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Original article

Prevalence and Clinical Profile of Celiac Disease in Children with Type 1 Diabetes Mellitus in Al Jabal Al Akhdar

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Abstract
To estimate the prevalence of celiac disease (CD) in children with type 1 diabetes mellitus (T1DM) and to evaluate the epidemiological and clinical profiles of CD in screened patients during follow-up. This observational study enrolled 250 children with T1DM attending the pediatric endocrinology clinic at Al-Bayda Medical Center Teaching Hospital between May 2020 and May 2022. Patients were screened for CD by evaluating immunoglobulin A (IgA) and immunoglobulin G (IgG) anti-tissue transglutaminase (anti-tTG) antibodies. A total of 250 patients (104 boys [41.6%] and 146 girls [58.4%]) with a mean age of 9.46 ± 3.28 years were included. Anti-tTG antibodies were positive in 27 patients, indicating a seroprevalence of 10.8%. Among the seropositive cases, 55.6% (15/27) were girls and 44.4% (12/27) were boys. Intestinal biopsy was performed on 7 of these patients, all of whom exhibited histological changes consistent with CD; the remaining seropositive patients declined the biopsy. Classical presentations of the disease were lacking in the majority of patients. The most frequent clinical presentation in patients with co-occurring CD and T1DM was anemia (37.0%), followed by chronic diarrhea (11.1%) and short stature (11.1%). The occurrence of anemia and chronic diarrhea was significantly higher in patients with CD compared to those with T1DM alone ($p < 0.001$ and $p = 0.029$, respectively). Celiac disease is prevalent among children with T1DM (10.8% seroprevalence) and often presents atypically, with anemia being the most common symptom rather than classical gastrointestinal features. Routine autoantibody screening is highly recommended for the early diagnosis and effective management of CD in patients with T1DM.
Keywords. Celiac Disease, Type 1 Diabetes Mellitus, Children, Anti-tTG, HLA-DQ2, HLA-DQ8.

Introduction

Diabetes mellitus (DM) is one of the most frequently seen endocrine diseases across all age groups [1]. Celiac disease (CD) is an autoimmune enteropathy characterized by a lifelong hypersensitivity to gluten, which affects the proximal intestine in genetically predisposed individuals subsequent to the intake of foods containing gluten [2, 3]. Chronic exposure to gluten can result in a higher incidence of autoimmune diseases such as autoimmune thyroid disease, connective tissue disease, Addison's disease, and type 1 DM (T1DM) [4]. The prevalence of CD in patients with T1DM is reportedly more than 20-fold higher than that seen in the general population [5, 6]. Both T1DM and CD result from a complex interplay between genetic susceptibility and environmental exposure. CD and T1DM have common autoimmune origins, both being associated with the major histocompatibility complex class II antigen DQ2 encoded by the alleles DQA1*0501 and DQB1*0201, thus providing a common genetic basis for disease expression [7, 8].

Recent research has also revealed several shared non-HLA loci associated with CD and T1DM [9]. This shared genetic basis strongly suggests a common etiology for both conditions. An increasing body of evidence suggests that T1DM and CD share many causative genetic and environmental factors, highlighting the emerging role of dietary antigens in T1DM development [10, 11]. Recent estimates indicate that the global pooled CD seroprevalence in T1DM is approximately 9%, with confirmed CD prevalence around 6% [12]. The classic presentation of CD describes symptoms related to gastrointestinal malabsorption and includes malnutrition, failure to thrive, diarrhea, anorexia, constipation, vomiting, and abdominal pain. This predominance of gastrointestinal symptoms is most common in children younger than three years of age [13].

Non-gastrointestinal or atypical symptoms of CD include short stature, pubertal delay, fatigue, vitamin deficiencies, and iron deficiency anemia, which are more commonly observed in older children [14]. The classical presentation of CD can occur in T1DM patients, but many patients with CD and T1DM are either asymptomatic (silent CD) or present with only mild symptoms [15]. The introduction of serologic testing has facilitated screening in at-risk populations for CD, including those with T1DM. Among the antibodies found in CD, screening tests for tissue transglutaminase (tTG) IgA have been reported to be the most sensitive and specific for initial detection [16].

The present study is designed to determine the prevalence of celiac disease among children diagnosed with type 1 diabetes mellitus, thereby providing insight into the extent of comorbidity between these two conditions. In addition, it seeks to evaluate the epidemiological and clinical profile of celiac disease in the screened population, with the aim of identifying characteristic patterns that may inform both early detection and effective management strategies. By integrating prevalence data with clinical and epidemiological observations, the study endeavors to contribute to a more comprehensive understanding of the intersection between autoimmune disorders in pediatric patients.

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Methods

Study Design and Population

This was an observational case-series study conducted at the pediatric endocrinology clinic of Al-Bayda Medical Center, Libya. The study enrolled 250 children diagnosed with T1DM who were receiving insulin therapy over a two-year period from May 2020 to May 2022. The study was approved by the Institutional Ethics Committee. Informed consent was obtained from the parents, as well as from children over 7 years of age, prior to enrollment.

Inclusion and Exclusion Criteria

Inclusion Criteria

The study population consisted of children between the ages of 1.5 and 16 years who had been diagnosed with type 1 diabetes mellitus. All participants were under regular follow-up at the endocrinology clinic, which provided a consistent framework for clinical monitoring and facilitated systematic screening for celiac disease within this cohort.

Exclusion Criteria

Children diagnosed with type 2 diabetes mellitus were excluded from the study, as were those with secondary forms of diabetes resulting from genetic defects in beta-cell function or insulin action. Additional exclusions included patients with diabetes secondary to pancreatitis, cystic fibrosis, or hemochromatosis. These criteria were established to ensure that the study population was restricted to individuals with type 1 diabetes mellitus, thereby maintaining homogeneity and minimizing confounding factors in the assessment of celiac disease prevalence and clinical characteristics.

Data Collection and Clinical Assessment

A comprehensive medical history and complete physical examination were performed for all patients. Patient records were reviewed to register information, including age of onset of DM, duration of the disease, and the presence of gastrointestinal or atypical symptoms suggestive of CD (e.g., diarrhea, abdominal pain, loss of weight, failure to gain weight, anemia, and stunted growth). Anthropometric parameters, including height and weight, were measured for all patients and plotted on appropriate growth charts.

Laboratory Investigations and Diagnosis

Patients were screened for CD using specific serological markers, primarily anti-tissue transglutaminase (anti-tTG) IgA and IgG class antibodies evaluated by ELISA. According to the study protocol, any patient testing positive for anti-tTG antibodies was referred for endoscopy to obtain a biopsy from the distal part of the second portion of the duodenum to confirm CD. The histopathologic diagnosis of CD was based on characteristic changes such as partial or complete villous atrophy associated with crypt hyperplasia and a lymphoplasmacytic infiltration in the lamina propria (Marsh classification).

Statistical Analysis

Data were analyzed using appropriate statistical methods. For comparisons between anti-tTG-positive and anti-tTG-negative groups, qualitative data were analyzed in the form of frequencies and percentages. The association between discrete variables was assessed using the Chi-square test and Fisher's exact test where appropriate. Quantitative data were represented by mean ± standard deviation (SD) and median. A p-value of ≤ 0.05 was considered statistically significant.

Results

A total of 250 patients with T1DM were included in the study, comprising 104 males (41.6%) and 146 females (58.4%). The age of the patients ranged from 1.5 to 16.0 years, with a mean age of 9.46 ± 3.28 years (Table 1).

Table 1. Distribution of the studied cases according to demographic data.

Demographic Characteristics	Number (n = 250)	Percentage (%)
Sex		
Male	104	41.6
Female	146	58.4
Age Groups (years)		
< 5	23	9.2
5 – 10	127	50.8
> 10	100	40.0
Age Statistics		
Min – Max	1.5 – 16.0	-
Mean ± SD	9.46 ± 3.28	-
Median (IQR)	10.0 (8.0 – 12.0)	-

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Anti-tTG antibody testing revealed that 27 patients (10.8%) were seropositive for CD. Among these 27 positive cases, 15 were female (55.6%), and 12 were male (44.4%). There was no statistically significant difference in CD prevalence between genders (p = 0.751).

Table 2. Distribution of cases according to anti-tTG antibodies and biopsy confirmation.

CD Screening Results	Number	Percentage (%)
Anti-tTG positive	27	10.8
Biopsy confirmed	7	2.8

Of the 27 seropositive patients, 7 consented to and underwent duodenal biopsy. All 7 patients (100%) showed positive histopathological changes consistent with CD. The remaining 20 patients refused the biopsy procedure. Consequently, the prevalence of biopsy-confirmed CD in the total study population was 2.8%. The mean age at the diagnosis of CD was 6.56 years. The majority of CD diagnoses (74%) occurred in children between the ages of 4 and 8 years. Regarding clinical presentation, the majority of the total study population (90.4%, n=226) were asymptomatic for CD-related complaints, while 9.6% (n=24) exhibited symptoms. When comparing the clinical profiles of T1DM patients with and without CD (Table 3), atypical presentations were prominent.

Table 3. Comparison of clinical parameters between T1DM patients with and without CD. (* Statistically significant)

Clinical Parameter	T1DM without CD (n = 223)	%	T1DM with CD (n = 27)	%	p-value
Chronic abdominal pain	18	8.1	2	7.4	1.000
Chronic diarrhea	4	1.8	3	11.1	0.029*
Short stature (below -2 SD)	6	2.7	3	11.1	0.061
Anemia	2	0.9	10	37.0	<0.001*

Anemia was the most frequent clinical presentation in patients with co-occurring CD and T1DM, affecting 37.0% of these patients, compared to only 0.9% of patients with T1DM alone (p < 0.001). Chronic diarrhea was also significantly more common in the CD group (11.1% vs. 1.8%, p = 0.029). Short stature was observed in 11.1% of the CD group compared to 2.7% of the non-CD group, though this difference approached but did not reach statistical significance (p = 0.061).

Discussion

The current study identified a seroprevalence of CD in children with T1DM of 10.8%, with a biopsy-confirmed prevalence of 2.8% (limited by biopsy refusal). This seroprevalence aligns closely with recent global meta-analyses, which report a pooled CD seroprevalence of 9% (95% CI 8%-10%) in T1DM patients, with higher rates observed in the Middle East and North Africa [12]. Our findings are consistent with studies from Egypt (11.2%) [17] and Saudi Arabia, reflecting the higher prevalence rates frequently observed in Arab populations compared to Western countries. For instance, lower prevalence rates have been reported in Germany (6.4%) and the US [18]. Although girls constituted a slightly higher proportion of the seropositive cases (55.5%), the difference was not statistically significant. This trend is consistent with other international studies that often show a slight female predominance in autoimmune comorbidities [19]. A critical finding of our study is the clinical profile of CD in these patients. The classical presentation of CD, such as chronic abdominal pain, was not the predominant feature. Instead, atypical presentations, particularly anemia, were highly significant. Anemia was present in 37.0% of the CD group compared to only 0.9% of the T1DM-only group (p < 0.001). This emphasizes that the absence of classic gastrointestinal symptoms does not rule out CD. Recent literature supports this shift in clinical presentation; a North American study reported that over 70% of children with diabetes reported no gastrointestinal symptoms at the time of a positive CD screen [20]. Furthermore, short stature was observed in 11.1% of our CD patients. While the statistical significance was marginal (p = 0.061), likely due to sample size, it highlights the impact of unrecognized malabsorption on growth. Height was significantly above the 3rd percentile in most diabetics without CD, whereas a higher proportion of those with CD fell below the 3rd percentile. This indicates the importance of monitoring linear growth in patients with T1DM, as a decline in growth velocity may be an early indicator of co-occurring CD [21]. The primary limitation of this study was the low rate of biopsy confirmation, as 20 out of 27 seropositive patients refused the invasive procedure. While the ESPGHAN guidelines permit a non-biopsy approach for diagnosing CD in certain pediatric populations (if TGA levels exceed 10 times the upper limit of normal and EMA is positive), the evidence for applying this non-biopsy approach specifically in asymptomatic children with T1DM remains limited and requires further prospective validation [22, 23]. Therefore, reliance on serology alone may overestimate the true prevalence, but it underscores the necessity of rigorous screening.

Conclusions

Celiac disease is highly prevalent among children with T1DM in our region, with a seroprevalence of 10.8%. The disease frequently presents atypically; anemia is significantly more common than classical gastrointestinal features like

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abdominal pain. Because CD can present either asymptomatically or with non-specific symptoms in T1DM patients, reliance on clinical suspicion alone is insufficient.

Recommendations

Routine serological screening for celiac disease, employing anti-tTG IgA and total IgA assays, should be considered mandatory for all children diagnosed with type 1 diabetes mellitus, particularly within the first five years following diagnosis. Clinicians are urged to maintain a high index of suspicion for celiac disease in patients presenting with atypical or non-classical manifestations, such as unexplained anemia or impaired linear growth, as these may represent subtle indicators of underlying pathology. In addition to clinical vigilance, greater emphasis on public health education is required to enhance patient and parental acceptance of intestinal biopsy as the definitive diagnostic tool. At the same time, future research should continue to explore the safety and reliability of non-biopsy diagnostic criteria within the type 1 diabetes population, thereby balancing diagnostic accuracy with patient-centered care.

Conflict of interest. Nil

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