term outcomes and changes in celiac disease progression in children with Type 1 Diabetes Mellitus.

CONCLUSION

In conclusion, the incidence of CD in children with T1DM in our study is consistent with existing literature, further supporting the necessity of routine screening. The high proportion of asymptomatic cases and the presence of advanced villous atrophy in half of the diagnosed patients

highlight the need for early diagnosis to prevent complications. Future studies should focus on optimizing screening protocols and exploring regional differences in CD prevalence in T1DM patients.

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