

Autoantibody Status at Diagnosis in Children and Adolescents with Type 1 And Type 2 Diabetes Attending the Paediatric Diabetes Care and Research Center (PDRC) in Bangladesh

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Abstract

Background: The rising prevalence of T1D and T2D in South Asia has created diagnostic challenges due to overlapping clinical features, underscoring the need for diabetes-associated autoantibodies (DAA) testing.

Objective: To evaluate the prevalence of GAD and IAA and their clinical and biochemical correlates in Bangladeshi children and adolescents with newly diagnosed diabetes.

Methods: A cross-sectional study was conducted among 91 children (aged 1–19 years) with newly diagnosed diabetes at the Paediatric Diabetes Care and Research Center (PDRC), BIRDEM, Bangladesh (2019–2022), classified as T1D or T2D using international and local criteria. Clinical, biochemical, and immunological data were extracted from records, with GADA and IAA measured within six months of diagnosis.

Results: Of the 91 participants, children with T2D were older at diagnosis (median 11.5 vs. 9.0 years, $p = 0.0001$), more likely to have a family history of diabetes (98% vs. 84%, $p = 0.031$), and had higher C-peptide levels (2.69 vs. 0.45 ng/mL, $p = 0.0001$). DKA at onset was more common in T1D (30% vs. 5%, $p = 0.003$). Autoantibody positivity (≥ 1 DAA) was observed in 76% of T1D and 22% of T2D patients ($p = 0.0001$). GADA positivity was found in 58.0% of T1D and 19.5% of T2D, while IAA was positive in 42.0% of T1D and 12.2% of T2D.

Conclusion: This study highlights lower DAA prevalence in Bangladeshi children with T1D compared to Western cohorts and reveals that many clinically suspected T2D cases also harbor antibodies, underscoring diagnostic complexity in South Asia.

Keywords: Type 1 diabetes, Type 2 diabetes, Children, Autoantibodies, Bangladesh, GADA, IAA, C-peptide.

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia due to defects in insulin secretion, insulin action, or both.¹ In children and adolescents, type 1 diabetes mellitus (T1D) is the most common form and results from autoimmune destruction of pancreatic β -cells, leading to absolute insulin deficiency.² However, the increasing prevalence of type 2 diabetes mellitus (T2D) in youth, particularly in South Asia, has introduced diagnostic challenges due to overlapping clinical features.³

The presence of diabetes-associated autoantibodies (DAAs), such as those against glutamic acid decarboxylase (GADA), insulin (IAA), serves as a hallmark of autoimmune T1D and plays a critical role in differentiating it from T2D at diagnosis.

Diabetes-associated autoantibodies (DAAs), notably glutamic acid decarboxylase antibody (GADA), insulin autoantibody (IAA) and islet antigen-2 (IA2A) are key markers of autoimmune T1D and assist in distinguishing T1D from T2D at diagnosis.^{4,5} Western cohorts report >90% antibody positivity in T1D at

onset,^{5,6} whereas several Asian studies show lower rates, suggesting population and environmental differences.⁷⁻⁹

Interestingly, DAA positivity has also been reported in children with clinical features of T2D, suggesting either misclassification or an underlying autoimmune component in some cases.¹⁰ In Bangladesh, where the dual burden of malnutrition and obesity is contributing to a changing diabetes phenotype, the accurate classification of diabetes in children is essential. However, there is limited local data on the prevalence and profile of DAAs in Bangladeshi children with newly diagnosed diabetes. This study evaluated DAA (GADA, IAA) patterns in Bangladeshi children with newly diagnosed diabetes and compared profiles between clinically classified T1D and T2D.

The aim of the study was to examine diabetes-associated autoantibodies (GADA, IAA), clinical and biochemical profile in new-onset diabetes and compare between children and adolescents with type 1 and type 2 diabetes.

2. MATERIALS AND METHODS

We conducted a cross-sectional study among children and adolescents aged 1–19 years with newly diagnosed DM who presented to the BADAS Paediatric Diabetes Care and Research Centre (PDRC) at BIRDEM Women and Children Hospital, Bangladesh. Data retrieved from the medical records diagnosed during 2019–2022. New-onset diabetes (diagnosed within the past 6 months), Age between 1 and 19 years were included randomly. Patients with monogenic diabetes, secondary diabetes, or incomplete autoantibody data were excluded. Previous diagnosis of diabetes, Secondary diabetes (e.g., due to drugs or pancreatic disease) were excluded.

Diagnosis and classification were done by International (WHO/ISPAD) and local criteria.¹¹⁻¹⁴ T1D was defined by one or more of these criteria: insulin requirement from diagnosis; abrupt symptom onset; diabetic ketoacidosis (DKA) at diagnosis; or positivity for ≥ 1 DAA; typically without obesity or acanthosis. T2D was diagnosed in patients who were overweight/obese, often had a slower onset of symptoms or were asymptomatic had strong family history had normal or elevated C-peptide levels, exhibited features of insulin resistance, acanthosis nigricans, dyslipidaemia, and did require minimum insulin for initial glycemic control

(unless needed for acute hyperglycemia or ketosis).

Data were collected from medical records, including demographic variables: age, sex, family history, and anthropometry (height, weight, BMI and clinical features (presence of acanthosis nigricans, DKA at diagnosis), and biochemical (fasting plasma glucose, HbA1c, random C-peptide). Diabetes-associated autoantibodies (DAAs): glutamic acid decarboxylase antibody (GADA) and Insulin autoantibody (IAA) measured within 6 months of diagnosis. Autoantibodies were measured using standardized ELISA kits.

2.1. Ethics Approval

The study was approved by the Ethical Review Committee of the Diabetic Association of Bangladesh. Written informed consent was obtained from patients and/or their guardians prior to participation.

2.2. Statistical analysis.

Data analysis was performed by Statistical Package for the Social Sciences program version 26. Descriptive statistics are presented as mean (\pm SD) scores for normally distributed data and median (interquartile range or range) for skewed data. Continuous data were compared using parametric test Anova and skewed data using the non-parametric test Kruskal-Wallis test. Differences in clinical and biochemical characteristics between T1 D and T2D were tested using chi-squared analysis. All applied statistical tests were two-sided, p-values < 0.05 were considered as statistically significant.

3. RESULT

3.1. Clinical and biochemical characteristics of study subjects

A total of 91 patients were analyzed. The median age at diagnosis was 10.5 years (IQR 8.9–13.2), and the median age at registration was 11.0 years (IQR 9.0–13.9). Thirty-nine (42.9%) were male and 52 (57.1%) were female. Fifty (55.0%) had type 1 diabetes and 41 (45.0%) had type 2 diabetes.

The clinical and biochemical characteristics of participants with T1D and T2 D were analysed. Age at diagnosis was higher in T2 D compared to T1 D. Family history of diabetes was more frequent in T2D (98%) than T1D; history of DKA was significantly more common in T1D. BMI and weight were higher in T2D, while fasting C-peptide was markedly higher in T2D (2.69 [1.57–

4.26] ng/mL) than in T1D (0.45 [0.14–0.78] ng/mL; $p=0.0001$). Fasting glucose and HbA1c did not differ significantly between groups. Children with T2 D were older at diagnosis (median 11.5 years [IQR 10.2–13.9]) compared to those with T1D (9.0 years [5.6–11.0], $p = 0.0001$). [Table1] Family history of diabetes was more frequent among T2 D patients (98%) compared to T1 D whereas H/O DKA was

significantly more common in T1 D. BMI and weight were higher in T2 D. No significant differences were found in fasting blood glucose ($p = 0.262$) or HbA1c ($p = 0.098$) between the groups. C-peptide level was markedly higher in T2 D (2.69 ng/mL [1.57–4.26]) compared to T1 D (0.45 ng/mL [0.14–0.78], $p = 0.0001$). Detailed clinical and biochemical characteristics were provided in Table 1.

Table 1. Clinical and biochemical characteristics of Type 1 and Type 2 diabetes

Characteristics	Type 1	Type 2	P value
Age at diagnosis	9.0[5.6-11.0]	11.5[10.2-13.9]	0.0001
Age at registration	9.7[7.0-12.0]	12.3[11.0-14.4]	0.0001
Gender	16(44)	38(39)	
	25 (54)	52(61)	0.564
F/H of diabetes	42 (84)	40(98)	0.031
H/O DKA	15(30)	2(5)	0.003
Height	139.0[125.0-150.0]	152.5[146.0-159.2]	0.007
Weight	30.0[23.0-38.7]	51.0[43.7-66.7]	0.0001
BMI	15.5[13.7-17.3]	23.1[19.9-26.4]	0.0001
FBS	18.2[14.6-22.4]	12.0 [8.1-16.5]	0.262
HbA1c	11.7[9.2-14.1]	11.0[9.1-12.8]	0.098
C peptide	0.45 [0.14-0.78]	2.69[1.57-4.26]	0.0001

3.2. Autoantibody status in T1D and T2D

GADA was positive in 40.7% of patients, while IAA was positive in 28.6%, as shown in Fig. 1.

GADA positivity was significantly higher in T1D (58.0%) than in T2D (19.5%) ($p=0.0001$), while IAA positivity was also greater in T1D (42.0%) compared with T2D (12.2%) ($p=0.0001$). [Fig.2]

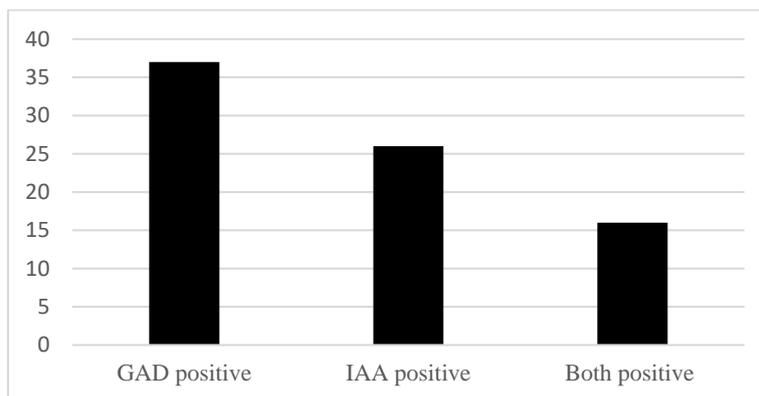


Fig 1. Autoantibody status of the patients

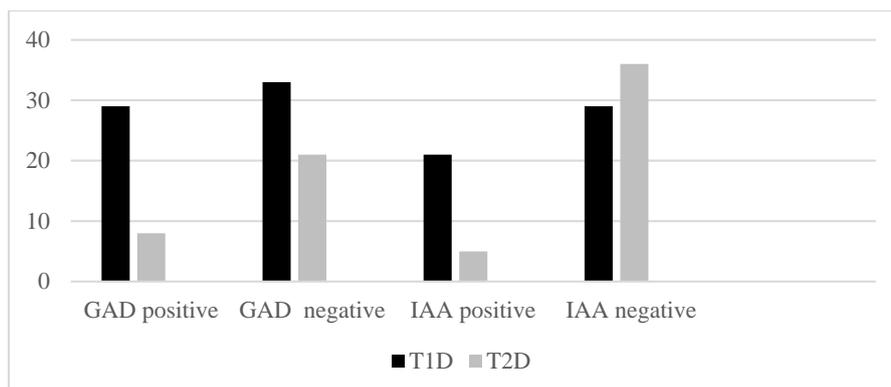


Fig2. Autoantibody status in patients with type 1 diabetes mellitus (T1D), and type 2 diabetes (T2D) GAD65 autoantibody and insulin autoantibody (IAA)

4. DISCUSSION

This study provides new insights into significance of diabetes-associated autoantibodies (DAAs) among Bangladeshi children and adolescents with newly diagnosed diabetes. Our results demonstrate that a substantial proportion of children with type 1 diabetes (T1D) were antibody positive with glutamic acid decarboxylase antibody (GADA) and insulin autoantibody (IAA) demonstrating comparable frequencies (58.0% and 42.0%, respectively). The overall positivity rate was lower than that reported in Western populations, where over 90% of newly diagnosed T1D cases are antibody positive at onset. These findings are consistent with previous studies from Asia that reported lower autoantibody positivity compared with Western cohorts, where more than 90% of newly diagnosed children with T1D are antibody positive at onset. Studies from Japan, China, and India have reported positivity rates of 81%, 61%, and 72%, respectively, confirming regional variation in immune-mediated diabetes.⁷⁻⁹ These variations highlight regional differences in the immunogenetic and environmental factors influencing the development of T1D. In our previous study we found that 29.8% was positive for one more autoantibodies in T1D and 14.3% in T2D.¹³

The lower prevalence of DAAs in Bangladeshi children compared with European cohorts may reflect ethnic, genetic, and environmental differences. Variation in HLA allele distribution and immune susceptibility genes may explain part of this discrepancy.¹⁵ In addition, nutritional status, early-life infections, and gut microbiota differences have been hypothesized to influence the autoimmune phenotype of diabetes.^{16, 17}

An important finding of this study was the detection of DAAs in a subset of children clinically diagnosed with type 2 diabetes (T2D). In this group, 19.5% were positive for GADA and 12.2% for IAA, with 22% positive for at least one antibody. Similar findings have been described in other populations, where children with clinical features of T2D but positive for islet antibodies often progress to insulin dependence more rapidly, suggesting a form of latent autoimmune diabetes in youth.^{18, 19} These results align with previous reports suggesting that between 10% and 20% of children with a clinical diagnosis of T2D may harbor islet autoantibodies.²⁰⁻²⁴ This subgroup is often referred to as having latent autoimmune diabetes in youth (LADY), which

represents a heterogeneous phenotype with features of both T1D and T2D. The clinical implications are significant: antibody-positive youth initially managed as T2D frequently show more rapid decline in β -cell function and earlier progression to insulin dependence.^{25, 26}

The prevalence of islet-related autoantibodies among individuals aged 15–30 yr with a type 2 diabetes phenotype has been reported at 9.0–11.8%.^{27, 28} In low-resource settings such as Bangladesh, where treatment decisions must balance clinical features with limited access to diagnostics and therapies, antibody testing could play a critical role in early identification of these children. Future follow-up of our cohort would therefore be valuable to clarify disease progression.

Our data also emphasize the complementary role of C-peptide measurements. As expected, C-peptide levels were significantly lower in T1D compared with T2D, confirming β -cell dysfunction in the former. However, overlap in C-peptide values between groups was observed, consistent with prior studies showing that reliance on a single biochemical marker may lead to misclassification. To overcome this limitation, diagnostic accuracy can be improved by combining C-peptide with a broader panel of antibodies, including IA-2A and ZnT8, both of which have been shown to add predictive value in distinguishing autoimmune from non-autoimmune diabetes.^{29, 30}

The strengths of this study deserve emphasis. Recruitment from a national referral center ensured standardized diagnostic and management protocols, while antibody assays were performed within six months of diagnosis, minimizing underestimation due to antibody decline. Furthermore, the integration of demographic, clinical, biochemical, and immunological data provides a comprehensive view of the evolving diabetes phenotype in Bangladesh. Finally, by demonstrating antibody positivity in a subset of clinically defined T2D patients, the study provides novel insights into the evolving diabetes phenotype in South Asia and underscores the importance of incorporating antibody testing into diagnostic algorithms in resource-limited settings.

Nevertheless, several limitations must be considered. First, only two antibodies (GADA and IAA) were measured. Unfortunately, due to resource constraints, we were unable to include these additional antibodies in our study, which

represents a limitation. The inclusion of IA-2A and ZnT8 could have improved sensitivity and diagnostic accuracy. Second, the cross-sectional design limited our ability to assess longitudinal outcomes, particularly among antibody-positive children classified as T2D, who may progress to insulin dependence over time.

5. CONCLUSION

This study provides important new data on the antibody status of children with type 1 and type 2 diabetes in Bangladesh and highlights the diagnostic complexities posed by overlapping phenotypes. The findings underscore the value of integrating antibody testing and C-peptide measurement into diagnostic pathways, which can improve classification accuracy and guide therapeutic decisions in resource-limited settings.

Incorporating these tools into routine pediatric diabetes care could enhance early identification of autoimmune diabetes, ensure more appropriate treatment strategies, and ultimately improve long-term outcomes. Expanding antibody panels to include markers such as IA-2A and ZnT8, together with prospective longitudinal studies, will be essential to clarify disease progression in antibody-positive children with atypical features and to refine clinical management algorithms for this population.

6. FUNDING

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7. COMPETING INTERESTS

The authors declare that they have no competing interests.

8. DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are not publicly available due to patient confidentiality but are available from the corresponding author (BZ) on reasonable request.

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