Medical Science Journal for Advance Research

Copyright © The Author(s)
Vol. 7, No. 3, September 2026
e-ISSN: 2774-4892

Celiac-related Antibody Profiles and Glycemic Control in Iraqi Children and Adolescents with Type 1 Diabetes: A Cross-Sectional Study

Mohammed Abd Al-Hussein Khalil
Department of Chemistry and Biochemistry, College of Medicine, Ibnsina University for Medical and Pharmaceutical Science, Baghdad, Iraq.
Corresponding Author Email: mohammed.abdalhussain@ibnsina.edu.iq

ABSTRACT

Background: *Celiac disease is associated with type 1 diabetes mellitus (T1DM), but differences in continuous antibody concentrations do not establish celiac disease. This study compared celiac-related antibody profiles between Iraqi children with T1DM and healthy controls and examined associations with glycemic control.* ***Methods:*** *A cross-sectional study in Baghdad, conducted from 2 June 2025 to 15 January 2026, included 60 participants with T1DM and 40 controls aged 2–15 years. Total immunoglobulin A (IgA), tissue transglutaminase antibodies (tTG-IgA/IgG), and deamidated gliadin peptide antibodies (DGP-IgA/IgG) were compared using Mann–Whitney tests. Log-linear regression with HC3 robust standard errors estimated covariate-adjusted geometric mean ratios (GMRs). Holm correction addressed multiple comparisons. HbA1c–antibody associations were assessed within the T1DM group.* ***Results:*** *Median total IgA was higher in T1DM than controls (137.00 vs 109.00 mg/dL), whereas tTG-IgA (0.99 vs 2.33 U/mL) and DGP-IgG (0.88 vs 1.39 reported units) were lower; all three comparisons remained significant after Holm correction. Adjusted GMRs were 1.31 (95% CI 1.15–1.48) for total IgA, 0.48 (0.36–0.65) for tTG-IgA, and 0.51 (0.35–0.75) for DGP-IgG. Differences in tTG-IgG and DGP-IgA were not statistically significant. Within T1DM, no HbA1c–antibody association was supported after covariate adjustment and multiplicity correction.* ***Conclusions:*** *The groups differed in total IgA, tTG-IgA, and DGP-IgG concentrations without evidence of an association between HbA1c and antibody levels. Missing assay thresholds and confirmatory celiac diagnoses preclude estimating celiac prevalence or diagnostic accuracy. The unexpected antibody pattern requires laboratory and source-record verification.*

Keywords: Type 1 Diabetes Mellitus; Celiac Disease; Tissue Transglutaminase; Deamidated Gliadin Peptide; Children; Hba1c.

Article Information
Received: July 30, 2026; Revised: August 27, 2026; Online: September 2026y

INTRODUCTION

Celiac disease is a common immune-mediated disorder in people with type 1 diabetes mellitus (T1DM). A systematic review which involved 26,605 people with T1DM reported a prevalence of biopsy-confirmed celiac disease of 6.0% (although substantial between-study heterogeneity) with the pediatric subgroup estimate at 6.2% [1]. These findings justify screening in pediatric diabetes care, but their interpretation depends on the type of outcome being measured seropositivity, confirmed enteropathy, or a continuous antibody concentration. Iraqi studies provide relevant local context. At the Children Welfare Teaching Hospital in Baghdad, 25 of 152 children with T1DM tested positive for tissue transglutaminase antibodies — 15 had a biopsy, and 13 had findings consistent with celiac disease [2]. Because only some seropositive children were biopsied, this 8.6% is an observed biopsy-confirmed cases instead of the whole disease ascertainment. Another study from Baghdad described silent celiac disease in 11.2% of 62 patients with T1DM after serology and duodenal biopsies (a wider range in age) [3]. Neither estimate can be directly compared with unclassified antibody concentrations. Current American Diabetes Association recommendations support screening children with T1DM using tTG-IgA together with

https://doi.org/10.46966/msjar.v7i3.472
This work is licensed under a Creative Commons Attribution 4.0 International License

documentation of adequate total IgA, with IgG-based assays used when IgA is deficient [4]. The European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) similarly recommends total IgA and tTG-IgA for initial testing and discourages routine first-line DGP testing in IgA-competent children [5]. Its non-biopsy diagnostic pathway requires assay-specific tTG-IgA concentrations at least ten times the upper limit of normal and positive endomysial IgA antibodies in a second sample [5]. Raw antibody values alone cannot substitute for these criteria.

Temporal variation also complicates the interpretation of pediatric serology. Prospective data on children with T1DM have shown that tTG antibody levels are erratic and can vary over time independent of continuing eating of gluten [6]. tTG-IgA was the most consistent test in screens for children and adolescents in the general population, while adding DGP-IgG at low level remained a marginally better screening test [7]. This exploratory study examined total IgA and four celiac-related antibody measurements in children and adolescents with T1DM and healthy controls in Baghdad. The sub-analysis examined association between HbA1c and antibody concentrations within the T1DM group. A study of this kind is not intended to provide an estimated prevalence of confirmed celiac disease from the data supplied.

MATERIALS AND METHODS

Study design and setting

This was a cross-sectional comparative study carried out in Baghdad Province, Iraq, from 2 June 2025 to 15 January 2026. The provided dataset included the data of 100 children and adolescent under 16 years, of which 60 were labeled with clinically known T1DM and 40 were healthy controls. They were between the ages of 2 and 15 years at the time of being contacted. The statistical analysis on the individual-level was taken from the provided workbook The relevant studies are described in the accompanying Word document. Reporting was performed in accordance with STROBE guidance for observational studies [8].

Inclusion and exclusion criteria

Here, children and adolescents under 16 years of age of either sex were eligible participants. The T1DM group was defined as children with an established diagnosis of T1DM at the time of enrollment. Controls were described as asymptomatic for celiac disease and free of chronic disease. The source doesn't indicate controls were excluded based on celiac serology.

The stated exclusion criteria included acute or chronic illnesses other than the index diagnosis of type 1 diabetes mellitus, including type 2 diabetes mellitus, Down syndrome, Turner syndrome, intellectual disability, autism, epilepsy, nonceliac gluten sensitivity, wheat or other food sensitivities, malignancy, hemoglobinopathies, and acute or chronic infections. In here, the check of presence of these conditions during clinical assessment or laboratory services is not mentioned. Only inclusion criteria regarding medical histories or information reported in case of children by their parents or guardians is given. Data set includes no verified diagnosis of celiac disease, endomysial antibody result, or intestinal histology.

Sample collection and laboratory measurements

These measurements of available records were identified as Fast Blood Sugar (FBS), Random Blood Sugar (RBS), HbA1c, Total IgA, tTG-IgA, tTG-IgG, DGP-IgA, and DGP-IgG. FBS and RBS were given in mg/dL, HbA1c in percent, total IgA in mg/dL, and there were tTG antibodies in U/mL.The DGP column headers were abreviated as "U/m"; DGP values as xxx reported units, and there are figures that will be reviewed by the authors when U/mL is shown in figures..

Anthropometry, diabetes duration, and data handling

For every participant, data on age, sex, weight in kilograms, and height in centimeters were available. The worksheet column labeled "BMI" ranged from 0.01 to 1.31 and did not reflect the mass index expressed as kg/m² derived from the recorded weight and height. Consequently, the original column was retained in the accompanying analysis file but did not represent a conventional BMI. The Z-score supplied separately was not examined because it's growth reference and definition were delayed. Age- and sex-specific nutritional categories were not based on absolute BMI.

 Copyright © The Author(s)

Diabetes duration was initially recorded as years, months, days, and weeks, but standardized to years: months were divided by 12, days by 365.25, and weeks multiplied by 7/365.25. Duration was not applicable to controls and therefore not imputed. All of the variables needed for analysis were complete and there were no repeat participant records with all of the same values (i.e., perfect duplicates). All 100 observations were retained; extreme measurements were not removed or altered. HbA1c values in controls were unusually low, including 21 below 4.0% and nine below 3.0%, and were retained as recorded while flagged for source-record and assay verification.

Statistical analysis

Age and anthropometric measurements were summarized as mean ± standard deviation and compared using Welch's t-test. Sex was summarized as counts and percentages and compared using Fisher's exact test. Glycemic measurements and immunological markers were summarized as medians with first and third quartiles and compared using two-sided Mann–Whitney U tests with asymptotic inference and tie correction. Rank-biserial correlations quantified immunological group differences, with positive values indicating larger measurements in T1DM. HC3 heteroskedasticity-robust standard errors and t-based 95% confidence intervals were used. These are conditional associations, not causal effects or risk ratios for celiac disease. Spearman rank correlations explored the relationships between HbA1c and each antibody among the 60 individuals with T1DM. Subsequently, separated log-linear models were employed to generate arthritis data by relating each antibody to HbA1c, diabetes duration, age, gender, resized BMI, and log total IgA. Antibody concentration ratios were defined by exponentiated HbA1c coefficients per one-percentage-point greater HbA1c. The Holm's correction was applied separately to each of the four families of multiple analyses: five methodological uncorrected immunological contrasts, five relative to group coefficient adjustments, four HbA1c regression parameters, and four HbA1c-antibody correlations. Two-sided corrected P values below 0.05 were considered as term for hypothesis testing and nominally uncorrected baseline comparisons are described as exploratory. Confidence intervals were single-point ratios, no correction for multiplicity was imparted.

RESULTS

All 100 participants were included in the analysis. Mean age was 9.58 ± 3.78 years in T1DM and 9.20 ± 3.63 years in controls (P = 0.612). The T1DM group included 34 boys and 26 girls, compared with 23 boys and 17 girls among controls (Fisher's exact P = 1.000). Weight, height, and recalculated BMI showed no statistically significant group differences (Table 1). Among participants with T1DM, median diabetes duration was 1.00 year (quartiles 0.42–2.00), ranging from five days to three years. Median FBS was 160.00 mg/dL, RBS 493.50 mg/dL, and HbA1c 9.50%; corresponding control medians were 88.55 mg/dL, 105.00 mg/dL, and 3.90%. All glycemic comparisons had P < 0.001.

Table 1. Participant characteristics and glycemic measurements.

Characteristics	Control (n = 40)	T1DM (n = 60)	P value
Age (years)	9.20 ± 3.63	9.58 ± 3.78	0.612
Girls, n (%)	17 (42.5)	26 (43.3)	1.000
Weight (kg)	34.52 ± 13.31	35.50 ± 13.93	0.726
Height (cm)	134.50 ± 21.10	136.13 ± 23.46	0.718
Recalculated BMI (kg/m²)	18.19 ± 1.95	18.12 ± 1.87	0.869
FBS (mg/dL)	88.55 (79.00–96.72)	160.00 (141.75–180.00)	<0.001
RBS (mg/dL)	105.00 (99.00–109.25)	493.50 (366.50–598.50)	<0.001
HbA1c (%)	3.90 (3.00–4.72)	9.50 (8.60–11.00)	<0.001
Diabetes duration (years)	Not applicable	1.00 (0.42–2.00)	—

Age, weight, height, and recalculated BMI are mean ± SD; other continuous measurements are median (Q1–Q3). Sex is n (%). P values are from Welch's t-test for age/anthropometry, Fisher's exact test for sex, and Mann–Whitney

Copyright © The Author(s)

U tests for glycemic variables; they are unadjusted and descriptive.

Total IgA was higher in the T1DM group, with a median of 137.00 mg/dL (117.50–199.25) compared with 109.00 mg/dL (99.75–119.00) in controls (Holm-adjusted P < 0.001). In contrast, tTG-IgA was lower in T1DM: 0.99 U/mL (0.75–1.49) versus 2.33 U/mL (1.37–3.30), with Holm-adjusted P < 0.001. DGP-IgG was also lower: 0.88 reported units (0.61–1.22) versus 1.39 (1.23–2.44), with Holm-adjusted P < 0.001 (Table 2; Figure 1). Median tTG-IgG was 1.19 U/mL in T1DM and 1.35 U/mL in controls, without evidence of a distributional difference (Holm-adjusted P = 0.479). DGP-IgA was numerically higher in T1DM (1.99 vs 1.45 reported units), but this comparison was not statistically significant (Holm-adjusted P = 0.168). Rank-biserial correlations were 0.556 for total IgA, −0.573 for tTG-IgA, and −0.434 for DGP-IgG,

Table 2. Unadjusted Immunochemical group comparisons.

Markers	Control (n = 40)	T1DM (n = 60)	Rank-biserial r	P value	Holm P
Total IgA (mg/dL)	109.00 (99.75–119.00)	137.00 (117.50-199.25)	0.556	<0.001	<0.001
tTG-IgA (U/mL)	2.33 (1.37–3.30)	0.99 (0.75–1.49)	-0.573	<0.001	<0.001
tTG-IgG (U/mL)	1.3 (0.77–2.15)	1.19 (0.86–2.53)	0.084	0.479	0.479
DGP-IgA (reported units)	1.45 (0.78–2.47)	1.99 (1.34–2.97)	0.205	0.084	0.168
DGP-IgG (reported units)	1.39 (1.23–2.44)	0.88 (0.61–1.22)	-0.434	<0.001	<0.001

Values are median (Q1–Q3). Two-sided Mann–Whitney U tests were used; Holm correction covers five markers. Positive rank-biserial values indicate larger concentrations in T1DM.

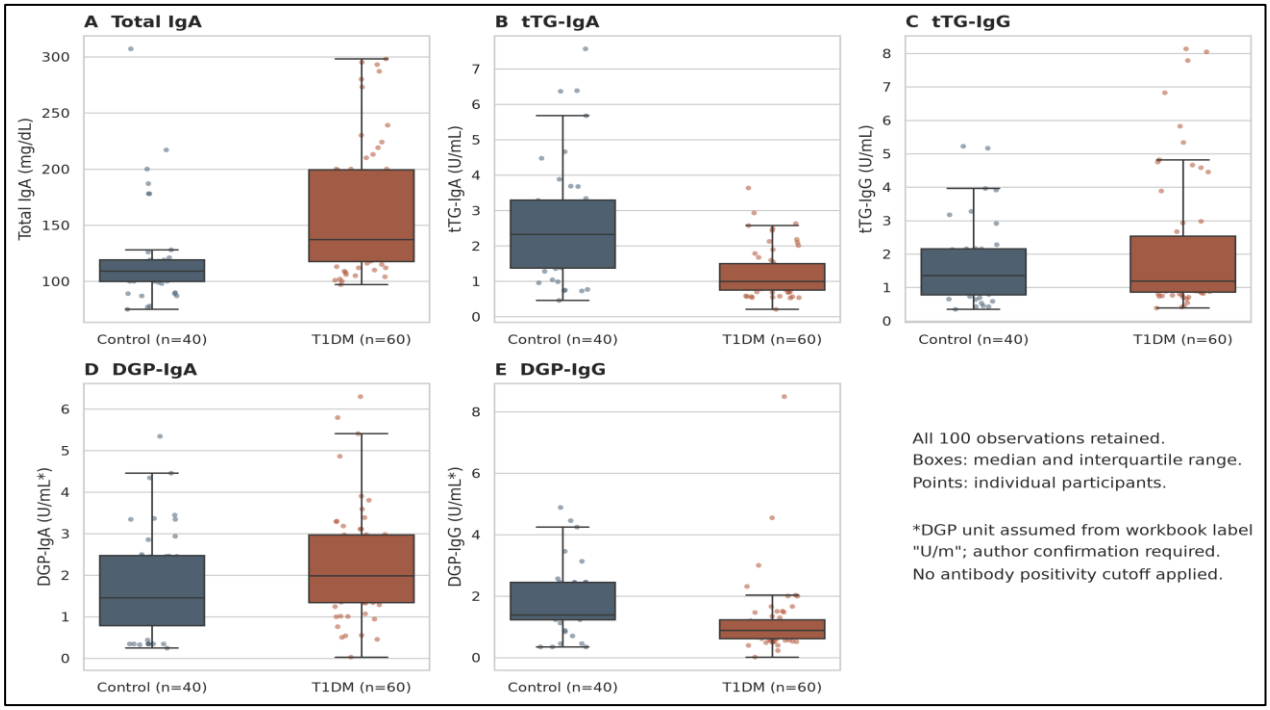


Figure 1. Immunological marker distributions. *A, total IgA; B, tTG-IgA; C, tTG-IgG; D, DGP-IgA; E, DGP-IgG. Boxes show medians and interquartile ranges; whiskers extend to the most extreme values within 1.5 interquartile ranges of the box. Points show every participant; horizontal jitter is used only to separate points visually. No observation was removed. DGP units are provisional pending author confirmation.*

 Copyright © The Author(s)

Adjusted analyses were consistent with the unadjusted findings. The T1DM-to-control GMR was 1.31 (95% CI 1.15–1.48; Holm-adjusted P < 0.001) for total IgA and 0.48 (0.36–0.5; P < 0.001) for tTG-IgA. For DGP-IgG, the adjusted GMR was 0.51 (0.35–0.75; Holm-adjusted P = 0.002). The GMRs for tTG-IgG and DGP-IgA were 1.15 (0.80–1.65; P = 0.440) and 1.36 (0.96–1.94; P = 0.172), respectively, with both confidence intervals including one (Table 3; Figure 2).

Table 3. Adjusted immunological group differences.

Outcome	GMR (95% CI)	P value	Holm P	Model R^2
Total IgA	1.31 (1.15–1.48)	<0.001	<0.001	0.247
tTG-IgA	0.48 (0.36–0.65)	<0.001	<0.001	0.276
tTG-IgG	1.15 (0.80–1.65)	0.440	0.440	0.028
DGP-IgA	1.36 (0.96–1.94)	0.086	0.172	0.100
DGP-IgG	0.51 (0.35–0.75)	<0.001	0.002	0.147

GMR = geometric mean ratio, T1DM/control. All log-outcome models adjust for age, sex, and recalculated BMI; antibody models additionally adjust for log total IgA. CIs use HC3 robust standard errors and t-based inference.

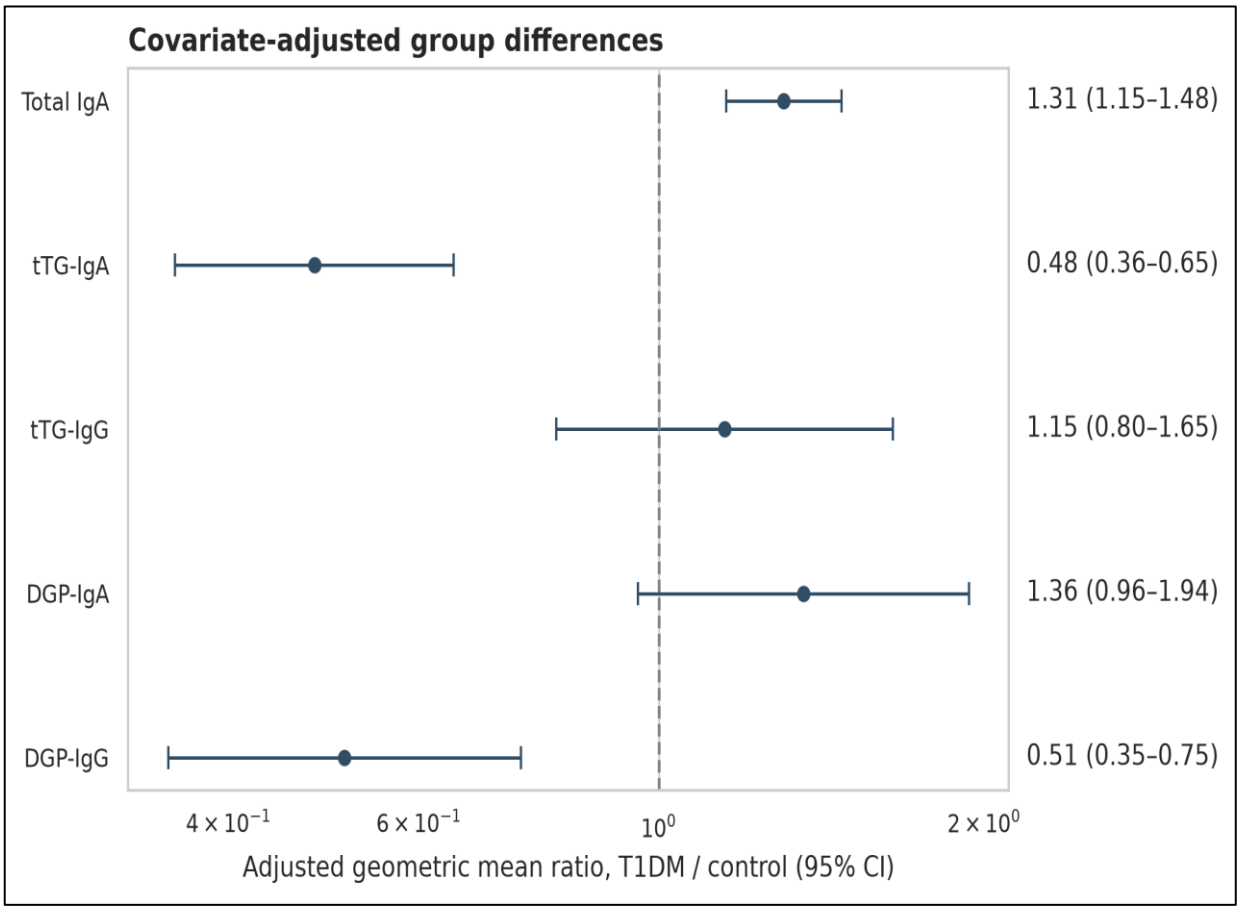


Figure 2. Covariate-adjusted group ratios, Points show adjusted T1DM-to-control geometric mean ratios; bars are pointwise 95% confidence intervals using HC3 robust standard errors. *The dashed line denotes no group difference. Models adjust for age, sex, and recalculated BMI, with log total IgA additionally included in antibody models.*

Copyright © The Author(s)

Group models explained approximately 2.8%–27.6% of variation in log biomarker concentrations. Sensitivity models omitting total-IgA adjustment produced GMRs of 0.49 for tTG-IgA and 0.59 for DGP-IgG; Huber-regression estimates were 0.46 and 0.51, respectively (Table 4). Their directions therefore persisted across these specifications. Several log-scale models still had non-normal residuals and influential observations, particularly for DGP antibodies. Maximum variance inflation factors were 5.55 in antibody group models and 7.14 in within-T1DM models, indicating that some covariate coefficients may be imprecisely estimated. Robust standard errors and sensitivity analyses do not eliminate these limitations.

Table 4. Sensitivity of adjusted group estimates to model specification.

Marker	Main GMR (95% CI)	No total-IgA adjustment GMR (95% CI)	Huber GMR
Total IgA	1.31 (1.15–1.48)	1.31 (1.15–1.48)	1.33
tTG-IgA	0.48 (0.36–0.65)	0.49 (0.38–0.64)	0.46
tTG-IgG	1.15 (0.80–1.65)	1.14 (0.83–1.57)	1.12
DGP-IgA	1.36 (0.96–1.94)	1.36 (0.96–1.93)	1.32
DGP-IgG	0.51 (0.35–0.75)	0.59 (0.42–0.83)	0.51

All models adjust for age, sex, and recalculated BMI. Main antibody models and Huber antibody models additionally include log total IgA; total-IgA outcome models do not adjust for themselves.

Spearman correlations with HbA1c were weak: −0.086 for tTG-IgA, 0.076 for tTG-IgG, −0.195 for DGP-IgA, and −0.097 for DGP-IgG. None remained statistically significant after Holm correction; the smallest adjusted P value was 0.541 for DGP-IgA (Figure 3). In covariate-adjusted models, the antibody concentration ratios per one-percentage-point higher HbA1c were 1.02 (95% CI 0.97–1.08) for tTG-IgA, 1.01 (0.91–1.13) for tTG-IgG, 0.95 (0.84–1.07) for DGP-IgA, and 0.94 (0.83–1.07) for DGP-IgG. All Holm-adjusted P values were 1.000 (Table 5).

Table 5. Adjusted associations between HbA1c and antibodies within T1DM

Antibody	Ratio per 1%-point HbA1c (95% CI)	P value	Holm P	Model R^2
tTG-IgA	1.02 (0.97–1.08)	0.411	1.000	0.216
tTG-IgG	1.01 (0.91–1.13)	0.792	1.000	0.012
DGP-IgA	0.95 (0.84–1.07)	0.355	1.000	0.098
DGP-IgG	0.94 (0.83–1.07)	0.342	1.000	0.106

Ratios are exponentiated HbA1c coefficients from log-antibody models adjusting for diabetes duration, age, sex, recalculated BMI, and log total IgA. CIs use HC3 robust standard errors and t-based inference. Holm correction covers four HbA1c coefficients. CIs are pointwise. All models include 60 participants with T1DM.

Copyright © The Author(s)

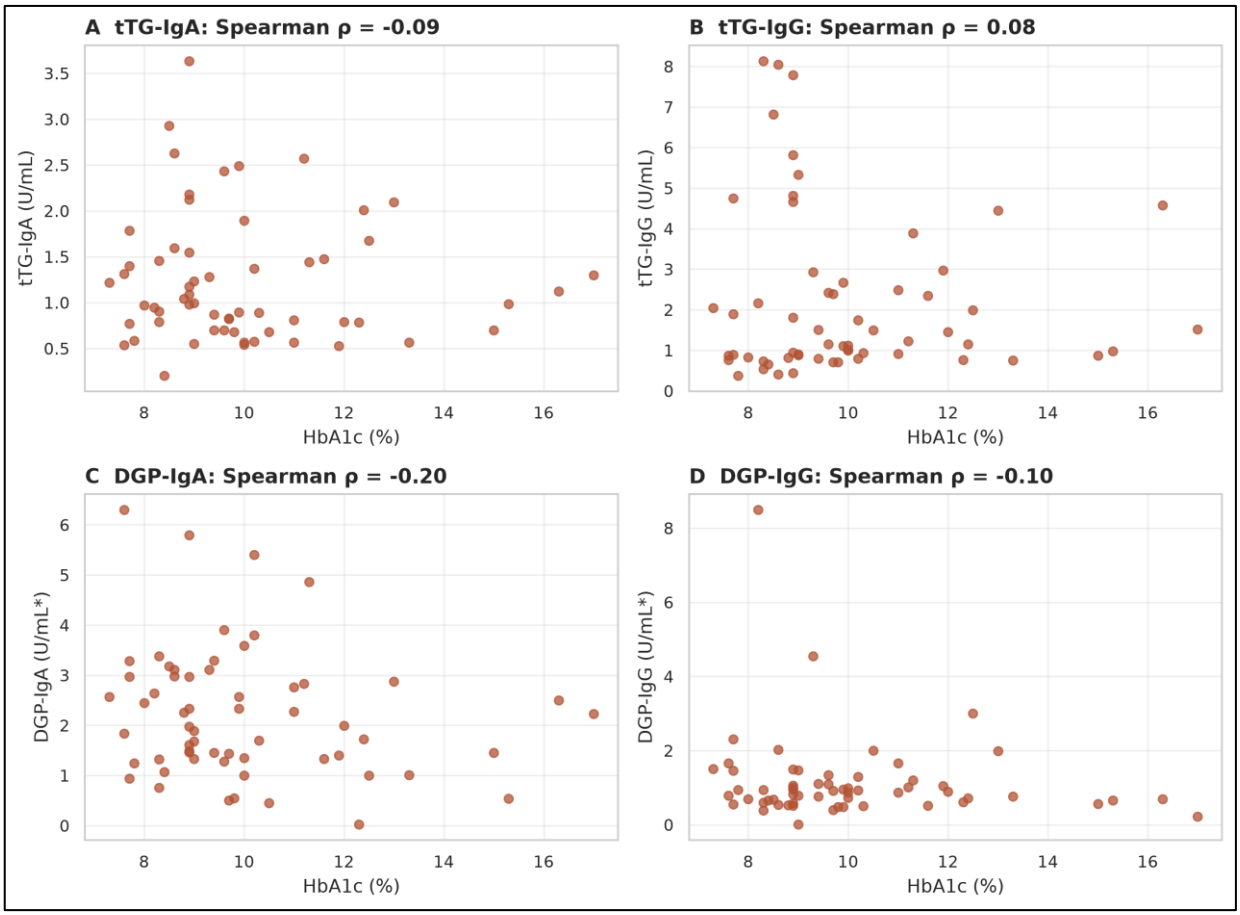


Figure 3. Antibody concentrations in relation to HbA1c within T1DM.

With higher values consistently treated as predicting T1DM, AUCs were 0.778 (95% bootstrap CI 0.678–0.868) for total IgA, 0.213 (0.124–0.314) for tTG-IgA, 0.542 (0.423–0.655) for tTG-IgG, 0.602 (0.485–0.717) for DGP-IgA, and 0.283 (0.176–0.397) for DGP-IgG (Table 6; Figure 4). The AUCs below 0.5 reflect lower, rather than higher, concentrations in T1DM. They were not inverted.

Table 6. Exploratory ROC analysis of T1DM group membership

Marker	AUC	95% bootstrap CI
Total IgA	0.778	0.678–0.868
tTG-IgA	0.213	0.124–0.314
tTG-IgG	0.542	0.423–0.655
DGP-IgA	0.602	0.485–0.717
DGP-IgG	0.283	0.176–0.397

Higher concentrations predict T1DM for every marker; AUCs were not inverted. CIs are percentile intervals from 5,000 stratified resamples of observed participants.

Copyright © The Author(s)

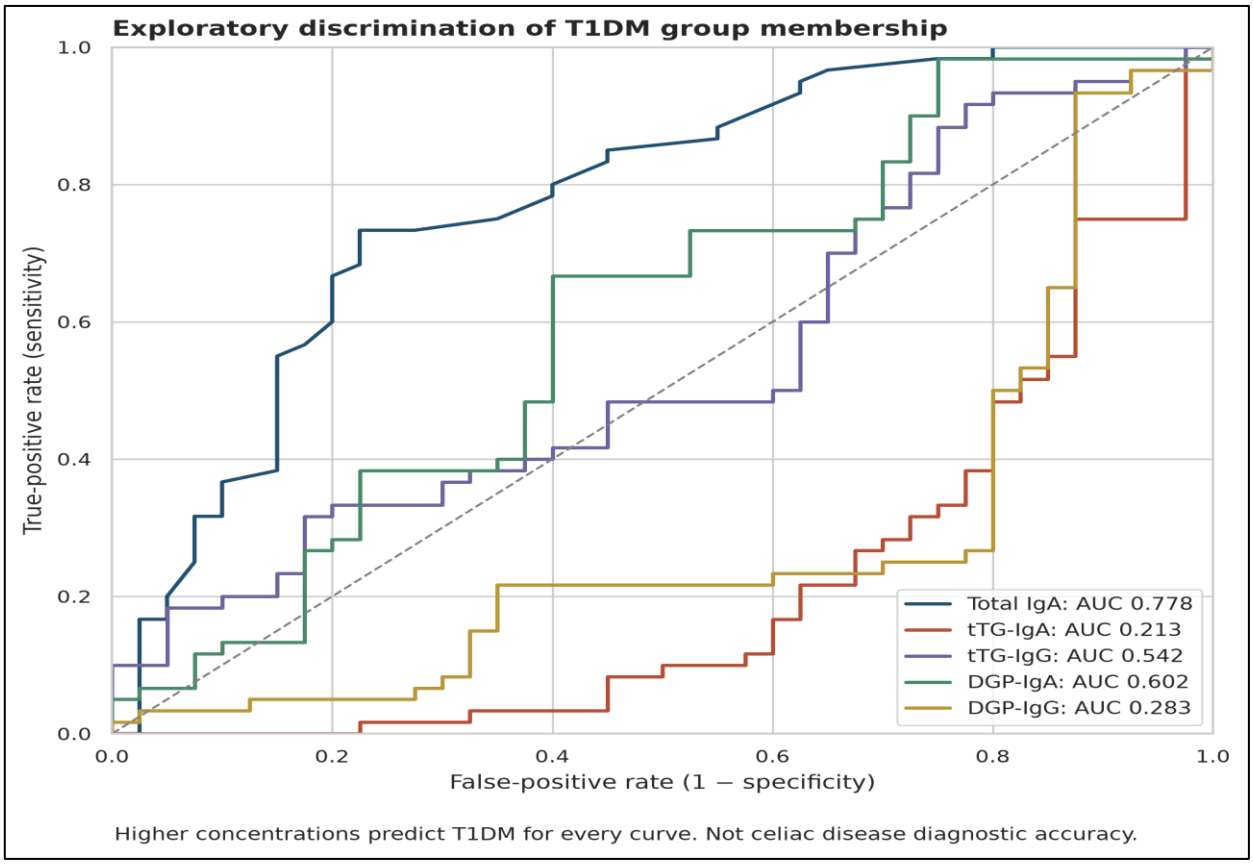


Figure 4. Exploratory ROC curves for recorded T1DM group membership.

DISCUSSION

In this exploratory cross-sectional comparison of 60 Iraqi children and adolescents with T1DM and 40 controls aged 2–15 years, the groups differed in three continuous measurements after adjustment for age, sex, recalculated BMI, and, for antibody models, log total IgA. Total IgA was higher in T1DM (adjusted GMR 1.31, 95% CI 1.15–1.48), whereas tTG-IgA (GMR 0.48, 95% CI 0.36–0.65) and DGP-IgG (GMR 0.51, 95% CI 0.35–0.75) were lower. tTG-IgG and DGP-IgA were not statistically different, and no HbA1c–antibody association was supported within T1DM after covariate adjustment and multiplicity correction. These are differences in measured concentrations, not estimates of seropositivity, biopsy-confirmed celiac disease (CD), diagnostic accuracy, or future CD risk.

The lower tTG-IgA and DGP-IgG concentrations are unexpected in light of the established association between T1DM and CD. The meta-analysis by Elfström et al. estimated biopsy-confirmed CD prevalence at 6.0% overall and 6.2% in children with T1DM, but its endpoint was confirmed enteropathy, not an unclassified antibody distribution [1]. Likewise, Singh et al estimated a global sero prevalence at 1.4% and a biopsy-confirmed prevalence at 0.7% in broadly screen populations, based on the studies analysed, although the prevalence was markedly variable; no studies on T1DM only were included [9]. Given that no estimate is generalisable to an unselected T1DM sample considering every antibody concentration, the current lower values cannot be regarded as a lowered CD risk, a reason to please discard screening, or even a conclusion of absence of disease.

This distinction is reinforced by the local context, a separate effort on the children welfare teaching hospital report, 25 of 152 cases with positive tTG antibodies, 15 had biopsy and 13 a histology of CD; the 13 / 152 cases used for biopsy confirmation are not fully representative of the detection of the true cases [2]. Mansour and Najeeb reported 7 Marsh III cases among 62 T1DM patients from Baghdad who have had serology and duodenoscopy, but the study was not particularly pediatric [3]. These diagnostic events cannot be meant to be in direct comparison with the current continuous values of the present manuscript. The unexpected trend

 Copyright © The Author(s)

in the current study therefore calls for the original group labels followup, units, calibration, specimen records and assay platform to be corrected before any biological explanation is put forth.

Higher total IgA did not coincide with a uniform increase in celiac-related antibodies. The measured total IgA pool is not equivalent to celiac-specific autoimmunity; guidelines use total IgA to support interpretation of IgA-based serology rather than as a diagnostic celiac marker [4] [5]. Although the lowest recorded total IgA was 75 mg/dL, formal age-specific IgA classification was not undertaken because local reference intervals were unavailable. Antibody models adjusted for total IgA, and sensitivity models omitting that covariate preserved the lower tTG-IgA and DGP-IgG directions. Neither specification isolates a causal diabetes effect, because total IgA itself could be associated with processes accompanying diabetes.

Longitudinal T1DM cohorts show that CD is clinically relevant in children, but they do not imply that continuous antibodies must be higher in every cross-sectional subgroup. Pham-Short et al. synthesized nine cohorts including 11,157 children and adolescents and reported a weighted pooled prevalence of biopsy-proven CD of 5.1%; among cases arising after T1D, 40% were diagnosed within one year, 55% within two years, and 79% within five years [10]. In the large Italian cohort of Cerutti et al., biopsy-confirmed CD occurred in 6.8% of 4,322 young people with T1DM; female sex and younger diabetes onset were associated with coexisting disease, but these were diagnostic and clinical associations rather than antibody-level comparisons [11]. The present participants had a median diabetes duration of one year, yet no participant-level diagnostic classification or longitudinal testing was supplied, so these studies cannot identify how many current observations represent early, absent, transient, or established CD.

The international registry comparison by Craig et al. included 52,721 youths with T1DM from Europe, North America, England/Wales, and Australia and found biopsy-confirmed CD in 3.5%, with site-specific prevalence from 1.9% to 7.7% [12]. Differences across registries were accompanied by variation in screening and diagnostic practice. The TEDDY birth cohort also illustrates how population structure matters: 12% of studies in genetically selected children, either DQ224 or DQ8 homozygous, developed celiac autoimmunity, but risk of CD by age five varied by HLA haplotype and country [13]. These prospective findings about incident autoimmunity or confirmed disease in genetically or clinically selected populations and do not offer thresholds interpreting Iraqi z scores.

Regional evidence is, likewise, heterogenous. The systematic review of studies from Arab Country of El-Metwally S et.al mentioned both studies, not only the diagnostic test-tier studies, of children with T1DM related estimates of CD 5.5% and 20%, yet stressed variation by populations, assays, as well as case definitions; It reported indigenous data on a population-based server of 62 individuals with T1DM, of whom 11.2% had CD [14]. According to Camarca et al., prior reports of the prevalence of T1DM/CD ranged between 4.4% and 11.1%; however, many affected children were asymptomatic. It was a narrative review of heterogeneous studies rather than single cohort study [15] These findings reinforce the clinical relevance of screening for Arab and Iraqi diabetes care, but we do not know the direction or shape of our current continuous antibody profile.

A single antibody measurement may not represent a stable disease state in a child with T1DM. In a prospective cohort of 446 children, Castellaneta et al. reported positive celiac serology in 14.5%; among seropositive children, titers fluctuated or normalized in a substantial proportion despite continued gluten consumption [6]. Retrospective studies are consistent with this temporal caution. Waisbourd-Zinman et al. found that 17 of 48 T1DM children with elevated anti-tTG levels normalized while continuing gluten, whereas Unal et al. reported spontaneous normalization in 24 of 103 children with positive tTG-IgA and biopsy-proven CD in 46 of 668 tested T1DM patients [16] [17]. In a Saudi cohort selected for elevated tTG-IgA, 47.1% normalized, with normalization strongly related to the initial multiple of the assay upper limit of normal [18]. These findings support repeat, assay-defined evaluation when clinically appropriate; they

Copyright © The Author(s)

cannot explain the present cross-sectional lower concentrations or establish that any current participant would normalize.

The diagnostic meaning of tTG-IgA depends on assay context and specificity. Maheshwari et al. reported that, in a clinically referred histology cohort, tTG-IgA sensitivity and specificity differed substantially between children with and without T1DM, and that many tTG-IgA-positive T1DM children had normal biopsies [19]. Their cutoff findings were derived from a particular laboratory and ELISA dataset and therefore cannot be transferred to the Iraqi U/mL values. ESPGHAN recommends total IgA plus tTG-IgA for initial testing and reserves IgG-based testing for low or undetectable IgA; its non-biopsy pathway requires at least 10 times the assay-specific upper limit of normal plus a second-sample endomysial antibody result [5]. ADA guidance likewise recommends tTG-IgA with documentation of adequate IgA and repeat screening after diagnosis and during follow-up, with IgG-based tests when IgA is deficient [4]. None of these recommendations permits classification from the present raw values.

DGP results require even more restraint. In a systematic review focused on children under two years, Catassi et al. found high summary sensitivity for both DGP-IgG and tTG-IgA but higher specificity for tTG-IgA; the authors considered DGP-IgG an adjunct in selected very young children rather than an interchangeable first-line test [20]. This evidence does not directly cover our participants, whose observed ages were 2–15 years and therefore included no child younger than two. In school-aged Saudi mass screening, Al-Hussaini et al. found tTG-IgA to be the most reliable first screen, with DGP-IgG adding only marginal benefit and DGP-IgA performing poorly as a standalone test [7]. Vootukuru et al. further reported a low positive predictive value for isolated DGP-IgG elevation with negative tTG-IgA in an endoscopy-selected pediatric cohort [21]. Thus, the present lower DGP-IgG and nonsignificant DGP-IgA findings cannot be translated into lower or higher CD probability, and the two DGP isotypes should not be treated as equivalent.

Within T1DM, the current study did not support an association between HbA1c and tTG-IgA, tTG-IgG, DGP-IgA, or DGP-IgG. The adjusted ratios per one-percentage-point higher HbA1c were close to one, with all Holm-adjusted P values equal to 1.000. Restricting the analysis to T1DM avoided an artificial pooled relationship driven by the marked glycemic difference between T1DM and controls. However, the analysis included only 60 participants, was cross-sectional, and had collinearity and influential observations; a null result indicates that an association was not detected, not that glycemic control and CD-related biology are equivalent or unrelated.

Clinical outcome studies generally provide no strong basis for expecting a simple HbA1c relationship. In the multinational registry study, mean HbA1c was similar in youths with T1DM plus biopsy-confirmed CD and those with T1DM alone (8.3% versus 8.4%) [12]. In the CD-DIET study, a 12-month gluten-free-diet intervention among biopsy-confirmed, asymptomatic participants did not produce a between-group HbA1c difference [22]. A systematic review by Mozzillo et al. likewise found no significant differences in HbA1c, growth, hypoglycemia episodes, or total daily insulin dose when comparing youth with T1DM plus CD on a gluten-free diet with youth with T1DM alone, although the evidence was heterogeneous and postprandial glucose may differ [23]. These studies assess diagnosed CD and clinical management, not antibody concentrations, so they provide context rather than validation of the present null antibody associations.

The clinical implication may be that it would be premature to adapt screening based on the direction of the antibody. Decisions on screening in terms of total IgA and tTG-IgA should adhere to local laboratory procedures and guideline-driven pathways, including repeat testing when warranted, presenting of symptoms and family-history, and nutrition practitioner confirmation of abnormal results prior to nutritional changes [4] [5]. This gluten-free diet should not be started just because a continuous value is above an undocumented limit, and the current lower tTG-IgA or DGP-IgG should not be used to postpone screening. Reference-study cutoffs, whether from Saudi-Style, U.S. or European assay, are not locally relevant until the Iraqi assay manufacturer, calibration, units,

 Copyright © The Author(s)

reference interval, and quality-control records are in place.

Strengths, limitations, and priorities for verification

A strength of the study is that it directly compared the two new, clinically validated biomarkers, rather than CD diagnosis. They kept the same 100 subjects, the main group estimates were age- and sex-adjusted (and also adjusted for revised BMI), antibody models were powered with total IgA, filtered families were protected by Holm correction, and sensitivity models maintained the sign of the tTG-IgA and DGP-IgG results. A significant strength of the study is that, it included a healthy-control comparator and investigates HbA1c within T1DM rather than using a baseline pooled group contrast. These are all descriptive features, useful for hypothesis generation, of an odd laboratory pattern pattern, not for a screening-validation study.

The limitations are obvious. Source information on recruitment setting and sampling, duration of diabetes, gluten intake, symptoms, family history, pubertal status, insulin treatment, and control allocation were all incomplete. Source BMI was not the conventional BMI but required recalculation; the supplied growth Z-score does not have a defined reference. Control HbA1c values were consistently low, often below 4%, and will need to be verified against source record and assay characteristics. Practice details are still incomplete (e.g., specimen handling, platform, manufacturer, calibration, analytical precision, reference intervals and positivity cutoffs); DGP units are not fully labeled. Ethics intake, ethics approvals and age-appropriate assent also need to be completed. Residual non-normality, influential DGP cases, modest sample sizes and a potential choice of a non-optimal base causative model. Though STROBE can direct accessible reporting it cannot fill in these gaps in study description [8].

The exploratory ROC results are also subject to further qualification. Their outcome was recorded T1DM group membership, not clinically verified CD and the same higher concentration direction was revised to be the most appropriate in every marker e.g. AUCs below 0.5 for tTG-IgA and DGP-IgG reflect the group relationships that were observed and not the lack of false positives; and if significant, they would have reversed the stated direction but wouldn't add to the diagnostic evidence. Bootstrap CI represents uncertainty using the current sample, but not recruitment bias, assay imprecision, or external validity. Therefore, such borderline results cannot claim the existence of a clinically relevant celiac screening threshold or a validated diagnostic performance measure of the T1DM population.

A prospective Iraqi pediatric cohort to establish pre-determined recruitment, age-based reference intervals, symptoms and known gluten exposure, serial tTG-IgA and total IgA measurements, endomysial antibody testing where indicated, and clinically relevant biopsy confirmation could estimate seroprevalence and disease prevalence separately. Such a design could also determine if transient serology, age, diabetes duration or metabolic state causes the variability. The most justifiable conclusion to this study, until it is done, is that this sample showed higher total IgA and lower tTG-IgA and DGP-IgG concentrations in T1DM, with no identified HbA1c–antibody association, but the clinical significance of these differences remains unclear.

CONCLUSIONS

In this exploratory cross-sectional analysis of 60 children and adolescents with T1DM and 40 healthy controls, T1DM was associated with higher total IgA and lower tTG-IgA and DGP-IgG concentrations after covariate adjustment and multiplicity correction. No statistically supported association between HbA1c and antibody concentrations was identified within T1DM. These results describe continuous immunological measurements, not celiac disease prevalence or diagnostic performance. Source-record and laboratory verification, followed by assay-defined serology and appropriate confirmatory evaluation, is required before drawing clinical conclusions from the unexpected antibody pattern.

DECLARATIONS

Ethics approval and consent to participate

This investigation obtained ethical approval from Ibn Sina University of Medical and Pharmaceutical Sciences. All procedures carried out during the study followed the ethical guidelines set forth by the institutional and

Copyright © The Author(s)

national research ethics committee, along with the principles detailed in the Declaration of Helsinki (1964) and its later revisions.

Availability of data and materials

The data available from the corresponding author on reasonable request.

Competing interests

None

Funding

None

Author contributions

Mohammed Abd Al-Hussein Khalil: Conceptualisation, Investigation, Data Curation, Writing – Original Draft, Methodology, Validation, Formal Analysis, Visualisation, Conceptualisation, Supervision, Project Administration, Writing – Review & Editing, Resources, ANA: Investigation, Methodology, Data Curation, Software

REFERENCES

1. Elfström P, Sundström J, Ludvigsson JF. Systematic review with meta-analysis: associations between coeliac disease and type 1 diabetes. Aliment Pharmacol Ther. 2014;40(10):1123–1132. doi:10.1111/apt.12973.

2. Abduljabbar HA, Matloub HY, Yassin BAG. Prevalence of Celiac Disease in type 1 Diabetes Mellitus in children and adolescents attending Children Welfare Teaching Hospital. J Fac Med Baghdad. 2012;54(1):28–32. doi:10.32007/jfacmedbagdad.541766.

3. Mansour AA, Najeeb AA. Coeliac disease in Iraqi type 1 diabetic patients. Arab J Gastroenterol. 2011;12(2):103–105. doi:10.1016/j.ajg.2011.04.007.

4. American Diabetes Association Professional Practice Committee for Diabetes. 14. Children and Adolescents: Standards of Care in Diabetes—2026. Diabetes Care. 2026;49(Suppl 1):S297–S320. doi:10.2337/dc26-S014.

5. Husby S, Koletzko S, Korponay-Szabó I, et al. European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020. J Pediatr Gastroenterol Nutr. 2020;70(1):141–156. doi:10.1097/MPG.0000000000002497.

6. Castellaneta S, Piccinno E, Oliva M, et al. High rate of spontaneous normalization of celiac serology in a cohort of 446 children with type 1 diabetes: a prospective study. Diabetes Care. 2015;38(5):760–766. doi:10.2337/dc14-2890.

7. Al-Hussaini A, Al-Jurayyan A, Alharbi S, Salman Bashir M, Troncone R. Performance of deamidated gliadin peptide antibodies as first screening for celiac disease in the general pediatric population. Front Pediatr. 2023;11:1279825. doi:10.3389/fped.2023.1279825.

8. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. PLoS Med. 2007;4(10):e296. doi:10.1371/journal.pmed.0040296.

9. Singh P, Arora A, Strand TA, Leffler DA, Catassi C, Green PH, et al. Global prevalence of celiac disease: systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2018;16(6):823–836.e2. doi:10.1016/j.cgh.2017.06.037.

10. Pham-Short A, Donaghue KC, Ambler G, Phelan H, Twigg S, Craig ME. Screening for Celiac Disease in Type 1 Diabetes: A Systematic Review. Pediatrics. 2015;136(1):e170–e176. doi:10.1542/peds.2014-2883.

11. Cerutti F, Bruno G, Chiarelli F, Lorini R, Meschi F, Sacchetti C; Diabetes Study Group of 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;27(6):1294–1298. doi:10.2337/diacare.27.6.1294.

12. Craig ME, Prinz N, Boyle CT, Campbell FM, Jones TW, Hofer SE, et al. Prevalence of Celiac Disease in 52,721 Youth With Type 1 Diabetes: International Comparison Across Three Continents. Diabetes Care. 2017;40(8):1034–1040. doi:10.2337/dc16-2508.

13. Liu E, Lee HS, Aronsson CA, Hagopian WA, Koletzko S, Rewers MJ, et al.; TEDDY Study Group. Risk of pediatric celiac disease according to HLA haplotype and country. N Engl J Med. 2014;371(1):42–49. doi:10.1056/NEJMoa1313977.

 Copyright © The Author(s)

14. El-Metwally A, Toivola P, AlAhmary K, Bahkali S, AlKhathaami A, AlSaqabi MK, et al. The Epidemiology of Celiac Disease in the General Population and High-Risk Groups in Arab Countries: A Systematic Review. Biomed Res Int. 2020;2020:6865917. doi:10.1155/2020/6865917.

15. Camarca ME, Mozzillo E, Nugnes R, Zito E, Falco M, Fattorusso V, et al. Celiac disease in type 1 diabetes mellitus. Ital J Pediatr. 2012;38:10. doi:10.1186/1824-7288-38-10.

16. Waisbourd-Zinman O, Hojsak I, Rosenbach Y, Mozer-Glassberg Y, Shalitin S, Phillip M, Shamir R. Spontaneous normalization of anti-tissue transglutaminase antibody levels is common in children with type 1 diabetes mellitus. Dig Dis Sci. 2012;57(5):1314–1320. doi:10.1007/s10620-011-2016-0.

17. Unal E, Demiral M, Baysal B, Ağın M, Devecioğlu EG, Demirbilek H, Özbek MN. Frequency of Celiac Disease and Spontaneous Normalization Rate of Celiac Serology in Children and Adolescent Patients with Type 1 Diabetes. J Clin Res Pediatr Endocrinol. 2021;13(1):72–79. doi:10.4274/jcrpe.galenos.2020.2020.0108.

18. Al Sarkhy A, Al Hassan A, Assiri H, Alabdulkarim H, AlAnazi N, Alshammari N, et al. Frequency and predictive factors for spontaneous normalization of anti-tissue transglutaminase-IgA serology among Saudi children with type 1 diabetes mellitus: a cohort study. Saudi J Gastroenterol. 2023;29(5):278–285. doi:10.4103/sjg.sjg_25_23.

19. Maheshwari A, He Z, Weidner MN, Lin P, Bober R, Del Rosario FJ. Influence of age and type 1 diabetes mellitus on serological test for celiac disease in children. Pediatr Gastroenterol Hepatol Nutr. 2021;24(2):218–229. doi:10.5223/pghn.2021.24.2.218.

20. Catassi GN, Pulvirenti A, Monachesi C, Catassi C, Lionetti E. Diagnostic Accuracy of IgA Anti-Transglutaminase and IgG Anti-Deamidated Gliadin for Diagnosis of Celiac Disease in Children under Two Years of Age: A Systematic Review and Meta-Analysis. Nutrients. 2021;14(1):7. doi:10.3390/nu14010007.

21. Vootukuru N, Singh H, Giles E. Isolated positive deamidated gliadin peptide-IgG has limited diagnostic utility in coeliac disease. J Paediatr Child Health. 2022;58(9):1648–1652. doi:10.1111/jpc.16071.

22. Mahmud FH, Clarke ABM, Joachim KC, Assor E, McDonald C, Saibil F, et al. Screening and Treatment Outcomes in Adults and Children With Type 1 Diabetes and Asymptomatic Celiac Disease: The CD-DIET Study. Diabetes Care. 2020;43(7):1553–1556. doi:10.2337/dc19-1944.

23. Mozzillo E, Franceschi R, Di Candia F, Rosanio FM, Leonardi L, Fedi L, et al. The impact of gluten-free diet on growth, metabolic control and quality of life in youth with type 1 diabetes and celiac disease: A systematic review. Diabetes Res Clin Pract. 2022;191:110032. doi:10.1016/j.diabres.2022.110032.

Copyright © The Author(s)