

## Latent Autoimmune Diabetes of Adults Presenting as Recurrent Diabetic Ketoacidosis

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### ABSTRACT

Diabetes mellitus encompasses a spectrum of metabolic disorders characterized by hyperglycaemia, resulting from genetic and environmental interactions that impair insulin secretion, glucose utilization, and production. The World Health Organization (WHO) revised its diabetes classification in 2019 to include six categories: Type 1 (insulin-dependent), Type 2 (insulin-resistant), hybrid forms (e.g., Latent Autoimmune Diabetes in Adults [LADA] and ketosis-prone diabetes), other specific types, unclassified diabetes, and hyperglycaemia first detected during pregnancy. LADA is a hybrid form of diabetes characterized by gradual autoimmune beta-cell destruction, commonly misdiagnosed as Type 2 diabetes. Diagnostic criteria include onset after 30 years, islet autoantibodies (e.g., GAD), and delayed insulin dependence. LADA risk factors include low BMI, autoimmune history, and progressive hyperglycaemia despite oral antidiabetic therapy. High-risk patients undergo GAD antibody testing for confirmation. Accurate identification of LADA is essential for appropriate management, as it bridges features of Type 1 and Type 2 diabetes.

### ARTICLE DETAILS

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### INTRODUCTION

Diabetes mellitus refers to group of common metabolic disorders that share the phenotype of hyperglycaemia. Several distinct types of Diabetes Mellitus are caused by complex interaction of genetic and environmental factors characterised by reduced insulin secretion, decreased glucose utilization and increased glucose production.<sup>1</sup> Revised classification of diabetes by WHO in 2019 provide the best possible compromise between an etiological and clinical classification that is feasible to implement in different settings throughout the globe which divides Diabetes into six broad groups 1) Type 1 (Insulin dependent), 2) Type 2 (Insulin resistant), 3) Hybrid forms of diabetes - slowly evolving immune mediated diabetes in adults previously known as LADA - Latent Autoimmune Diabetes of Adults and ketosis prone Type2 diabetes mellitus previously known as Flatbush diabetes. 4) Other specific types like monogenic diabetes, disease of exocrine pancreas, endocrinopathies, drug or chemical induced diabetes, infection related diabetes, uncommon form of immune mediated diabetes and other genetic syndromes associated with diabetes 5) Unclassified diabetes. 6) Hyperglycaemia first detected during pregnancy - Diabetes Mellitus in pregnancy or Gestational Diabetes

Mellitus.<sup>2</sup> LADA is a hybrid group of Diabetes Mellitus characterised by slowly progressive beta cell loss due to autoimmunity in adults. Most of the patients are phenotypically closer to Type 1 Diabetes Mellitus. Criteria for diagnosis include - adult age of onset (>30years), presence of any islet cell autoantibody, absence of insulin requirement for at least 6 months after diagnosis. The commonest islet cell autoantibodies are GAD (Glutamic acid decarboxylase), ICA, IA-2A, ZnT8A and tetraspanin7. As per European multicentre study 90% of LADA patients were positive for GADA, less frequent were-ICA, IA-2A, ZnT8A and tetraspanin7.<sup>3</sup> LADA has to be suspected in patients diagnosed as Type 2 diabetes with normal weight, personal or family history of autoimmune diseases such as Thyroid disease, Rheumatoid Arthritis, Lupus, Multiple Sclerosis and in patients with significant deterioration of blood sugar over a period of year despite treatment with oral anti diabetic drugs and carbohydrate restriction. The parameters for Clinical Risk Assessment in suspected LADA includes 1) Age less than 50 years 2) BMI less than 25 3) Acute symptoms of hyperglycaemia at onset 4) History of autoimmune diseases 5) Family history of autoimmune disease <sup>4</sup>. Patient having score of equal or more than 2 are at High risk of LADA were

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measured for GADA. Patient having score of one clinical feature are at Mild risk of LADA and are measured with C-

Peptide, patients with low C-Peptide are measured for GADA. Patient is diagnosed as LADA who are positive For GADA.

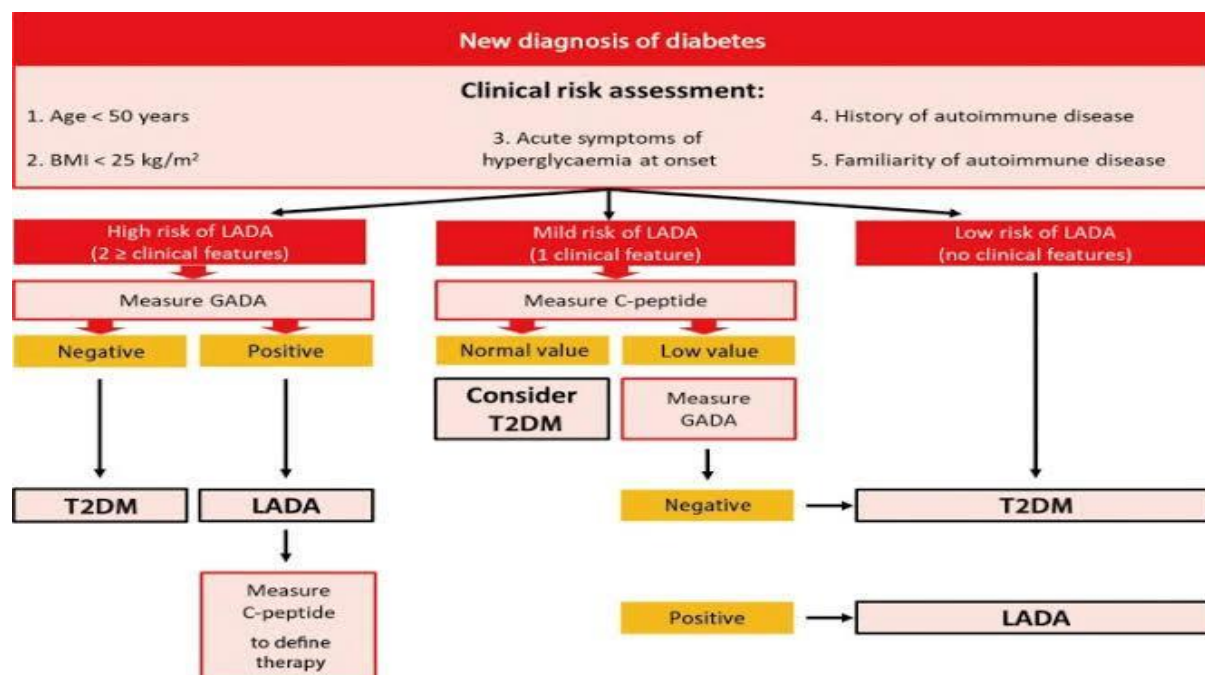


Fig 1 Clinical Risk Assessment of LADA in newly diagnosed Diabetes Mellitus<sup>3</sup>

### CASE PRESENTATION

A 24 year female known case of diabetes mellitus since 2 years on regular injection Human Mixtard 20 -0 -25 units presented to Emergency ward with tiredness, continuous vomiting, pain abdomen. On evaluation patient is conscious and tachypneic, pulse 116 per minute, Blood pressure 100/60 mm hg, Respiratory rate-26 cycles per minute, spo2-98% at room air, lower abdominal tenderness present. Blood glucose was 350mg/dl. Urine was positive for ketone bodies, Arterial Blood Gas analysis shows acute metabolic acidosis with Ph 7.24, Pco2 was 20.7, Po2 was 71.4, Bicarbonate 11.1. Routine investigations were Hb of 13.9 gm/dl, Total leukocyte count 15,320, Platelet 3.05lakh, Blood Urea 23mg/dl, Serum Creatinine 0.6 mg/dl, Bilirubin 0.8mg/dl, SGPT 20U, SGOT 38U, Sodium 136 mmol/l, Potassium 5.8 mmol/l, Chloride 106 mmol/l. History of admission for Diabetic Ketoacidosis 7 and 11 months back. Patient was diagnosed as Diabetes mellitus 20 months back in July 2022 was on oral anti diabetic drugs and carbohydrate restriction. Patient was also having significant history of Hashimoto's Thyroiditis since 2020 when USG of the neck showed coarse echotexture in thyroid with ill-defined small hypoechoic nodules possibly due to Hashimoto's thyroiditis which was confirmed by Fine needle aspiration and cytology, however thyroid profile was within normal limits patient was not started on any treatment, As the patient was not under good glycaemic control she was evaluated further and found to have high titres of GAD-65 antibody 85.8 Iu/ml (<10.0 negative, >10.0 positive), Anti Microsomal/ Thyroperoxidase antibody >1300.0 u/ml

(<0.60), Anti Thyroglobulin Antibody >500.00 IU/ml (<60.0) and insulin antibodies 0.47 units/ml (<0.95-negative, >1.05-positive). No family history of Diabetes Mellitus and autoimmune diseases. Her HbA1c was constantly on higher side 14.5% on 20/05/23 and 23/09/23, 12.1% on 31/03/24. Patient was diagnosed as Diabetic ketoacidosis and managed as per the protocol.

### DISCUSSION

LADA usually presents above the age of 30 years with presence of any islet cell antibody and absence of requirement of insulin early in the diagnosis. Most of the patients are phenotypically similar to Type 1 diabetes mellitus. Most of the patient will have family or personal history of autoimmune diseases and significant deterioration of blood sugar despite of carbohydrate restriction and oral anti diabetic drugs. This patient got diagnosed at the age of 22years, phenotypically similar to Type 1 diabetes mellitus with BMI of 17.3. There is history of Hashimoto's thyroiditis with confirmed histological report, presence of significant titres of islet cell autoantibody in the form of GAD 65- 85.8 Iu/ml (<10.0 negative, >10.0 positive). There is significant rise in the autoimmune antibodies in the form of Anti Microsomal/ Thyroperoxidase >1300.0 u/ml (<0.60) and Anti Thyroglobulin Antibody >500.00 IU/ml (<60.0). As patients have residual beta cell function treatment should aim to protect and stimulate beta cell regeneration. Hence patient started on insulin but patient had recurrent admissions for Diabetic ketoacidosis inspite of compliance to insulin therapy

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which suggests progressive beta cell destruction. Insulin, DPP4 inhibitors, thiazolidinediones and GLP1 receptor agonists have shown promise in achieving glycaemic control and preserving beta-cell function.

### CONCLUSION

This case highlights the importance of clinical recognition of LADA in the patient Diabetes Mellitus patients who presents in early age, not under control with oral antidiabetic drugs and with carbohydrate restriction. LADA to be considered in patients with phenotypically Type 1 diabetes mellitus presenting in early adulthood.

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