Clin Chem Lab Med 2008;46(9):1326–1327 © 2008 by Walter de Gruyter • Berlin • New York. DOI 10.1515/CCLM.2008.269

Letter to the Editor

What's in a name? Standardisation of HbA_{1c}: a response

W. Garry John[1], Gunnar Nordin[2] and Mauro Panteghini[3,*]

[1] Clinical Biochemistry, Norfolk and Norwich University Hospital, and School of Medicine, Health Policy and Practice, UEA, Norwich, NR4 7UY, UK
[2] External Quality Assurance in Laboratory Medicine in Sweden, Uppsala, Sweden
[3] Centre for Metrological Traceability in Laboratory Medicine (CIRME) and Department of Clinical Sciences ''Luigi Sacco'', University of Milan, Milan, Italy

Keywords: haemoglobin A_{1c}; nomenclature; standardisation; traceability.

We are grateful to McLaughlin and Bakker for highlighting their concern that confusion still exists regarding the reported results and nomenclature of haemoglobin A_{1c} (HbA_{1c}) (1). The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Working Group on HbA_{1c} standardisation (WG-HbA1c) has been working for a number of years to develop reference measurement procedures and reference materials for HbA_{1c}, and also to establish a network of reference laboratories; this work has been completed and published (2). The new reference measurement system has traceability to the International System (SI) and offers better trueness. More recently, the IFCC Committee on Nomenclature, Properties and Units (C-NPU) has been considering the systematic name of the quantity measured by the IFCC reference measurement procedure and the units according to the SI in which HbA_{1c} should be reported (3). Finally, in a recent publication (4) the IFCC WG-HbA_{1c} has shown stable linear relationships between results traceable to the IFCC reference system for HbA_{1c} and previous national and regional aligned methods, allowing the conversion of clinical decision limits from one system to another [see Table 1 in ref. (5)]. It was also clearly demonstrated that the transformation based on the so-called ''master equations'' from IFCC standardised values to, e.g., the National Glycohaemoglobin Standardisation Programme (NGSP) aligned values adds further uncertainty to the derived values [0.05%–2% (relative percentage), depending on the HbA_{1c} concentrations] (4).

*Corresponding author: Prof. Mauro Panteghini, Laboratorio Analisi Chimico Cliniche, Ospedale Luigi Sacco, via GB Grassi 74, 20157 Milano, Italy
Phone: +39-02-39042806, Fax: +39-02-50319835, E-mail: sd.chair@ifcc.org

To discuss issues related to the reporting of HbA_{1c} in the clinical setting, in 2007 the IFCC hosted a meeting with the American Diabetes Association (ADA), the European Association for the Study of Diabetes (EASD), and the International Diabetes Federation (IDF). The outcome of this meeting was a Consensus Statement, which was published in a number of journals (6–8). In summary, the workgroup agreed on three main recommendations. First, the IFCC system represents the only valid reference to implement standardisation of the HbA_{1c} measurement. Second, in order to guarantee a smoother passage to the new SI units, the HbA_{1c} result should be reported both in the SI unit (mmol/mol) and the derived NGSP unit (%) using the IFCC-NGSP master equation. Finally, as an aid for interpretation of the HbA_{1c} results, the calculation of a HbA_{1c}-derived average glucose (ADAG) value was suggested, but only after appropriate validation of the corresponding equation(s) (9).

Quite recently, the IFCC has also organised a meeting with manufacturers of HbA_{1c} methods to define the requirements for implementing the Consensus Statement recommendations and a timeframe for this implementation (10). The main outcomes of this meeting were that: 1) all manufacturers should implement worldwide assays for HbA_{1c} giving results traceable to the IFCC reference system; 2) the deadline for implementing traceability to the IFCC reference system is December 31, 2009; and 3) all new instruments sold after January 1, 2011 should report HbA_{1c} results in both SI (mmol/mol) and NGSP derived units (%).

Name

The IFCC reference measurement procedures measure glycation at the N-terminal valine of the haemoglobin beta-chain as a glycated hexapeptide. The C-NPU considered the correct name that should be applied to the quantity being measured; following much debate, it was agreed that the correct descriptive term should be ''haemoglobin beta-chain (blood) –N-(1-deoxyfructos-1-yl) haemoglobin beta-chain; substance fraction'' (3). Of course, this systematic name cannot be used in clinical practice and the C-NPU also offered for discussion the abbreviation ''DOF haemoglobin'', well aware of the difficulties to standardise language. After discussion, the WG-HbA1c recommended that the old term haemoglobin A_{1c} (abbreviated as HbA_{1c}) should be used when reporting results for this new quantity from the clinical laboratory (2). The use of this term was agreed during both the joint meeting of the clinical societies with the IFCC and the implementation meeting with

industry (7, 10). It was unfortunate that in one publication the term A1C was used in the Consensus Statement (6), whereas in other publications the agreed abbreviation HbA_{1c} was used (7, 8). However, the issue was only related to the journal style.

Units

In considering the units that should be used when reporting HbA_{1c}, the C-NPU proposed that mmol/mol should represent the SI unit for this measurand (3). But, maybe more importantly, this reporting option, i.e., the use of a completely different unit (mmol/mol instead of percentage), also avoids confusion when recalculating old HbA_{1c} targets to the new IFCC standardised values when clinical laboratories wish to implement HbA_{1c} results traceable to the IFCC reference system (5).

Estimated average glucose

In a collaborative effort, the ADA, EASD and the IDF set up the HbA_{1c}-Derived Average Blood Glucose (ADAG) study; this study has recently been published (9). The estimated average glucose (eAG) has undergone several name changes before and during the gestation of the study; at the time of publishing the Consensus Statement the abbreviation ADAG was the preferred term, but it was eventually considered that eAG was a better term for use in clinical practice. In all the documents, it was recommended that eAG should be used as an interpretation of HbA_{1c} results (6–8, 10). This should be carried out after having considered the outcome of the ADAG study and its scientific evidence (9).

References

1. McLaughlin PM, Bakker AJ. What's in a name? Standardization of HbA1c. Clin Chem Lab Med 2008;46:878–9.
2. Mosca A, Goodall I, Hoshino T, Jeppsson JO, John WG, Little RR, et al. Global standardization of glycated hemoglobin measurement: the position of the IFCC Working Group. Clin Chem Lab Med 2007;45:1077–80.
3. Nordin G, Dybkaer R. Recommendation for term and measurement unit for ''HbA1c''. Clin Chem Lab Med 2007;45:1081–2.
4. Geistanger A, Arends S, Berding C, Hoshino T, Jeppsson JO, Little R, et al. Statistical methods for monitoring the relationship between the IFCC Reference Measurement Procedure for Hemoglobin A1c and the designated comparison methods in the United States, Japan, and Sweden. Clin Chem 2008;54:doi:10.1373/clinchem.2008.103556.
5. Panteghini M, John WG. Implementation of haemoglobin A1c results traceable to the IFCC reference system: the way forward. Clin Chem Lab Med 2007;45:942–4.
6. The American Diabetes Association, European Association for the Study of Diabetes, International Federation of Clinical Chemistry and Laboratory Medicine, and the International Diabetes Federation Consensus Committee. Consensus Statement on the worldwide standardization of the hemoglobin A1C measurement. Diabetes Care 2007;30:2399–400.
7. The American Diabetes Association, European Association for the Study of Diabetes, International Federation of Clinical Chemistry and Laboratory Medicine, and the International Diabetes Federation Consensus Committee. Consensus Statement on the worldwide standardization of the hemoglobin A_{1c} measurement. Diabetologia 2007;50:2042–3.
8. Consensus Statement on the worldwide standardization of the hemoglobin A1c measurement. American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), and International Diabetes Federation (IDF). Clin Chem 2007;53:1562–4.
9. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine R for the A1c-Derived Average Glucose (ADAG) Study Group. Translating the A1c assay into estimated average glucose values. Diabetes Care 2008;31:doi: 10.2337/dc07-0545.
10. Implementation of standardization of HbA1c measurement. Summary of the meeting with manufacturers held in Milan, Italy, December 12, 2007. Clin Chem Lab Med 2008;46:573–4.