HbA1c

Diabetes constitutes a heavy burden for the patient and the society. It is associated with many complications and increased mortality.

Complication and mortality rates further increase with smoking, obesity, hypertension, increased cholesterol and triglyceride, proteinuria, and poor glucose control. Early diagnosis, good glucose monitoring and control are crucial to reduce the burden of diabetes.

The fraction of hemoglobin that is bound to glucose - HbA1c - now serves as a powerful tool for assessing long-term glycemic control. HbA1c also correlates well with the risk of development of complications related to diabetes, which is a very important aspect. In the future HbA1c is likely to become a useful tool also for the diagnosis and evaluation of all forms of diabetes mellitus and patients at risk of developing diabetes, making it possible to discover diabetes earlier.

The new Clover A1c developed by Infopia and based on a patented test method makes it possible to easily and rapidly determine HbA1c at the physician’s office. This system will simplify monitoring of any type of diabetes facilitating treatment management, and prevention of late complications. It may also increase the patient’s motivation to comply with treatment and lifestyle changes to optimise prognosis.

What is HbA1c?

HbA1c designates a stable minor glycated sub fraction of hemoglobin. It is a reflection of the mean blood glucose levels during the last 6-8 weeks, and is expressed in % of total hemoglobin. HbA1c does correlate well with average blood glucose, but does not say anything about the blood glucose fluctuations. An HbA1c value of 7.5% will, however, correspond to fasting blood glucose values of 5-8 mmol/L or a mean blood glucose value of somewhat lower than 10 mmol/L. The first clinically useful method for determining of HbA1c was described in 1978. Since then about 20 methods of determination of HbA1c, based on HPLC, electrophoresis, immunology and affinity methods have been developed. Different methods, however, do not measure identical adducts. Some methods measure all adducts, others not. Therefore values have to be standardized, and international standardisation work is well underway. The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) have presented an approved reference method for the measurement of HbA1c. It is the basis for the uniform standardization of HbA1c routine assays worldwide.

Why measure HbA1c?

HbA1c has gained acceptance as an accurate index of long-term blood glucose control. Longitudinal studies have shown that good metabolic control, reflected by stable HbA1c level can prevent or postpone micro- and macrovascular and other complications or slow down the progress of such complications in both Type 1 and
Type 2 diabetics.

The Diabetes Control and Complications Trial (DCCT), and the United Kingdom Prospective Diabetes Study (UKPDS), clearly demonstrated that there is a good correlation between glycemic control and the incidence of late complications. In this study of 1,141 patients with Type 1 diabetes, with or without complications at baseline, the mean HbA1c values over the nine-year study period were 7.2% with intensive therapy and 9.1% in the conventional group. Even more important; late complications were rarer in the group with lower HbA1c treated intensively. The results showed that intensive treatment with lower and more stable HbA1c values delayed the onset or slowed the progression of clinically important retinopathy, including vision-threatening lesions, nephropathy and neuropathy by 35% to more than 70%. The study established HbA1c as the gold standard of glycemic control, with levels 7% deemed appropriate for reducing the risk of vascular complications in diabetic patients. In another longitudinal study: the Barbados Eye Study, 324 diabetic patients at risk for developing diabetic retinopathy was followed-up for 9 years. Diabetic retinopathy risk increased with 30% for each increase of HbA1c of 1%.

In the UKPDS, a study of over 4,000 patients with newly diagnosed Type 2 diabetes, treated with different regimens, a 1% reduction of HbA1c was associated with a 35% reduction in macrovascular endpoints, an 18% reduction in myocardial infarction, and a 17% reduction in all-cause mortality. Also in this study there was a correlation between HbA1c values obtained and the rate of complications. Over the 10-year study period, the average HbA1c was 7.0% in the intensively treated group compared with 7.9% in the conventional group. The benefit of intensive treatment appeared to be independent of type of treatment. The EURODIAB study conducted in 31 European centres, that followed HbA1c in 3,250 patients with Type 1 diabetes, found that HbA1c was a predictor for the development of retinopathy and neuropathy, and also for worsening of albuminuria.

It was recently reported from the Atherosclerosis Risk in Communities Study that raised HbA1c could be an independent risk factor for stroke with similar relative risk as for coronary heart disease, and not only in diabetics, but also in adults without diabetes. The study included 10,886 participants without diabetes and 1,635 with diabetes that were followed up for 8-10 years. It is also interesting that a significant joint effect of HbA1c and another risk factor for vascular disease, C-reactive protein (CRP) were found on the atherosclerotic progression in both diabetic as well as non-diabetic subjects in a population-based German study of 3,534 persons followed for 2 years.

Most of the cost of diabetes - in suffering, in lost years of working capacity, and in health care - comes from its complications.

Efficient glucose control and monitoring using HbA1c can thus reduce diabetes complications efficiently.
Interpretation of HbA1c

Although the glycohemoglobin value reflects the average blood glucose levels over the previous 2-3 months, it is not possible to logistically determine the precise mathematical relationship between a particular glycohemoglobin level and mean plasma glucose. Several studies have shown that the closer the glycohemoglobin level is to normal range, the lower is the mean plasma glucose value. Ideally, an important diabetes care goal would be to maintain glycohemoglobin levels in the non-diabetic range. It must be determined, however, if such a goal is realistic.

The outcome of the Diabetes Control and Complications Trial (DCCT study) has been and is important concerning treatment of Type 1 diabetes mellitus. The goal for the participants receiving intensive therapy was HbA1c levels <6.05%. 44% of the patients receiving intensive therapy achieved the goal of glycated hemoglobin value of 6.05% or less at least once during the study. Less than 5% maintained an average value in this range.

The recommendation from the DCCT study is that most patients with Type 1 diabetes should be treated with closely monitored intensive regimens, with the goal of maintaining the glycemic status as close to the normal range as safely possible. Because of the risk of hypoglycemia, intensive therapy should be implemented with caution.

Capital outlay

Cost per machine: R14 000 with Printer (excl vat) No Printer R12500 (excl vat)
Cost per test : R72 (excl vat) (R720 per box of 10)
Nappi Code : 627926-002
Procedure Code: 4064

Additional Information

HbA1c (Haemoglobin A1c)

- What is Haemoglobin A1c (HbA1c)?
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- Can you diagnose diabetes using HbA1c?
- The risk of complications is not linear!
• How often should I have my HbA1c checked?
• What is the target HbA1c?
• Why do I find it impossible to hit the target HbA1c?

What is Haemoglobin A1c (HbA1c)?
Haemoglobin is the substance in the blood that carries oxygen within red blood cells. Over time, glucose binds very slowly to haemoglobin and results in glycated haemoglobin. This glycated haemoglobin can be measured and provides an estimate of average blood sugar levels. In people who do not have diabetes levels between 4 and 6% are observed.

The life span of a red blood cell is 90 to 120 days in circulation. This is why the HbA1c measurement tells us what your blood sugars have been doing over the past three months.

What is the importance of measuring HbA1c?
The HbA1c is the best single measurement available to clinicians to assess your overall diabetes control and the risk of complications of diabetes.

The Diabetes Control and Complications Study, a landmark study of people with Type 1 diabetes conducted in the early 1990s, showed that the risk of development and progression of complications of diabetes increased with HbA1c.

Can you diagnose diabetes using HbA1c?
Yes. Recently the ADA issued a statement that certified A1c as an acceptable method to diagnose diabetes.

December 31, 2009 — The American Diabetes Association (ADA) revised clinical practice recommendations for diabetes diagnosis promote hemoglobin A1c (A1c) as a faster, easier diagnostic test that could help reduce the number of undiagnosed patients and better identify patients with prediabetes. The new recommendations are published December 29 in the January supplement of Diabetes Care.

"We believe that use of the A1c, because it doesn't require fasting, will encourage more people to get tested for type 2 diabetes and help further reduce the number of people who are undiagnosed but living with this chronic and potentially life-threatening disease," Richard M. Bergenstal, MD, ADA president-elect of medicine & science, said in a news release. "Additionally, early detection can make an enormous difference in a person's quality of life. Unlike many chronic diseases, type 2 diabetes
actually can be prevented, as long as lifestyle changes are made while blood glucose levels are still in the pre-diabetes range."

The A1c test, which measures average blood glucose levels for a period of up to 3 months, was previously used only to evaluate diabetic control with time. An A1c level of approximately 5% indicates the absence of diabetes, and according to the revised evidence-based guidelines, an A1c score of 5.7% to 6.4% indicates prediabetes, and an A1c level of 6.5% or higher indicates the presence of diabetes.

For optimal diabetic control, the recommended ADA target for most people with diabetes is an A1c level no greater than 7%. It is hoped that achieving this target would help prevent serious diabetes-related complications including nephropathy, neuropathy, retinopathy, and gum disease.

Unlike fasting plasma glucose testing and the oral glucose tolerance test, A1c testing does not require overnight fasting. Compliance with screening may therefore be improved through use of the A1c test, which can be determined from a single nonfasting blood sample.

**The risk of complications is not linear!**

With increasing haemoglobin A1c the risk of complications of diabetes tends to rise disproportionately.

As you can see from the graph the risk of complications increases substantially with a small increase in HbA1c of 1%. 
How often should I have my HbA1c checked?
We recommend you have an HbA1c at least twice a year. For those who are consistently well controlled once a year should suffice.

What is the target HbA1c?
Targets in many ways depend on the individual patient as there are many variable factors which would influence your ability to achieve a given target. In general an Hba1c of 6.5% represents ‘good’ control, a level of 7% ‘satisfactory’ or ‘fair’ and a level greater than 7.5% is indicative of poor control. It is worth emphasizing that it may not be appropriate to aim for a level of 6.5% in someone who is elderly or prone to recurrent hypoglycaemia.

A1C and Complications
The DCCT was the pivotal trial that provided the link between A1C levels and the risk of diabetes-associated complications. The results of the Diabetes Control and Complications Trial (DCCT) shown below are considered definitive for patients with type 1 diabetes. Relative risk increased with A1C for retinopathy, nephropathy, and microalbuminuria, and the risk of retinopathy and nephropathy accelerated at the highest levels of A1C. In this study, improved glycemic control following intensive diabetes therapy delayed the onset and slowed the progression of diabetic retinopathy, nephropathy and neuropathy in patients with type 1 diabetes. [5]
Patients with type 1 diabetes (n=1,441)
Adapted from DCCT. Diabetes 1995;44:968-43.

The United Kingdom Prospective Diabetes Study (UKPDS) was a large-scale trial that investigated the effect of intensive blood glucose control versus conventional treatment in patients with type 2 diabetes, with a median follow-up of 10 years. This observational
analysis of data from the UKPDS demonstrated a direct relationship between the risk of diabetic complications and glycemia over time. Each 1% absolute reduction in mean A1C levels was associated with a 37% decrease in the risk of microvascular complications and a 21% reduction in the risk of any diabetes-related complication or death.

Therefore, any improvement in A1C levels is likely to reduce the risk of diabetic complications. [6]

Lowering A1C levels reduces the risk of diabetes complications in people with type 2 diabetes
UKPDS: 21% risk reduction per 1% absolute decrease in A1C levels (p<0.0001)
Real-time results. Better outcomes.

1. The ADA recommends that healthcare professionals use A1C point-of-care testing for timely decisions on therapy changes [2]
2. Giving diabetes patients on-the-spot feedback on their A1C number may result in a 1% point reduction in their A1C [3]
3. A 1% point reduction lowers the risk of serious complications by 40% [1]

A1C Standards of Care
The American Diabetes Association (ADA) recommends A1C testing to determine a patient’s average blood glucose control. For patients whose therapy has changed or who are not meeting glycemic goals, the A1C test should be performed quarterly. The A1C test should be performed at least two times a year in patients who are meeting treatment goals and who have stable glycemic control. Guidelines about A1C testing by the American Diabetes Association, International Diabetes Federation, and National Institute for Health and Clinical Excellence are summarized in the table below.

Guidelines for A1C testing in patients with diabetes
The goal of therapy is to achieve an A1C as close to the non-diabetic range as possible without severe hypoglycemia

<table>
<thead>
<tr>
<th>A1C target</th>
<th>Frequency of A1C testing</th>
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<tbody>
<tr>
<td>ADA</td>
<td>General population: ≤7%</td>
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<tr>
<td></td>
<td>Individuals: ≤6%</td>
</tr>
<tr>
<td></td>
<td>≥2 tests per year if meeting glycaemic goals</td>
</tr>
<tr>
<td></td>
<td>Every 3 months if not meeting glycaemic targets</td>
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<tr>
<td>NICE</td>
<td>6.5–7.5%</td>
</tr>
<tr>
<td>IDF</td>
<td>&lt;6.5%</td>
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<tr>
<td></td>
<td>Every 2–6 months depending on level and stability of blood glucose control</td>
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</tbody>
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1. ADA Diabetes Care 2007;30(Suppl 1):S4-41
2. NICE 2002. www.nice.org.uk
Less stringent treatment goals than those noted in the chart above may be appropriate for patients with a history of severe hypoglycemia, patients with limited life expectancies, very young children or older adults, and individuals with comorbid conditions.[1]

**How Does A1C Relate to Glucose Control?**

A strong relationship exists between A1C and plasma glucose – an increase in A1C equates to an increase in plasma glucose.[1, 2] Although a single plasma glucose measurement or a single daily glucose profile may not reliably predict A1C, plasma glucose levels measured over time can provide a reasonably accurate estimation of A1C, which allows patients and their HCPs to set day-to-day glucose targets to achieve long-term A1C goals.

The table below shows the range or blood glucose that corresponds to an A1C value. The relationship between average blood glucose and A1C was derived through a combination of Continuous Glucose Monitoring (CGM) and 7- and 8- point self monitoring of capillary blood glucose. Corresponding blood glucose values and ranges below are updated as prior relationship between average blood glucose and A1C did not use CGM and relied on infrequent self blood glucose monitoring.[2]

<table>
<thead>
<tr>
<th>A1C Value (%)</th>
<th>Blood Sugar Level (mg/dl)</th>
<th>Blood Sugar Level (mmol/l)</th>
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<tbody>
<tr>
<td>5</td>
<td>97 (76-120)</td>
<td>5.4 (4.2-6.7)</td>
</tr>
<tr>
<td>6</td>
<td>126 (100-152)</td>
<td>7.0 (5.5-8.5)</td>
</tr>
<tr>
<td>7</td>
<td>154 (123-185)</td>
<td>8.6 (6.8-10.3)</td>
</tr>
<tr>
<td>8</td>
<td>183 (147-217)</td>
<td>10.2 (8.1-12.1)</td>
</tr>
<tr>
<td>9</td>
<td>212 (170-249)</td>
<td>11.8 (9.4-13.9)</td>
</tr>
<tr>
<td>10</td>
<td>240 (193-282)</td>
<td>13.4 (10.7-15.7)</td>
</tr>
<tr>
<td>11</td>
<td>269 (217 – 314)</td>
<td>14.9 (12.0 – 17.5)</td>
</tr>
<tr>
<td>12</td>
<td>298 (240-347)</td>
<td>16.5 (13.3 – 19.3)</td>
</tr>
</tbody>
</table>

Data in parentheses are 95% Confidence Intervals.

To convert (mmol/mol) A1C units (IFCC traceable) to (%)A1C (DCCT traceable) use the following equation:

\[ \%A1C = (0.0915 \times A1C \text{ mmol/mol}) + 2.15. \]


   * Study results with healthcare professionals showed that the accuracy of A1CNow+ with fingerstick samples was, on average, 99%. This means that, on average, a true 7.0% A1C could read approximately 6.9%A1C. An individual A1CNow+ result may differ by as much as -1.0% A1C to +0.8% A1C from the true result. This represents the 95% confidence limits of a Bland-Altman plot.
