Technical Brief

Hemoglobin A1C

Background Information

This assay (also known as HbA1c, A1c, Glycohemoglobin, Glycated hemoglobin and Glycosylated hemoglobin) is useful in evaluating the long-term control of blood glucose concentrations in diabetic patients. Diabetes mellitus is a chronic disorder affecting 25.8 million adults and children, or 8.3% of the U.S. population. More than 1.9 million new cases were diagnosed in adults over age 20 in 2010, and another 79 million are estimated to have prediabetes.

Diabetes is characterized by hyperglycemia and is associated with disturbances in carbohydrate, fat and protein metabolism. Classic symptoms include polyuria, polydipsia and polyphagia due to hyperglycemia. Treatment is focused on effectively controlling blood glucose levels in order to prevent the acute complications of ketosis and hyperglycemia, as well as the long-term complications of retinopathy, neuropathy, nephropathy and cardiovascular disease.

Results of the Hemoglobin A1C assay reflect the mean glucose concentration in the blood over the previous two to three months. In many patients, it is considered a better indicator of long-term glycemic control than fasting plasma glucose (FPG) and oral glucose tolerance tests (OGTT) because the assay is more closely linked to the risk of complications than single or episodic measure of glucose levels.

Advantages of the Hemoglobin A1C test include:

- Provides an assessment of chronic hyperglycemia.
- Assay standardization efforts from the National Glycohemoglobin Standardization Program (NGSP) have been successful.
- Fasting is not necessary.
- Intra-individual variability is very low (CV of < 2%)
- Based on newer guidelines, this single test can be used for both diagnosing and monitoring diabetes.

Clinical Indications

The Hemoglobin A1C test is often ordered as part of a routine physical. It also is used if diabetes is suspected because of signs and symptoms of hyperglycemia, such as increased thirst, increased urination, blurred vision, fatigue, and slow-healing infections. In 2010, new clinical practice guidelines from the ADA stated that Hemoglobin A1c may be added to fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT) as an option for diabetes screening or diagnosis.

The Hemoglobin A1C test is useful in monitoring a patient’s metabolic control. The American Diabetes Association recommends the testing three to four times per year for type 1 and poorly controlled type 2 diabetes patients, and two times per year for well-controlled type 2 diabetes patients. More frequent monitoring may be recommended if the patient changes diabetes treatment or if they are not meeting blood glucose goals.

Methodology

Turbidimetric Inhibition Immunoassay (TINIA).

Interpretation

The Hemoglobin A1C assay is reported as a percentage based on NGSP derived units for monitoring glucose. A result below 5.7% is considered normal; prediabetes may be indicated with a 5.7 to 6.4% result, and diabetes is indicated at a level of 6.5% or higher. A diabetes diagnosis should be confirmed by a second test ordered by the patient’s physician.

The test report will include an eAG result, which is calculated based on the relationship between blood glucose concentrations and Hemoglobin A1C levels. Knowing the eAG helps patients to relate their results to everyday glucose monitoring levels obtained from home monitoring systems or laboratory tests. It’s important to understand that the eAG is an evaluation over a period of several months, and will not match exactly with any one daily glucose result. For example, a diabetic patient who has come under good control in recent weeks may for some time have a high concentration of Hemoglobin A1c. Conversely, a patient with a low concentration of Hemoglobin A1C may have had good control in previous weeks, but have poor control in recent weeks.
Limitations of the Assay
Since the Hemoglobin A1C will not indicate temporary, acute blood glucose changes, the assay will not reflect acute glucose swings. The assay may not be useful in patients with rare hemoglobin variants. In addition, test results may be falsely low for individuals who have iron-deficiency anemia, vitamin B12 anemia, hemolysis or heavy bleeding. It should not be used to diagnose diabetes in pregnant women.

This assay is not useful in determining day-to-day glucose control and should not be used to replace daily home testing of blood glucose.

References

Test Overview

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Hemoglobin A1C</th>
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<tbody>
<tr>
<td>Methodology</td>
<td>Turbidimetric Inhibition Immunoassay (TINIA)</td>
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<tr>
<td>Specimen Requirements</td>
<td>Volume/Size: 2 mL; Type: Whole blood; Tube/Container: EDTA (Lavender); Transport Temperature: Refrigerated</td>
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<tr>
<td>Alternate Specimen Requirements</td>
<td>Volume/Size: 2 mL; Type: Whole blood; Tube/Container: Lithium heparin (Green); Collection Temperature: Ambient; Transport Temperature: Refrigerated</td>
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<tr>
<td>Special Information</td>
<td>Limitations/Contraindications: hemoglobinopathies. The test requires the presence of intrinsically produced hemoglobin A. Patients with disorders causing significantly shortened life span of red blood cells (e.g. hemolytic anemias) should not be offered this test. In addition, elevated hemoglobin F (&gt; 10% of total hemoglobin) causes significant underestimation of hemoglobin A1c. In these cases, fructosamine or fasting glucose should be considered for monitoring glycemic control.</td>
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<tr>
<td>Clinical Information</td>
<td>Evaluation of control of diabetes mellitus; diagnosis of diabetes mellitus</td>
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<tr>
<td>Stability</td>
<td>3 days at 15-25°C; 7 days at 2-8°C</td>
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<tr>
<td>Reference Range</td>
<td>&lt; 5.7%</td>
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