Diabetes UK

NHS Diabetes

The Association for Clinical Biochemistry

HbA_{1c} Standardisation For Laboratory Professionals

Change to reporting of HbA_{1c}

From 1 June 2009, the way in which HbA_{1c} results are reported in the UK is changing. This leaflet explains why and how this will happen.

What is HbA_{1c}?

Glucose in the blood binds non-enzymatically to the N-terminal valine residue of the β-chain of haemoglobin A in red blood cells. After spontaneous chemical modification, the Amadori rearrangement, the irreversible product HbA_{1c} is formed; so the higher the glucose, the higher the HbA_{1c}. HbA_{1c} circulates for the lifespan of the red blood cell. It therefore reflects the prevailing blood glucose concentration over the preceding 2-3 months.

What does it tell us?

The Diabetes Control and Complications Trial (DCCT) in Type 1 diabetes and the UK Prospective Study (UKPDS) in Type 2 diabetes both demonstrated the association between the increasing risk of microvascular and macrovascular complications of diabetes and increasing HbA_{1c}. HbA_{1c} thus gives a measure of an individual's risk of the long-term complications of diabetes.

Why measure it?

Serial measurements of HbA_{1c} show how an individual's glucose control, and thus risk of complications, changes in response to alterations in management. HbA_{1c} should be measured 2-6 monthly. Target HbA_{1c} levels can be set for individual patients and therapy adjusted accordingly.

How is HbA_{1c} reported currently?

Current HbA_{1c} assays in the UK and other parts of the world are aligned to the assay used in the DCCT, so that an individual's risk of complications can be inferred from the result.

What are the current targets?

General targets for HbA_{1c} of 6.5 - 7.5% should be set for an individual, taking into consideration their risk of severe hypoglycaemia, cardiovascular status and co-morbidities.

Why change?

After the DCCT, a new standard specific for HbA_{1c} was prepared by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). In future, manufacturers will supply IFCC standardised values for their calibrators as well as DCCT-aligned values. The units for reporting HbA_{1c} will also be changed so that HbA_{1c} reported by laboratories is traceable to the IFCC reference method. Global comparison of HbA_{1c} results will therefore be possible.

What are the new units?

HbA_{1c} results traceable to the IFCC reference method derived will be expressed as *mmol per mol* of unglycated haemoglobin.

How do old and new relate?

The relationship between the new IFCC reference method and the current "DCCT aligned" assays has been stable over several years. When HbA1c results are expressed as % haemoglobin, the equation describing the relationship is:

IFCC-HbA_{1c} (mmol/mol) = [DCCT-HbA_{1c} (%) - 2.15] x 10.929

A guide to the new values expressed as mmol/mol is:

Current DCCT aligned HbA_{1c} (%)	New IFCC HbA_{1c} (mmol/mol)
4.0	20
5.0	31
6.0	42
6.5	48
7.0	53
7.5	59
8.0	64
9.0	75
10.0	86

What are the targets in new units?

The equivalent of the current DCCT HbA_{1c} targets of 6.5% and 7.5% are 48 mmol/mol and 59 mmol/mol in the new units, with the non-diabetic reference range of 4.0% to 6.0% being 20 mmol/mol to 42 mmol/mol.

When is the changeover to new units?

HbA_{1c} results expressed in the new units are obviously very different to those currently in use. From **1 June 2009**, results will be provided in the UK as both IFCC-standardised units (mmol/mol) and DCCT-aligned units (%). This will give everyone time to become familiar with the new units and how they relate to DCCT numbers, and

thus to the risk of complications. From **1 June 2011**, results will be reported only in the new IFCC units.

What are the limitations of HbA_{1c} measurement?

As with the current DCCT-aligned system, HbA_{1c} results will be misleading in certain situations eg a variety of haematological conditions where there is abnormal red cell turnover, where there is an abnormal haemoglobin, and in some patients with renal or liver disease.

Various chromatographic and immunochemical techniques are used to measure HbA_{1c} but only ion exchange high performance liquid chromatography (IE HPLC) detects abnormal haemoglobins. In some laboratories in the UK, HbA_{1c} is reported in the presence of abnormal haemoglobin with a rider saying the results may not be comparable to the DCCT but in others the results are not reported. It is not known whether the glycation rate is affected by conformational changes in abnormal haemoglobin.

Affinity chromatography measures glycation of both normal and abnormal haemoglobin and immunochemical methods glycation of some abnormal haemoglobin depending on antibody recognition.

If any condition leads to a change in red cell survival, then HbA_{1c} measurement can, at best, be used to track changes in glycaemia when the effects on turnover are not too severe. Other measures of glycaemia may then be required, such as more reliance on self monitored blood glucose values or the use of a serum fructosamine assay, if available.

Why not report eAG?

Conceptually, converting an HbA_{1c} result to the equivalent "average glucose" concentration might help our understanding and interpretation of HbA_{1c}. A large international study recently produced average glucose values (eAG) for HbA_{1c} from continuous glucose monitoring and capillary self-blood glucose measurements and HbA_{1c}.

However, the study was carried out in a restricted population and issues have been raised about the study design. In addition, eAG will have limited applicability to the majority of patients who do not measure their own blood glucose levels and in some patients, the estimates may be inaccurate enough to be misleading. It has been agreed in the UK that eAG results will not be reported at the moment. Research into the applicability and utility of eAG to a wider range of people with diabetes is on-going and welcomed.

Key References

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