The Role of Diabetes-Associated Autoantibodies in Confirming the Diagnosis of Type 1 Diabetes Mellitus in Children and Adolescents

Dr Ahmad Mahfuz bin Gazali

PhD in Immunology

Senior Lecturer, Universiti Malaysia Pahang (UMP)

Type 1 diabetes mellitus (T1DM) is a chronic condition caused by immune cell infiltration and destruction of the pancreas insulin-producing beta (β) cells. The death of β cells causes the loss of insulin secretion, causing hyperglycaemia. The Malaysian Diabetes in Children and Adolescents Registry published a report in 2007 stating that almost 70% of childhood and adolescent diabetes were T1DM patients[1].

Although T1DM is a metabolic disease, diabetes-associated autoantibodies (DAA) have been one of the markers used to confirm the diagnosis of T1DM. The Clinical Practice Guidelines recommended DAA testing, namely glutamic acid decarboxylase antibody (GADA), anti-islet antibody (ICA), insulin autoantibodies (IAA), protein tyrosine phosphatase antibody (IA-2A) and zinc transporter 8 autoantibody (ZnT8), to confirm T1DM diagnosis[2].

Despite DAA is a vital marker to confirm the diagnosis of T1DM, there are several limitations to using DAA in T1DM diagnosis. An American study reported 86% of children and adolescents with T1DM were positive for DAA (GADA, IAA and IA-2A), while 6% of Type 2 diabetes mellitus (T2DM) patients were positive for DAA[3]. Furthermore, 0.98% of young T2DM patients were positive with ZnT8[4], indicating that a positive titre of DAAs may not be diagnostic of T1DM. Another limitation of using DAAs is not all T1DM patients are positive for DAAs. These patients are autoantibody negative T1DM patients. 5.2% of young T1DM patients display no positive titre of DAAs[3]. At the same time, a study from Malaysia reported that 32% of young diabetes patients were seronegative despite being presented with the near or total destruction of β cells[5]. Therefore, the patient's history, blood glucose profile, glycated haemoglobin (HbA1c), DAA and possibly C-peptide levels are crucial before confirming a T1DM diagnosis.

Innoquest Pathology offers:

Panel Code	Tests	Specimen Requirements
GDA	GAD Autoantibodies	8ml Plain (Gel-YELLOW)
IAN	IA-2 Autoantibodies	8ml Plain (Gel-YELLOW)

References:

1. Md Zain, F, et al 2nd Annual Report of the Diabetes in Children and Adolescents Registry 2006-2008. Kuala Lumpur: Diabetes in Children and Adolescents Registry, Malaysia. 2012.
2. Malaysia Health Technology Assessment Section. Clinical Practice Guidelines: Management of Type 1 Diabetes Mellitus in Children and Adolescents. Putrajaya, Putrajaya. 2017.
3. von Oettingen, J. E., Wolfsdorf, J. I., Feldman, H. A., & Rhodes, E. T. Utility of diabetes-associated autoantibodies for classification of new onset diabetes in children and adolescents. Pediatric Diabetes, 2015, 17(6), 417–425.
4. Higgins, J., Zeitler, P., Drews, K. L., Arslanian, S., Copeland, K., Goland, R., Klingensmith, G., Lipman, T. H., & Tollefsen, S. ZNT8 autoantibody prevalence is low in youth with type 2 diabetes and associated with higher insulin sensitivity, lower insulin secretion, and lower disposition index. Journal of Clinical & Translational Endocrinology, 2022, 29, 100300.
5. Wan Nazaimoon, W. M., Nor Azmi, K., Rasat, R., Ismail, I. S., Singaraveloo, M., Wan Mohamad, W. B., Letchuman, R., Sheriff, I. H., Faridah, I., Khalid, B. A. K. Autoimmune markers in young Malaysian patients with type 1 diabetes mellitus. Medical Journal of Malaysia; 2000; 55(3), 318–23.