Diabetes-Associated Autoantibodies

Diabetes mellitus (DM) refers to a group of metabolic disorders characterized by hyperglycemia that results from defects in insulin secretion, insulin action, or both. Type 1 DM (T1DM) is less common than type 2 DM (T2DM) and is characterized by insulin deficiency, which often results from the autoimmune-mediated destruction of insulin-producing cells. The detection of diabetes-associated autoantibodies confirms an autoimmune etiology for that individual.

Indications for Insulin Antibody Testing

<table>
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<tr>
<th>Indications for Insulin Antibody Testing</th>
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<tbody>
<tr>
<td><strong>T1DM</strong></td>
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<tr>
<td>Patient should have been previously diagnosed with DM.</td>
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<tr>
<td>- Antibody testing is not useful for the diagnosis of DM.</td>
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<td>- Patients should be receiving insulin ≤2 wks, ideally.</td>
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<tr>
<td>- Testing is not recommended for patients receiving insulin &gt;2 wks, as insulin antibody formation may occur (false-positive result possible).</td>
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Most useful in children or in adults without traditional risk factors for T2DM

- Traditional risk factors include excess weight/obesity (BMI ≥25 kg/m² or ≥23 kg/m² in Asian individuals), a first-degree relative with diabetes, being a high-risk race/ethnicity, physical inactivity, etc.
- For a full list of traditional risk factors, see Table 2.3 in the Standards of Medical Care in Diabetes.²

It may be useful in difficult adult cases to help differentiate between T1DM or T2DM.³

| **T2DM**                                |
| No indication for routine evaluation or management.¹ |

| **Screening**                            |
| Acceptable only for first-degree relatives of a proband with T1DM or in research settings |

| **Limited use**                          |
| Differentiate LADA from T2DM⁴ |
| Rule out autoantibodies as a cause of DM in patients with suspected genetic DM types (eg, monogenic DM, MODY) |

### Diabetes Mellitus Type 1 Overview

**Prevalence**

1.25 million in the United States

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Prevalence

1.25 million in the United States
Age of Onset

Most common in children but can develop in individuals of any age, especially in late 30s or early 40s

Symptoms

- Excessive thirst, hunger, and urination
- Fatigue, nausea, blurred vision
- Unexplained weight loss (obesity is rare at initial diagnosis)
- Possible co-occurring autoimmune disorders

Physiology

- Caused by autoimmune-mediated destruction of insulin-producing beta cells of the islets of Langerhans in the pancreas
- Five major autoantibodies of diagnostic interest:
  - GAD
  - IAA
  - IA-2
  - ICA
  - ZnT8
- Antibodies may be present in individuals years before the onset of clinical symptoms.
  - A presence in individuals with diabetes confirms an autoimmune etiology.

Test Interpretation

Sensitivity/Specificity

- Moderate sensitivity, high specificity in newly diagnosed T1DM
- The presence of antibodies may decrease with long-term disease.
- Insulin antibody testing loses specificity once the patient has been on exogenous insulin for >2 weeks.

Results

- The presence of multiple insulin antibodies (GAD, IA-2, IAA, ICA, and ZnT8) is predictive of T1DM.
- If one autoantibody is found, others should be assayed; the risk of T1DM increases (>90%) if an individual tests positive for two or more autoantibodies.
- For further risk stratification, HLA-DR or HLA-DQ genotyping may be helpful.

Limitations

- Negative test results do not rule out autoimmune diabetes; autoantibody response varies by individuals.
- Presence of a single autoantibody in the absence of clinical symptoms has low predictive value (1-2% in healthy individuals).
- Not all individuals with antibodies will develop T1DM.
- Do not use to monitor or diagnose T1DM.
- IAA testing does not differentiate between antibodies specific for endogenous and exogenous forms of insulin.

References


Related Information

*Dietetics Mellitus - Type 1, Type 2, and Gestational*