ORIGINAL RESEARCH ARTICLE

Prevalence of Autoantibodies in Type 1 Diabetes Mellitus and the Clinical Utility of Diabetes Antibody Testing in the Indian Population: A Retrospective Study of 3 Years

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Abstract

Background: Type 1 diabetes or insulin-dependent diabetes is rising at 2–3% per year and contributes to almost 90% of juvenile diabetes and 10% of adult-onset diabetes. The presence of autoantibodies to glutamic acid decarboxylase-65 (GAD65), insulin antibodies (IA-2), islet cell antibodies, insulin antibodies, and zinc transporter 8 (ZnT8) indicates autoimmune destruction of beta cells and thus has the highest predictive value for type 1 diabetes. The risk of developing diabetes is also higher when an individual exhibits more than one antibody. Our study aimed to compare the predictive value of diabetes positivity for a specific type of autoantibody.

Materials and methods: A retrospective study was conducted at the Global Reference Lab in Mumbai over a period of 3 years (from January 2020 to July 2023) on patients and children undergoing testing for diabetes type 1 profile. Data were analyzed based on age, gender, and antibody positivity.

Results: Out of the 547 patients tested, 41.68% were female, and 58.32% were male. The positivity rate for the type 1 diabetes profile was 53.75%. Glutamic acid decarboxylase-65 antibodies were detected in 45.16% of patients, followed by IA2 insulin in 15.17% of patients. 48.68% of females were positive for GAD-65 compared to 42.63% positivity in males. The prevalence of GAD-65 positivity was higher in children up to 12 years of age, at 58.86%, followed by 43.50% positivity among the 19–30 years age group.

Conclusion: Our study found that more than half of the individuals (53.75%) who underwent testing, exhibited type 1 diabetes antibodies. GAD-65 positivity rates were higher in females compared to males.

Clinical significance: The study provides valuable insights into the prevalence and significance of type 1 diabetes antibodies in the Indian population, offering a foundation for targeted strategies in diabetes prevention and management.

Keywords: Autoantibodies, Autoimmunity, Anti GAD-65, Islet cell antibody, Type 1 diabetes mellitus.

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Introduction

Type 1 diabetes mellitus (TIDM) is an auto-immune disease in which the insulin-producing cells beta cells in the pancreas are damaged resulting in an insulin deficiency.[1] The presence of autoantibodies is the first sign of beta cell immunity, increasing with a 3–5% increase/year trend. Their appearance years before the onset of diabetes serves as an early marker of risk of progression to diabetes type 1 and detection of two or more antibodies is associated with a higher risk. The initial antibodies detected were islet cell antibodies. The disease-related antibodies available for testing are Glutamic acid decarboxylase-65 (GAD-65) Total antibody, islet cell antibody (ICA)-512, insulin antibodies (IA2), insulin antibody (IAA), zinc transporter 8 (ZnT8) antibody.[2]

Testing for autoantibodies helps in differentiating type 1 diabetes from other types of diabetes. The presence of multiple autoantibodies confirms type 1 diabetes and Autoantibodies may be absent in other non-autoimmune diabetes.[3]

Type 1 diabetes mellitus is rising at a rate of 2–3% per year and constitutes about 5–10% of all diabetes cases.[4] It comprises 90% of childhood-onset diabetes and 5–10% of adult-onset diabetes. Type 1 diabetes mellitus may be autoimmune or due to other processes.[5]

The probability of developing type 1 diabetes is difficult to determine however it can be due to genetic factors, environmental factors, and faulty immune regulatory mechanisms. The rate of progression to diabetes is dependent on the age of detection of antibodies, and the number and titer of autoantibodies.[6]

Type 1 diabetes autoantibody screening in the general population helps in educating and preparing families for disease symptoms and treatment. This could significantly delay the onset of TIDM, helping improve the quality of life with early diabetes management.

Our study conducted a retrospective analysis to assess the predictive value of diabetes positivity associated with a specific autoantibody within the general population.

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Table 1: Diabetes type 1 profile interpretation

Test	*Method*	*Interpretation*	*Remarks*
Glutamic acid decarboxylase (GAD)-65 antibody	Chemiluminescent immunoassay (CLIA)	Negative < 17 IU/mL Positive ≥ 17 IU/mL	Seen in prediabetes and insulin-dependent (type 1) diabetes mellitus (DM)
Islet cell antibody ICA-512	Immunofluorescence (IF)	Negative	Indicates a risk of developing type 1 diabetes and a future need for insulin therapy. Distinguish between autoimmune type 1 DM and DM due to other causes. (Obesity and insulin resistance)
IA2 insulin antibodies-protein tyrosine phosphate	Enzyme-linked immunoassay (ELISA)	Negative < 10 IU/mL, Positive ≥ 10 IU/mL	Indicates a risk of developing type 1 diabetes and a future need for insulin therapy
Insulin antibody IAA	Enzyme-linked immunoassay (ELISA)	Negative < 10 U/mL, Positive ≥ 10 U/mL	Indicate the likelihood of the development of future type 1 diabetes during the asymptomatic phase
Zn transporter 8 ZnT8 antibody	Chemiluminescent immunoassay (CLIA)	Non-reactive < 10 AU/mL, Reactive ≥ 10 AU/mL	Marker of childhood-onset type 1 diabetes
Insulin fasting	Electrochemiluminescence immunoassay (ECLIA)	02–25 µIU/mL	Decreased insulin level seen in diabetes. Increased insulin resistance
C-peptide	Chemiluminescent microparticle immunoassay (CMIA)	0.78–5.19 ng/mL	Decreased in insulin dependent diabetes. Increased in insulinomas

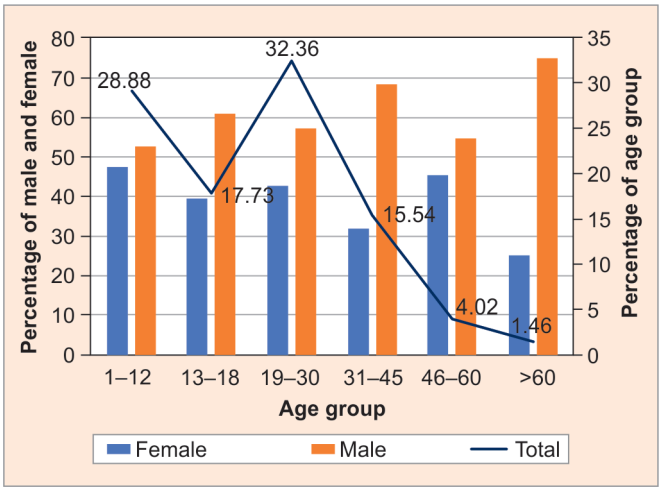

Fig. 1: Demographic distribution

Materials and Methods

A retrospective study was conducted over a period of 6 months (January 2020 to July 2023) at the Global Reference Laboratory in Mumbai, Maharashtra. Data was collected and analyzed in MS Excel format. Approval was obtained for the usage of Laboratory Information Management System (LIMS) data.

Inclusion Criteria

The study included data from a total of 547 patients, regardless of their clinical history. All patients, both children and adults, had their serum samples analyzed for the diabetes type 1 profile (Table 1).

Data Analysis and Results

- **Overall Demographic Distribution of Diabetes Type 1 Profile Tests:** Out of the 547 patients, 228 (41.68%) were females while 319 (58.32%) were males. The highest number of tests were conducted on children aged 12 and below, 158 (28.88%) cases, and 177 (32.36%), were conducted on individuals aged between 19 and 30 years old (Fig. 1).

Table 2: Distribution of diabetes type 1 profile

Diabetes type 1 profile	*N*	*%*
C-peptide, fasting		
Low	299	54.66%
Normal	230	42.05%
High	18	3.29%
GAD-65 antibody type 1 diabetes serum		
Negative	300	54.84%
Positive	247	45.16%
IA2-insulin		
Negative	464	84.83%
Positive	83	15.17%
Insulin antibody		
Negative	489	89.40%
Positive	58	10.60%
Insulin (fasting)		
Low	102	18.65%
Normal	366	66.91%
High	79	14.44%
Islet cell antibody		
Negative	478	87.39%
Positive	69	12.61%
Zinc transporter 8 (ZnT8) antibody		
Negative	45	95.74%
Positive	2	4.26%

N, number of participants; %, percentage

- **Overall Positivity Distribution of Diabetes Type 1 Profile:** Out of all the Diabetes autoantibodies, the GAD-65 antibody was found to have the highest positivity rate for type 1 diabetes. Out of the 547 patients, 247 (45.16%) were positive for GAD-65 antibody followed by 83 (15.17%) for IA2-insulin. C-peptide was low for 299 (54.66%) patients indicating an increase in Diabetes Mellitus among these patients (Table 2).

- **Positivity Distribution of Diabetes Auto Antibodies Gender Wise:** GAD-65 antibody had the highest positivity rate among females (48.68%) compared to males (42.63%), followed by ICA in females (15.79%). Additionally, a low C-peptide level was observed in 134 (58.77%) females and 165 (51.72%) males, indicating an increase in diabetes mellitus among these patients (Table 3).
- **Age-wise Prevalence of Diabetes Autoantibodies:** Among the different types of antibodies tested, GAD-65 antibody type 1 was found to be most prevalent in children up to 12 years old, with 93 cases (58.86%). The next most common antibodies were IA2 insulin, with 49 cases (31.01%), and ICA with 38 cases (24.05%). In the 19–30 age group, 77 patients (43.50%) tested positive for GAD-65 antibody, followed by 21 cases (11.86%) for IA. C-peptide hormone had the highest rate of positivity, with 124 cases (78.48%) among children up to 12 years old and 14 cases (63.64%) among those aged between 46 and 60 years. Similarly, insulin fasting hormone had the highest positivity rate of 7 cases (31.82%) among those aged between 46 and 60 years (Table 4).
- **Number of Autoantibodies in Patients:** Out of the 547 patients screened for type 1 diabetes, 46.25% of patients tested for antibodies. Meanwhile, 30.35% showed at least one positive test result, with 17.37% of patients having at least two positive test results, and 5.67% of patients testing positive for three autoantibodies. All four antibodies were positive in 2 patients (0.37%). The overall positivity rate for the type 1 diabetes profile antibodies was 53.76% (Fig. 2).
- **Comparison of C Peptide with Diabetes Antibodies:** Out of the 299 patients having low C-peptide, GAD-65 Antibody was positive in 176 (58.86%) patients (Table 5).

Table 3: Gender-wise distribution of diabetes type 1 autoantibody

	Gender				
	Female		*Male*		
Diabetes type 1 profile	*N*	*%*	*N*	*%*	*p-value*
C-peptide, fasting					
Low	134	58.77%	165	51.72%	0.2427
Normal	88	38.60%	142	44.51%	
High	6	2.63%	12	3.76%	
GAD-65 antibody type 1 diabetes serum					
Negative	117	51.32%	183	57.37%	0.1613
Positive	111	48.68%	136	42.63%	
IA2-insulin					
Negative	196	85.96%	268	84.01%	0.5307
Positive	32	14.04%	51	15.99%	
Insulin antibody					
Negative	197	86.40%	292	91.54%	0.0548
Positive	31	13.60%	27	8.46%	
Insulin (fasting)					
Low	46	20.18%	56	17.55%	0.5886
Normal	147	64.47%	219	68.65%	
High	35	15.35%	44	13.79%	
Islet cell antibody					
Negative	192	84.21%	286	89.66%	0.0589
Positive	36	15.79%	33	10.34%	

N, number of participants; %, percentage; $p < 0.05$ is considered statistically significant

Table 4: Age-wise prevalence of autoantibodies

	Age group												
	1–12		*13–18*		*19–30*		*31–45*		*46–60*		*Above 60*		
Diabetes type 1 profile	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*p-value*
C-peptide, fasting													
Low	124	78.48%	39	40.21%	79	44.63%	39	45.88%	14	63.64%	4	50.00%	0.0001
Normal	31	19.62%	57	58.76%	90	50.85%	42	49.41%	8	36.36%	2	25.00%	
High	3	1.90%	1	1.03%	8	4.52%	4	4.71%	0	0.00%	2	25.00%	
GAD-65 antibody type 1 diabetes serum													
Negative	65	41.14%	57	58.76%	100	56.50%	58	68.24%	13	59.09%	7	87.50%	0.0004
Positive	93	58.86%	40	41.24%	77	43.50%	27	31.76%	9	40.91%	1	12.50%	
IA2 insulin													
Negative	109	68.99%	80	82.47%	166	93.79%	81	95.29%	21	95.45%	7	87.50%	0.0001
Positive	49	31.01%	17	17.53%	11	6.21%	4	4.71%	1	4.55%	1	12.50%	
Insulin antibody													
Negative	139	87.97%	90	92.78%	156	88.14%	78	91.76%	18	81.82%	8	100.00%	0.4676
Positive	19	12.03%	7	7.22%	21	11.86%	7	8.24%	4	18.18%	0	0.00%	
Insulin (fasting)													
High	26	16.46%	9	9.28%	30	16.95%	10	11.76%	3	13.64%	1	12.50%	0.0002
Low	45	28.48%	16	16.49%	14	7.91%	17	20.00%	7	31.82%	3	37.50%	
Normal	87	55.06%	72	74.23%	133	75.14%	58	68.24%	12	54.55%	4	50.00%	
Islet cell antibody													
Negative	120	75.95%	85	87.63%	167	94.35%	80	94.12%	18	81.82%	8	100.00%	0.0001
Positive	38	24.05%	12	12.37%	10	5.65%	5	5.88%	4	18.18%	0	0.00%	

N, number of participants; %, percentage; $p < 0.05$ is considered statistically significant

Note: Four antibodies were used for the above table are GAD-65 antibody, IA2-insulin, Islet cell antibody, and insulin antibody used for the above table

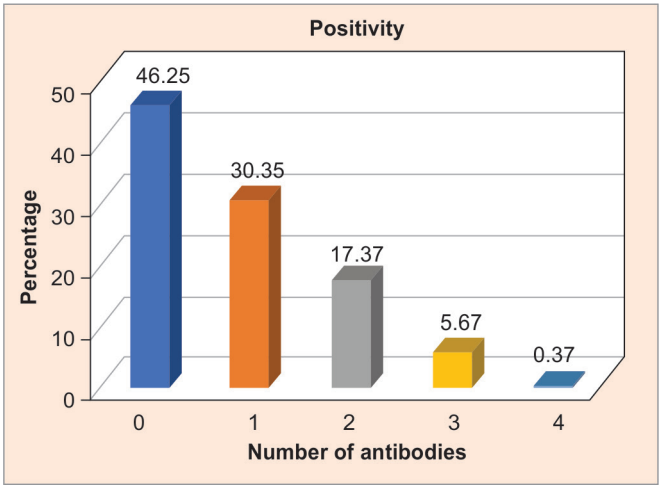

Fig. 2: Count of autoantibodies in patients

Table 5: Comparison of C-peptide with diabetes antibodies

Diabetes profile antibodies	*C-peptide, fasting*						
	Low		*Normal*		*High*		
	N	*%*	*N*	*%*	*N*	*%*	*p-value*
GAD-65 antibody type 1 diabetes serum							
Negative	123	41.14%	161	70.00%	16	88.89%	<0.0001
Positive	176	58.86%	69	30.00%	2	11.11%	
IA2-insulin							
Negative	238	79.60%	209	90.87%	17	94.44%	0.0008
Positive	61	20.40%	21	9.13%	1	5.56%	
Insulin antibody							
Negative	262	87.63%	210	91.30%	17	94.44%	0.3078
Positive	37	12.37%	20	8.70%	1	5.56%	
Islet cell antibody							
Negative	249	83.28%	212	92.17%	17	94.44%	0.0062
Positive	50	16.72%	18	7.83%	1	5.56%	

N, number of participants; %, percentage; $p < 0.05$ is considered statistically significant

Discussion

The incidence of type 1 Diabetes Mellitus is on the rise globally, accounting for 5–10% of all diabetes cases. Early intervention during the prediabetes phase can help manage the disease and prevent serious long-term complications. In type 1 diabetes, the immune system attacks beta cells and produces autoantibodies. While the likelihood of developing type 1 diabetes is unknown, testing positive for diabetes autoantibodies can increase the risk of the disease in the future. Repeated positive tests for two or three autoantibodies carry a higher risk. Thus, multiple antibody positivity can differentiate between health and disease and help predict the risk of developing type 1 diabetes.[7]

Our research on 547 patients showed that the percentage of those testing for diabetes type 1 autoantibody was higher in males, at 58.32%, compared to 41.68% in females. In the current study, those tested in the 19–30 years age group were slightly higher compared to those between 1 and 12 years (32.36 vs 28.88%).

Our retrospective study found that 53.75% of the Indian population had diabetes type 1 antibodies while 46.25% were negative for all antibodies. Additionally, 30.35% were positive for at least one antibody. These results are consistent with a study conducted by Unnikrishnan and Mohan in India, which indicated that 50% of patients clinically diagnosed with T1DM also tested positive for at least one antibody. Furthermore, over 10% of individuals tested positive for 2 antibodies, and 4% tested positive for all 3 antibodies.[8]

In another Moroccan study by Belhiba et al. 87.18 % of patients were positive for diabetes type 1 antibodies.[9]

When a screening test detects the presence of GAD65 autoantibodies, it serves as a crucial warning sign. This solitary positive result signals the need for further testing to assess the risk of developing type 1 diabetes (T1D) accurately and predict its onset. This area has seen numerous studies, leading to the development of various prediction models. For instance, some models suggest that if an individual test positive for three different islet protein autoantibodies, their risk of developing T1D within 5 years falls between 48% and 86% and over 10 years, it ranges from 64 to 86%. Other models propose that testing positive for three islet protein autoantibodies indicates a risk of developing T1D within 5 years approaching 100%.[10]

All of the studies conducted so far have failed to analyze all the antibodies collectively to diagnose type 1 diabetes.

Our retrospective study found that GAD-65 antibody positivity was the highest overall at 45.16%, followed by 15.17% for IA2 insulin. The positivity rate for GAD-65 was higher in females at 48.68% compared to males at 42.63%. Islet cell antibody was found to be 15.79% in females, while IA2 insulin was 15.99% in males. This difference could be attributed to the possible involvement of female hormones in autoimmune processes.[9]

Also, diabetes mellitus was indicated by low C-peptide levels of 58.77% in females and 51.72% in males. The highest percentage of positivity for GAD-65 was 58.86% in the 1–12 years age group followed by IA2 at 31.01% and islet cell antibody at 24.05%.

In a study conducted in Delhi by Dhanwal et al., 48% of patients with youth-onset diabetes had anti-GAD antibodies, 28% had insulin antibodies, and 14% had IA2 antibodies. This study reports high autoimmunity compared to other Indian studies.[11]

A recent study conducted in East India by Sanyal D et al. over ten years showed a trend of increasing autoantibody positivity. This surge in autoimmunity of T1DM could be triggered by changes in the enterobiome of the population, which could be a significant contributing factor towards the reported increased incidence of TIDM in India. T1DM is on the rise worldwide, with significant increases of 4.0% in Asia, 3.2% in Europe, and 5.3% in North America.[12]

A study conducted in Karachi by Khan YH et al. found that IAA and ZnT8 were present in children under 10 years of age, while the incidence of GAD 65 and IA2 occurs in children older than 10.[3]

A study conducted in Morocco by Derrou S et al. found that the incidence of GAD, IA2-insulin antibodies-protein tyrosine phosphate, and ICA was 74, 22, and 3.7%, respectively.[13]

Another study on the pediatric population in Morocco by Belhiba et al. showed that the proportion of positive results for anti-IA2 antibodies and anti-GAD antibodies was 76.92% and 62.82%, respectively.[9] Testing for anti-GAD antibodies alone may suffice as a diagnostic tool in young-onset diabetes mellitus.[11]

C-peptide is a commonly used tool in clinical settings to monitor beta cell function in diabetic patients and distinguish between type 1 and type 2 diabetes. About 80% of clinically classified type 1 diabetes patients test positive for autoantibodies. However,

it's important to highlight that autoantibody analyses are not consistently accessible in the standard local hospital laboratory. In contrast to most autoantibodies, C-peptide can be analyzed using a commercially available kit in the majority of laboratories. Therefore, patients with autoimmune markers would exhibit low C-peptide levels in the fasting state.[14] In our retrospective study of 547 patients with type 1 diabetes, 299 patients had low C-peptide levels. We found that 58.86% tested positive for GAD-65, 20.40% for IA2-insulin, 12.37% for IA, and 16.72% for ICA. While C-peptide measurement is utilized in diagnostic and therapeutic algorithms for autoimmune diabetes, its usefulness in predicting type 1 diabetes and managing type 2 diabetes is limited. The literature presents uncertainties, such as the lack of standardization of C-peptide measurement, C-peptide cutoff values, and the role of C-peptide as a marker of beta-cell competence.[15]

Conclusion

Our study found that 53.75% of the Indian population tested positive for type 1 antibodies. Additionally, GAD-65 showed higher positivity rates in females compared to males. Although GAD autoantibodies are commonly used to assess the risk of developing T1D, combining their detection with other islet autoantibodies can more accurately predict the likelihood of developing the disease. However, it's worth noting that the detection of GAD autoantibodies has unique clinical applications because its incidence varies based on age and susceptible populations. Currently, it is not possible to prevent type 1 diabetes in children who have developed multiple islet autoantibodies. Our research emphasizes the importance of finding ways to intervene and halt the development of these antibodies and delaying or preventing the onset of type 1 diabetes.

Clinical Significance

The study underscores that the risk of diabetes escalates with multiple autoantibodies, underscoring the need for a comprehensive risk assessment. It emphasizes the critical importance of early detection, particularly in specific demographics, providing valuable insights for targeted interventions and preventive strategies. The findings highlight the public health importance of addressing autoimmune diabetes through initiatives such as awareness campaigns, early screening, and interventions to mitigate the prevalence of type 1 diabetes.

Limitations

Zinc transporter 8 was excluded from further positivity analysis due to the low sample size ($n = 47$) as it is a newly added autoantibody for T1DM screening.

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References

1. Akil AAS, Yassin E, Al-Maraghi A, et al. Diagnosis and treatment of type 1 diabetes at the dawn of the personalized medicine era. J Transl Med 2021;19(1):137. DOI: https://doi.org/10.1186/s12967-021-02778-6.
2. Barker JM, Barriga KJ, Yu L, et al. Prediction of autoantibody positivity and progression to type 1 Diabetes: Diabetes autoimmunity study in the young (DAISY). The Journal of Clinical Endocrinology & Metabolism 2004;89(8):3896–3902. DOI: https://doi.org/10.1210/jc.2003-031887.
3. Khan YN, Ashfaq M, Nisa B, et al. IAA, GAD65 AND IA2 antibodies in type 1 diabetes mellitus children and adolescents. Annals ASH KMDC 2021;26(3):114–120. DOI: https://doi.org/10.58397/ashkmdc.v26i3.474.
4. Kumar KMP. Incidence trends for childhood type 1 Diabetes in India. Indian J Endocrinol Metab 2015;19(Suppl 1):S34–S35. DOI: 10.4103/2230-8210.155378.
5. Noemi Valdez S, Poskus E. Autoimmune Diabetes Mellitus: The importance of autoantibodies for disease prediction and diagnostic support. Current Immunology Reviews 2010;6(4):299–313. DOI: https://doi.org/10.2174/1573395511006040299.
6. ElSayed NA, Aleppo G, Aroda VR, et al. Introduction and methodology: Standards of Care in Diabetes—2023. Diabetes Care 2023;46 (Suppl 1): S1–S4. DOI: 10.2337/dc23-Sint.
7. Das AK. Type 1 diabetes in India: Overall insights. Indian Journal of Endocrinology and Metabolism 2015;19(Suppl 1):S31–S33. DOI: https://doi.org/10.4103/2230-8210.155372.
8. Unnikrishnan R, Mohan V. New directions for research into type 1 diabetes in India-An immunological perspective. The Indian journal of medical research 2014;140(3):336–338. PMID: 25366199.
9. Belhiba O, Aadam Z, Jeddane L. Research of anti-GAD and anti-IA2 autoantibodies by ELISA test in a series of Moroccan pediatric patients with diabetes type 1. African health sciences 2020;20(3):1337–1343. DOI: https://doi.org/10.4314/ahs.v20i3.40.
10. Towns R, Pietropaolo M. GAD-65 autoantibodies and their role as biomarkers of type 1 diabetes and latent autoimmune diabetes in adults (LADA). Drugs Future 2011;36(11):847. DOI: https://doi.org/10.1358/dof.2011.036.11.1710754.
11. Dhanwal DK, Agarwal S, Garg S, et al. Clinical and immunological profile of newly diagnosed patients with youth onset diabetes mellitus. Indian J Med Res 2014;140(3):356–360. PMID: 25366202.
12. Sanyal D, Batabyal SK, Maity S, et al. Changing profile of GAD and IA-2 antibody positivity in Indian children with recently diagnosed type 1 Diabetes Mellitus. Clinical Diabetology 2019;8(2):116–120. DOI: https://doi.org/10.5603/dk.2019.0005.
13. Derrou S, El Guendouz F, Benabdelfedil Y, et al. The profile of autoimmunity in type 1 Diabetes patients. Ann Afr Med 2021;20(1): 19–23. DOI: https://doi.org/10.4103/aam.aam_8_20.
14. Törn C, Landin-Olsson M, Scherstén B. Predictability of C-peptide for autoimmune diabetes in young adult diabetic patients. Pract Diab Int 2001;18(3):83–88. DOI: https://doi.org/10.1002/pdi.125.
15. Maddaloni E, Bolli GB, Frier BM, et al. C-peptide determination in the diagnosis of type of diabetes and its management: A clinical perspective. Diabetes, Obesity and Metabolism 2022;24(10): 1912–1926. DOI: https://doi.org/10.1111/dom.14785.