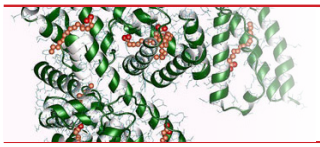
THE PATHCARE NEWS



DIABETES ANTIBODIES

Immune-mediated diabetes is characterized by the presence of circulating specific antibodies against the pancreatic islets such as glutamic acid decarboxylase autoantibodies (GADA), islet antigen-2 autoantibodies (IA-2A), or zinc transporter-8 autoantibodies (ZnT8A).

Type 1 Diabetes Mellitus (T1DM) is a chronic progressive disease characterized by autoimmune destruction of the insulin-secreting β-cells within the pancreatic islets. It occurs predominantly in young people and represents approximately 10% of all diabetes cases.

The development of islet cell antibodies precedes the clinical manifestation of T1DM by months or even years. One or more islet cell antibodies can be detected in approximately 90% of T1DM, even before the onset of clinical symptoms. GAD antibodies are the most commonly detected autoantibody, found in 50-80% of individuals diagnosed with T1DM, and are more frequently detected in adults. Autoantibodies against IA-2 can be found in 50-70% of children and adolescents and in 30-50% of adults with newly diagnosed T1DM. Anti-ZnT8 antibodies are detectable in the serum of approximately 60-80% of children at the onset of the disease and are found in up to 26% of cases that were previously classified as autoantibody negative. ZnT8 and IA2 antibodies persist until the manifestation of T1DM, then decline over the first years following the disease onset.

The combined determination of antibodies against GAD65, IA2, and ZnT8 can enable the identification of T1DM at disease onset in more than 90% of cases. In a study by Ziegler *et al*, the disease progression to T1DM in children were as follows:

Number of different autoantibodies present	Disease risk for T1DM
0	0.4%
1	12.7%
2	61.6%
3	79.1%

Although islet autoimmunity is responsible for the majority of childhood- and adolescent-onset diabetes, it can be detected in 4-10% of adults diagnosed with type 2 diabetes mellitus. This form of diabetes, described as latent autoimmune diabetes of the adult (LADA), is characterized by age > 30 years, the presence of diabetes-associated antibodies, and no insulin requirement within 6 months of diagnosis. GADA are the most prevalent autoantibodies observed in these patients (68-90%), with approximately 5% IA-2A and 2.3% with ZnT8-abs. Up to 24.1% of LADA have the presence of two autoantibodies.

In conclusion:

Islet cell antigen	Description
ZnT8	ZnT8 antibodies is often detected in the preclinical phase of autoimmune diabetes (T1DM). The presence of ZnT8A in asymptomatic patients increase the risk of developing T1DM. ZnT8A are detected in 60-80% of children at the onset of disease, and in approximately 10% of adult-onset diabetes. Up to 26% of autoantibody negative T1DM may have ZnT8A. ZnT8A are also associated with a greater risk of ketoacidosis. The presence of ZnT8A in patients who have undergone a pancreas transplant predicts beta-cell failure. ZnT8A levels decline after disease progression.
IA2	The presence of IA-2A in patients with diabetes indicated the presence of autoimmune T1DM. IA-2A in asymptomatic individuals indicate an increased risk of developing T1DM. IA2-A is more frequently detected in the younger patients, with a prevalence of 48-80% in children and adolescents, and 30-50% in adults with newly diagnosed T1DM.
GAD	GADA is found in 60-85% of T1DM, and is more frequently detected in adults than in children. The presence of GADA in asymptomatic individuals indicate an increased risk of autoimmune diabetes.
The risk of progression to T1DM in asymptomatic individuals is directly proportional to the number of different islet cell autoantibodies detected.	

Indications for diabetes autoantibody testing:

1. To establish an autoimmune aetiology in newly diagnosed T1DM patients.
2. To exclude autoimmune T1DM in diabetic adults without traditional risk factors for T2DM
3. To exclude possibility of autoimmune T1DM in overweight or obese paediatric patients suspected of having T2DM.

The combined detection of antibodies against ZnT8A, GADA and IA2 increases the detection rate of T1DM.

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References:

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