Research Article

Screening of celiac disease among children with type one diabetes mellitus in Rapareen teaching hospital for children in Erbil City

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Abstract

Background:
Celiac disease is autoimmune disorder characterized by immune mediated damage to the lining of small intestinal resulting from the consumption of gluten. A significant occurrence of Celiac disease is recorded in multiple autoimmune diseases like type 1 diabetes mellitus. Both disorders are associated with genetic loci on short arm of chromosome six. Aim of study: To determine the frequency of Celiac disease among a group of children diagnosed with type one diabetes mellitus.

Patients and methods:
A prospective observational cross sectional study conducted in Pediatric Endocrinology Clinics of Rapareen teaching hospital for children in Erbil City-Kurdistan region /Iraq through the period of six months from 01 July 2024 to 01 January 2025. 100 children and adolescent with type one diabetes mellitus were involved in the study ageing less than 18 years old.

Results:
From 100 patients with type one diabetes, 7% diagnosed with celiac disease were confirmed by duodenal biopsy and one patient with positive serology but duodenal biopsy was normal. The risk will be higher among diabetic children with anemia ,growth failure ,poorly controlled diabetes and positive consanguinity compared to non-celiac children, with the strongest associations observed for short stature (RR 6.64) and weight loss (RR 4.98).

Conclusions:
This research indicates a 7% prevalence of celiac disease confirmed by biopsy among children and adolescents with type one diabetes in Erbil city. The risk is higher in those with growth failure, anemia or poorly controlled diabetic patients and those with duration of diabetes more than 3 years.

Introduction

Background

Celiac disease (CD) is an autoimmune disorder characterized by immune-triggered damage to the small intestine's mucosa resulting from gluten consumption, a complex protein present in wheat, rye and barley (1). It affects about 1% of the overall population. A significant number of people with celiac disease exhibit HLA-DQ2, while a smaller subset tests positive for HLA-DQ8 (2).
CD and T1DM (type 1 diabetes mellitus) have shared autoimmune origins. The connection between the two is established through the major histocompatibility complex class II antigen DQ2, which is encoded by the alleles DQB1∗201and DQA1∗501, thereby providing a shared genetic foundation for disease manifestation.(3)
Recent studies have identified 7 common non-HLA loci linked to T1DM and CD, including RGS1 on chromosome 1q31, IL18RAP on chromosome 2q12, TAGAP on chromosome 6q25, PTPN2 on chromosome 18p11, CTLA4 on chromosome 2q33, SH2B3 on chromosome 12q24, and a 32-bp insertion-deletion variant located on chromosome 3p21 (4 ,5). Worldwide, the prevalence of CD in the overall population is around 1 percent, increasing 5 to 7 times in connection with T1DM (4)
Patients with T1DM can have the classical presentation of CD, though many patients with T1DM and CD are either have mild symptoms with the absence of both gastrointestinal and extra-intestinal signs or asymptomatic (silent CD) (3,6), some exhibit atypical features likeas short stature, osteopenia,delayed puberty, refractory anemia and

other autoimmune disorders like autoimmune hepatitis and thyroiditis (6).

Patients & Methods

This study was a prospective observational cross-sectional study conducted in Pediatric Endocrinology Clinics of Rapareen teaching hospital for children in Erbil City-Kurdistan region /Iraq through the period of six months from 01 July 2024 to 01 January 2025. A convenient sample of 100 type 1 diabetes patients aged 1 to 18 years were chosen from the endocrinology Consultation Clinic at Rapareen Teaching Hospital following the inclusion and exclusion criteria.

Inclusion criteria

1. Age 0- 18 years.
2. Known cases of type 1 diabetes mellitus.

Exclusion criteria

1. Children with type 2 diabetes, or diabetes resulting from confirmed genetic defects impacting beta cell function or insulin action, as well as those with pancreatitis, cystic fibrosis, and hemochromatosis, were not included in the study.
2. Who refused to participate.

Each of them has been asked questions in the questioner prepared include
general and clinical characteristics followed by investigations that include Hemoglobin level, HbA1C, Total IgA, Anti-tissue transglutaminase IgA (anti-tTG IgA) and Anti-tissue transglutaminase IgG.

For patients who tested positive for anti-tTG IgA, a duodenal biopsy has been performed. Biopsy samples has obtained through an endoscopic procedure at gastroenterology department and specimens then to be evaluated and classified according to Marsh classification (6). The WHO criterion was used to diagnose anemia and the degree of anemia was further categorized accordingly while diabetic control was categorized following SIPAD clinical guidelines (7)

Poor glycemic control is defined as HbA1c is more than 7.5% and Good glycemic control is defined as HbA1c is less than 7.5%.

Ethical considerations

Approval was received from the Arab Board of Health Specializations.

Verbal informed consent was obtained from the patients and caregivers participating in the study.

The data of all patients was inputted using computerized statistical software, specifically the Statistical Package for Social Sciences (SPSS), version 25. Descriptive statistics were expressed as (mean ± standard deviation) and frequencies as percentages. Various tables were created with the Chi square test applied to categorical variables and later estimate relative risks. The significance level (p value) established at ≤ 0.05, with results presented in tables.

Results

Majority of studied sample were of age group between 7-12 years ,with slight female predominance and around 10% are either short or not gain weight properly. Surprisingly 65% of patients have positive history of autoimmune disease in one or more of their first- or second-degree relatives, ten of them were proven celiac (table 1)

Only 8% were positive for Antitissue TGA IgA antibodies with no reported cases of low IgA. After endoscopic evaluation of those 8 children ,one was excluded as histopathologically was negative and remained 7 confirmed celiac (7%). All of them have duration of diabetes for more than 3 years with mean age of 9.14 ± 2.69. Four of the patients had Marsh class 3a while most frequent endoscopic findings was mosaic pattern.(table 2)

In table 3 , when compare confirmed cases with other cases (non-celiac) , Diabetic with Celiac are ~2 times more likely to have anemia (RR = 2.16) while poorly controlled diabetics and parental consanguinity slightly increase risks. Highest risks were related to weight loss (around 5 folds increase, RR 4.98) and short stature (around six folds increase, RR 6.64) ,also 4 folds increase with longer duration of diabetes.

Table 1 : General and clinical characteristics of participants

Variables	Category	*n*=100 (100%)
Age (years)	1-3	2 (2%)
	4-6	26 (26%)
	7-12	53 (53%)
	13-18	19 (19%)
Gender	Male	43 (43%)
	Female	57 (57%)
Weight for age	Below 3rd percentile	8(8%)
	Normal	92(92%)
Height for age	Below 3rd percentile	10(10%)
	Normal	90(90%)
Parental consanguinity present		65(65%)
Duration of diabetes	Below 3 years	70(70%)
	≥ 3 years	30(30%)
Family history of autoimmune disease		9(9%)
Family history of diabetes		3(3%)
Family history of celiac disease		10(10%)

Table 2 screening and diagnostic evaluation results of participants

Variables	Category	*n*=100 (100%)
Anemia		71(%)
HbA1c ,controlled		34(%)
anti-tTG IgA (U/ml) positive		8(%)
anti-tTG IgG (U/ml) positive		10(%)
Total IgA mg/dl	Normal	89(%)
	Above normal	11(%)
Endoscopic findings	Decrease doudenal folds	1(%)
	Granular pattern	2(%)
	Mosaic pattern	4(%)
	Normal	1(%)
Histopathological findings		7(%)
Marsh classification	0	1(%)
	3a	4(%)
	3b	2(%)

	3c	1(%)

Table 3: Comparison of Clinical Features and Risk Estimates Between Celiac and Non-Celiac Children

	Non celiac (93)	Celiac (7)	Relative risks	CI 95%	
Anemia	43	7	2.16	(1.74 to 2.69)	< 0.0001
Weight loss	8	3	4.98	1.6886 to 14.6995	0.0036
Short stature	10	5	6.64	3.1381 to 14.0617	< 0.0001
Parental consanguinity	65	7	1.28	1.1402 to 1.4300	< 0.0001
Poor controlled	59	7	1.58	1.3509 to 1.8392	< 0.0001
Duration of diabetes ≥ 3 years	23	7	4.044	2.8364 to 5.76	< 0.0001

Discussion:

The coexistence of type 1 diabetes and coeliac disease has historically been linked with the presence of common high-risk human lymphocyte antigen (HLA) genotypes (DR-DQ) (7,8). Recent studies suggest that environmental or non-genetic variables significantly contribute to the development of certain disorders (8). Individuals with Type 1 Diabetes Mellitus are at an elevated risk of developing Coeliac Disease (9). The risk to develop CD among T1DM patients is around 5%, though the general population risk is near 1% (9). Globally, the risk of both diseases coexisting together differs with rate of 0.6% in Germany, 1.6% in France, 2.4% in Finland, 6.8% in Italy, 9.7% in Sweden 10.4% in Denmark and 11.1%-16.4% in North India and Algeria (9,10,11,12). A study conducted on 152 diabetic patients in children welfare hospital for pediatrics in Baghdad revealed 8.6 rate confirmed by biopsy.(13) In our study the rate of celiac disease among T1DM patients is 7% and it is close to mentioned records.

Noticing the diagnosed celiac cases were in scholar age group and adolescent (5%-2%) subsequently. Nevertheless, age had no statistical significant association to the diagnosing with celiac disease, which was of similar results in other studies too.(2) In contrast to these results, few studies found out that the risk is higher in younger patients with type 1 diabetes, and mainly in childhood (6). Numerous studies indicate that being female is a risk factor for celiac disease, with female patients having nearly double the likelihood of developing the condition compared to male patients as our study revealed but with no major difference (6, 10,12).

The prevalence of CD in patients with T1DM has been claimed to be nearly 1% to 4% among first-degree relatives (5,14). In our study the first degree parent consanguinity among all T1DM patients was 65%, and 100% in CD patients with slight increase risk of developing celiac as demonstrated in table 3.

Presence of autoimmune diseases in the family has been mentioned in literatures to increase the odds of CD, and the coexistence of hypothyroidism (4). Another study as well agreed to this whereas the prevalence of overt hypothyroidism was 8.4% (5). Our patients had 9% positive family history of autoimmune disease from which 3 were positive for T1DM.

Within the study ,10% of the participants declared positive celiac disease history and all the celiac positive cases had a family history. These results were consistent with other studies as well.(14,15)

Only 8 patients with positive serology ,biopsy exclude one case and other 7

biopsy-confirmed celiac patients. Available data in Iraq revealed 23% positive serology with 13 proved by histopathological report ,this high serology prevalence is justified by using different screening test (Antigliadin Antibody).(13) Four patients showed Mosaic pattern of mucosa with 3a in Marsh classification ,an Italian study 50% of children and 25% of adults had nonfocal or “patchy” histopathologic lesions in their duodenal samples but there are no known significant reports support correlation of endoscopic findings with histological results (1,16)

Growth failure is known previously as a common presentation of celiac, nearly half of studied children either short or improperly gain weight and both highly increase risk of developing celiac. In some studies, researchers had reported about one third of children with celiac disease are short stature (13 ,17), another one reported that short stature was a presentation in 52.3% of CD-T1DM patients (5). Diabetic children with celiac exhibit lower weight and height when compared to non- Celiac. Duration of T1DM significantly associated with high risk of celiac with long lasting cases prone to have CD as most data validate it.(13)
Gluten-free diet therapy in patients with CD did not affect HbA1c levels (18) Limited data exist on HbA1c levels in older children with coexisting type 1 diabetes with celiac. Some reports showed higher HbA1c levels in (19), while others with no significant difference (20).
Anemia is seen often in patients with celiac disease in which Iron deficiency anemia is common among patients with CD and has been reported in as much as 46% of cases (5). In this study, 71% of the participants had anemia, and all the celiac disease patients had anemia with 2 fold risk increment. This was relevant to the results in another study where >50 % had anemia (5).

Limitations of the study: The celiac group is **very small (n = 7)** so Several cells likely have **very low** This can inflate relative risks and reduce reliability

Conclusions:
This research indicates a 7% prevalence of celiac disease confirmed by biopsy among children and adolescents with type one diabetes in Erbil city. The risk is higher in those with growth failure, anemia or poorly controlled diabetic patients and those with duration of diabetes more than 3 years.

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