P-ISSN: 2664-3685
E-ISSN: 2664-3693
www.paediatricjournal.com
IJPG 2025; 8(1): 01-04
Received: 06-11-2024
Accepted: 08-12-2024

Abeer Degan Abdul
Amir, Babylon Health Directorate, Babylon, Iraq

Jehan Jasim Kadhim
Al-Najaf Health Directorate, Al-Najaf, Iraq

Samaher Thamer Hamza
Babylon Health Directorate, Babylon, Iraq

Corresponding Author:
Abeer Degan Abdul
Amir, Babylon Health Directorate, Babylon, Iraq

Prevalence rate of antitussive transglutaminase antibodies in type 1 diabetic children

Abeer Degan Abdul, Jehan Jasim Kadhim and Samaher Thamer Hamza

DOI: https://doi.org/10.33545/26643685.2025.v8.i1a.253

Abstract
Background: The association of celiac disease and type I diabetes mellitus is known worldwide due to shared auto immunological background, since celiac disease could present in diabetic patients with nonspecific symptoms or asymptomatically, so follow up and screening is necessary for early diagnosis. To estimate the prevalence of celiac disease in children with TIDM.
Methods: This is a cross sectional study comprised all the Validate diabetic children seen in our wards, emergency unit consultation department in AL Zahraa Teaching Hospital for Maternity and Child health in AL Najaf AL-Ashraf city from November 2015 through October 2016.
Results: We enrolled 53 children with TIDM (25 males and 28 female) age of patients in this study ranging from I.3/12 to 15 years. Anti-tissue transglutaminase antibody was positive in 7/53 patients, more in girls (5/28), (2/25) of boys, making the prevalence of celiac disease 13.2%. Female number more than male, but without statistical significance. Anti-tissue transglutaminase antibody was positive in 7/53patients, more in girls (5/28), (2/25) of boys, making the prevalence of celiac disease 13.2%. Female number more than male, but without statistical significance.
Conclusion: The prevalence of celiac Disease in type I diabetes mellitus in our study show a relatively high prevalence compared with other studies. Therefore, screening and follow up of patients by Anti tissue transglutaminase antibodies is recommended for all patients with type I diabetes.

Keyword: Celiac disease, tissue transglutaminase antibodies, type I diabetes mellitus

Introduction

Type 1 Diabetes Mellitus (TIDM) and Celiac Disease (CD) are chronic autoimmune disorders characterized by an interplay of genetic susceptibility and environmental triggers [1]. The co-occurrence of these diseases has drawn significant attention due to their shared autoimmune etiology, with the prevalence of CD in TIDM patients reported to be 5-7 times higher than in the general population [2, 3]. This association was first hypothesized in 1954, marking the beginning of a longstanding interest in the interrelationship between these conditions [4]. TIDM is a chronic autoimmune disorder resulting in the immune-mediated destruction of pancreatic β-cells, leading to varying degrees of insulin deficiency [5]. It is primarily classified into type 1a (autoimmune) and type 1b (idiopathic) diabetes. The autoimmune form, accounting for the majority of cases, is associated with islet cell autoantibodies against insulin, GAD65, IA-2, and ZnT8, as well as specific high-risk HLA haplotypes (DR4, DQ8, and DR3/DQ2) [6]. TIDM represents 5-10% of diabetes cases globally and is most prevalent in children and adolescents, with incidence peaks at 5-7 years and near puberty [6, 7]. CD, an autoimmune enteropathy triggered by gluten ingestion, is characterized by small intestinal lesions and variable clinical presentations. It is commonly associated with HLA-DQ2 or HLA-DQ8 genotypes, with over 95% of CD patients carrying one of these haplotypes [8, 9]. Although initially considered rare outside of Europe, CD is now recognized worldwide, with a prevalence of 2-8% among TIDM patients in regions like Iran, Israel, and Saudi Arabia [10]. The pathogenesis of both TIDM and CD involves a complex interplay of genetic and environmental factors. In TIDM, T-cells reactive against β-cell antigens infiltrate the pancreas, leading to β-cell destruction and insulin deficiency [11]. Similarly, CD pathogenesis involves glia din-induced intestinal damage in genetically predisposed individuals, with contributing factors such as viral infections, timing of gluten introduction, and breastfeeding cessation [12, 13]. Both conditions pose significant diagnostic and management challenges. The diagnosis of TIDM is established based on hyperglycemia criteria, while CD diagnosis requires serological testing and small intestinal biopsy [14, 15].

Effective management of CD involves a strict gluten-free diet, which not only alleviates symptoms but also reduces the risk of complications such as osteoporosis and lymphoma [16, 17]. Similarly, TIDM management relies on glycemic control through insulin therapy, tailored nutrition, and regular exercise to mitigate acute and chronic complications [18, 19]. The overlapping nature of TIDM and CD underscores the need for a multidisciplinary approach to diagnosis, management, and long-term monitoring. Screening for CD in TIDM patients at diagnosis and during follow-up is crucial to detect silent or subclinical cases and initiate timely interventions [20]. This study aims to evaluate the seroprevalence of positive serology of celiac disease in type I diabetic patients and the risk of the disease in those patients.

Methods

This cross-sectional study included all validated diabetic children seen in the emergency and consultation departments of Al-Zahraa Teaching Hospital for Maternity and Child Health in Al-Najaf Al-Ashraf from November 2015 to October 2016. A total of 53 children with type 1 diabetes mellitus (TIDM) were enrolled, comprising 25 males and 28 females, with ages ranging from 13 months to 15 years. All patients had a prior diagnosis of TIDM based on the criteria of the American Diabetes Association and were on insulin therapy. After explaining the study's objectives, oral consent was obtained from the patients and their parents. The study involved physician interviews with parents and physical examinations of all enrolled patients. Data collected included patient age, gender, duration of diabetes, consanguinity, type of feeding during the first six months of life, and the age at which a gluten-containing diet was introduced. A 2 mL venous blood sample was collected from each patient, placed in a tube without anticoagulant, centrifuged for serum separation, and immediately stored at -20°C for later analysis. All samples were tested for anti-tissue transglutaminase (tTG) IgA and IgG antibodies using ELISA kits (CHORUS tTg-A code and tTg-G code 86060, Italy). The kit's cutoff value was set at 20 U/mL, values below 20 U/mL were considered normal, while values equal to or above 20 U/mL were deemed positive. Results, whether positive or negative, were recorded in each patient's medical record. Patients with positive celiac serology were referred to a gastroenterology clinic for further evaluation and management. Data analysis was conducted using SPSS software version 20. Results were expressed as frequencies and percentages. Chi-square tests were used for categorical variables, and independent t-tests were employed for comparisons of means. A p-value of ≤ 0.05 was considered statistically significant.

Results

There were 53 patients included in this study, about 28 of them (52.8%) were female and 25 (47.2%) were male, their age range were thirteen months to 15 years with a mean 93.9 ±42.6, mean age at time of diagnosis was 5.2+ 2.9 years ,while mean duration of disease 2.6±2.9 years. Celiac disease screen results shows that only 7 patients (13.2%) were positive entity antibodies, 5 of them (71.4%) were female and 2(28.6%) were male comparing to 46 patients with negative results 23 male (50%) and 23 female (50%) According to present data, the statistical analysis does not found significant association between gender and celiac screen, (P-Value 0.3), as shown in Table 1.

Table l: Distribution of the study group by gender and celiac screen

ATT	Gender		Total	P-Value
	Male	Female		
Positive	2(28.6%)	5 (71.4%)	7	0.3
Negative	23 (50%)	23 (50%)		
Total	25 (47.2%)	28 (52.8%)	53	

x^2-l. l, P=0.3

As shown in Table 2, there was a significant correlation between the age of children with TIDM and positivity for Anti- tTG antibody (P=0.03). The age at diagnosis of TIDM was less in patient positive for celiac screen (3.01±1.8) than those with negative results (5.5±2.9). Moreover, the duration of the disease in patients with negative Anti-tTG antibody was shorter than patients were positive for Anti-tTG antibody. While, there was no significant difference regarding duration of disease and positivity for Anti-tTG antibody (P=0.3).

Table 2: Distribution of the study group by Age at diagnosis of DM, duration of DM

Parameter	Positive, Mean ± SD	Negative, Mean ± SD	P-Value
Age at diagnosis of DM	3.01±1.8	5.5±2.9	0.03
Duration of DM	3.5±2.5	2.5±2.9	0.3

Even, Consanguinity was positive in 5 (71%) patient who were positive for celiac disease, comparing to 22(48%) who were negative, however there was no statistical differences among them P=0.2. as shown in Table 3.

Table 3: The distribution of consanguinity and their celiac screen results

ATT	Consanguinity (Not Relative)	Consanguinity (Relative)	Total	P-Value
Positive	2 (28.6%)	5 (71.4%)	7	0.2
Negative	24 (52.2%)	22 (48.8%)	46	
Total	26 (49.1%)	27 (50.9%)	53	

As shown in Table 4, and regarding Age of gluten introduction before or after 6 months, present study demonstrated that only one patient who was positive for celiac screen started gluten before 6 months, thus there was no significant correlation P=0.4.

Table 4: Age of gluten introduction and celiac screen results

ATT	Age of gluten introduction		Total	P-Value
	Before 6th month	After 6th month		
Positive	1(14.3%)	6 (85.7%)	7	0.4
Negative	13 (28.3%)	33 (71.7%)	46	0.4
Total	14 (26.4^0/0)	39 (73.6%)	53	

In Table 5. the patient with exclusive breast feeding during the I st 6 months of life higher than those with mixed or Bottle feeding (64.2%, 22.6%, 13.2%) respectively. According to present data we demonstrated that number and percentage of child with celiac disease was found to be less in exclusive breast feeding than those patients with mixed feeding (28.6%, and 57.1%) respectively). However, this results are statistically not significant p value =0.06.

Table 5: Type of feeding during Ist 6 months of life related to celiac screen result

ATT	Feeding			Total	P-Value
	Bottle	Breast	Mixed		
Positive	104.3%)	2 (28.6%)	4(57.1%)	7	0.06
Negative	6 (13%)	32 (69.6%)	807.4%)	46	
Total	7 (13.2%)	34 (64.2%)	12(22.6%)	53	

Discussion

The prevalence of celiac disease (CD) among children with type 1 diabetes mellitus (TIDM) in this study was 13.2%. This rate is consistent with findings from similar studies in the Middle East, including 11.6% reported in Baghdad [17] and 14.4% in southern Iran [21]. However, it was lower than the 16% prevalence observed in Children Welfare Teaching Hospital in Iraq [22] and higher than the 2.4% reported in Finland [23]. Globally, the prevalence of CD in TIDM varies significantly due to factors such as screening methods, sample size, age distribution, genetic predispositions, and environmental influences. The high prevalence in the Middle East may be related to higher rates of consanguinity and dietary dependence on wheat [24]. In this study, females were more commonly affected (71.4%) than males (28.6%), though the difference was not statistically significant (P=0.3). This trend aligns with studies by Al-Hussaini [25] and Kordonouri [26] but contrasts with findings by Araújo *et al*. [27]. The increased prevalence of autoimmune diseases in females may partially explain this gender disparity. Additionally, consanguinity was not significantly associated with CD in TIDM (P=0.2), a finding consistent with similar studies in the region. Age at diagnosis of diabetes was significantly lower in tTGA-positive patients than in tTGA-negative patients (P=0.03), highlighting the higher risk of CD in younger children. This observation agrees with study by Cerutti F *et al*. [28], which suggest an elevated CD risk in younger age groups. Regarding feeding practices, no significant relationship was found between exclusive breastfeeding or bottle feeding and CD development (P=0.06). This may reflect the strong genetic association between TIDM and CD, as over 90% of CD patients share high-risk HLA genotypes [22, 26]. Timing of gluten introduction before or after six months was also not significantly associated with CD risk, a finding consistent with Ziegler *et al*. [29] but differing from Ivarsson *et al*. in Sweden (P=0.001) [30]. These variations may result from genetic factors and the amount of gluten exposure rather than the timing. Most CD cases in TIDM patients are atypical or silent, detected only through screening. This highlights the importance of early detection to prevent complications such as poor growth and diabetic control. While biopsy remains the gold standard for CD diagnosis, anti-tTG tests, particularly IgA and IgG, offer a less invasive and cost-effective initial screening tool. This approach aligns with findings by Kordonouri *et al*. [26], emphasizing the utility of anti-tTG testing for early detection in TIDM patients.

Conclusion

The seroprevalence of CD among children with TIDM was 13.2%, with no significant association with gender (P=0.3) or consanguinity (P=0.2). Younger age at diabetes onset (P=0.03) and longer TIDM duration were associated with positive celiac serology. Feeding type and timing of gluten introduction during infancy showed no correlation with CD autoantibodies.

References

1. Fasano A. Clinical presentation of celiac disease in the pediatric population. Gastroenterology, 2005.
2. Smyth DJ, Plagnol V, Walker NM, Cooper JD, Downes K, Yang JH, Howson JM, Stevens H, McManus R, Wijmenga C, Heap GA, Dubois PC, Clayton DG, Hunt KA, van Heel DA, Todd JA. Shared and distinct genetic variants in type 1 diabetes and celiac disease. N Engl J Med. 2008 Dec 25;359(26):2767-77. DOI: 10.1056/NEJMoa0807917. EPUB 2008 Dec 10. PMID: 19073967; PMCID: PMC2840835.
3. Aktay AN, Lee PC, Kumar V, *et al*. The prevalence and clinical characteristics of celiac disease in juvenile diabetes in Wisconsin. J Pediatr Gastroenterol Nutr. 2001;33(4):462-465.
4. Mahmud FH, Murray JA, Kudva YC, Zinsmeister AR, Dierkhising RA, Lahr BD, *et al*. Celiac disease in type 1 diabetes mellitus in a North American community: prevalence, serologic screening, and clinical features. Mayo Clin Proc. 2005 Nov;80(11):1429-34. DOI: 10.4065/80.11.1429. PMID: 16295022; PMCID: PMC2128722.
5. Atkinson MA, Eisenbarth GS. Type 1 diabetes: New perspectives on disease pathogenesis and treatment.

Lancet. 2001;358:221-229.
6. Svoren BM, Jospe N. Diabetes mellitus in children. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, editors. Nelson Textbook of Pediatrics. 20th ed. Canada: Elsevier, 2016, p. 2760-2783.
7. Harjutsalo V, Sjöberg L, Tuomilehto J. Time trends in the incidence of type I diabetes in Finnish children: A cohort study. Lancet. 2008;371:1777-1782.
8. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. Gastroenterology. 2001 Feb;120(3):636-51. DOI: 10.1053/gast.2001.22123. PMID: 11179241.
9. Heap GA, van Heel DA. Genetics and pathogenesis of coeliac disease. Semin Immunol. 2009;21:346-354.
10. Ciclitira PJ, Moodie SJ. Transition of care between paediatric and adult gastroenterology. Coeliac disease. Best Pract Res Clin Gastroenterol. 2003 Apr;17(2):181-95. DOI: 10.1016/s1521-6918(02)00147-6. PMID: 12676114.
11. Kim HS, Lee M. Role of innate immunity in triggering and tuning of autoimmune diabetes. Curr Mol Med. 2009;9:30-44.
12. Kupper C. Dietary guidelines and implementation for celiac disease. Gastroenterology. 2005;128:S121-S127.
13. Shan L, Molberg Ø, Parrot I, Hausch F, Filiz F, Gray GM, *et al*. Structural basis for gluten intolerance in celiac sprue. Science. 2002 Sep 27;297(5590):2275-9. DOI: 10.1126/science.1074129. PMID: 12351792.
14. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010 Jan;33 Suppl 1(Suppl 1):S62-9. DOI: 10.2337/dc10-S062. Erratum in: Diabetes Care. 2010 Apr;33(4):e57. PMID: 20042775; PMCID: PMC2797383.
15. Hill ID, Dirks MH, Liptak GS, *et al*. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr. 2005;40:I-19.
16. Binkley N, Bilezikian JP, Kendler DL, *et al*. Summary of the International Society for Clinical Densitometry 2005 Position Development Conference. J Bone Miner Res. 2007;22(5):643-645.
17. Obaid A, Kubba R, Zaidan K, Al Hergani M. The detection of silent celiac disease in patients with type 1 diabetes mellitus by the use of anti-tissue transglutaminase antibodies. Al-Kindy Col Med J. 2012;8(2):131-135.
18. Silverstein J, Klingensmith G, Copeland K, Plotnick L, Kaufman F, Laffel L, *et al*. American Diabetes Association. Care of children and adolescents with type 1 diabetes: A statement of the American Diabetes Association. Diabetes Care. 2005 Jan;28(1):186-212. DOI: 10.2337/diacare.28.1.186. PMID: 15616254.
19. Palma Sisto PA, Heneghan MK. Endocrinology. In: Marcdante KJ, Kliegman RM, editors. Nelson Essentials of Pediatrics. 7th ed. Philadelphia: Elsevier; 2015. p. 572-578.
20. Karavanaki K, Kakleas K, Paschali E, *et al*. Screening for associated autoimmunity in children and adolescents with type 1 diabetes mellitus. Horm Res. 2009;71:201-206. DOI: 10.1159/000201108.
21. Honar N, Karamizadeh Z, Saki F. Prevalence of celiac disease in patients with type 1 diabetes mellitus in the south of Iran. Turk J Gastroenterol. 2013;24(2):122-126. DOI: 10.4318/tjg.2013.0541. PMID: 23934458.
22. Abduljabbar HA, Matloub HY, G B A. Prevalence of celiac disease in type 1 diabetes mellitus in children and adolescents attending Children Welfare Teaching Hospital. Fac Med Baghdad. 2012;54(1):28-32.
23. Saukkonen T, Savilahti E, Reijonen H, Ilonen J, Wolf TE, Akerblom HK. Coeliac disease: Frequent occurrence after clinical onset of insulin-dependent diabetes mellitus. Childhood Diabetes in Finland Study Group. Diabet Med. 1996 May;13(5):464-470. DOI: 10.1002/(SICI)1096-9136(199605)13:5<464::AID-DIA101>3.0.CO;2-R. PMID: 8737029.
24. Sari S, Yeşilkaya E, Eğritaş O, Bideci A, Cinaz P, Dalgiç B. Prevalence of celiac disease in Turkish children with type 1 diabetes mellitus and their non-diabetic first-degree relatives. Turk J Gastroenterol. 2010 Mar;21(1):34-38. DOI: 10.4318/tjg.2010.0045. PMID: 20533110.
25. Al-Hussaini A, Sulaiman N, Al-Zahrani M, Alenizi A, El Haj I. High prevalence of celiac disease among Saudi children with type 1 diabetes: A prospective cross-sectional study. BMC Gastroenterol. 2012 Dec 23;12:180. DOI: 10.1186/1471-230X-12-180. PMID: 23259699; PMCID: PMC3543703.
26. Kordonouri O, Dietrich W, Becker M, Muller C. Antibodies to tissue transglutaminase predict latent celiac disease in children with diabetes mellitus. Diab Res Clin Pract. 1999;44:S6.
27. Araújo J, da Silva GA, de Melo FM. Serum prevalence of celiac disease in children and adolescents with type 1 diabetes mellitus. J Pediatr (Rio J). 2006;82:210-214.
28. Cerutti F, Bruno G, Chiarelli F, Lorini R, Meschi F, Sacchetti C. Diabetes Study Group of the Italian Society of Pediatric Endocrinology and Diabetology. Younger age at onset and sex predict celiac disease in children and adolescents with type 1 diabetes: An Italian multicenter study. Diabetes Care. 2004 Jun;27(6):1294-1298. DOI: 10.2337/diacare.27.6.1294. PMID: 15161778.
29. Ziegler AG, Schmid S, Huber D, Hummel M, Bonifacio E. Early infant feeding and risk of developing type I diabetes-associated autoantibodies. JAMA. 2003;290(13):1721-8. DOI: 10.1001/jama.290.13.1721.
30. Ivarsson A, Maylèus A, Nordström F, *et al*. Prevalence of childhood celiac disease and changes in infant feeding. Pediatrics. 2013;131:e687-e694. DOI: 10.1542/peds.2012-1649.