Opinion paper

Standardization of the hemoglobin A_{1c} reporting: transferring global consensus to the local community - Special report

Marijana Vučić Lovrenčić [1*], Željko Metelko[2]

[1]Institute of Clinical Chemistry and Laboratory Medicine, Merkur Clinical Hospital, Zagreb, Croatia
[2]Vuk Vrhovac University Clinic, Merkur Clinical Hosiptal, Zagreb, Croatia

*Corresponding author: vucic@idb.hr

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Long-term controversies regarding hemoglobin A_{1c} (HbA_{1c}) standardization seem to have finally reached the global consensus point. Hemoglobin A_{1c}, an integrated measure of glycaemic control, has been widely used as a „gold-standard" in management of diabetes mellitus for decades (1). However, the standardization of the „gold-standard" has been very difficult to achieve, due to so far unprecedented conflict between analytical and clinical standardization concept.

Ever since the results of the Diabetes Control and Complication Trial (DCCT) showed positive relationship between the degree of glycaemic control (assessed as hemoglobin A_{1c}) and risk for development of diabetic complications, the goal for successful diabetes treatment has been anchored to the hemoglobin A_{1c} level <7% (2). However, the 7% cut-off has been derived from DCCT data by using highly reproducible, but non-specific HPLC method for hemoglobin A_{1c} measurement. Based on the „DCCT-method", the National Glycohemoglobin Standardization Programme (NGSP) has been designed to harmonize results from all the methods to the DCCT-traceable results. Thus, a clinical harmonization has been achieved and all the results obtained by the NGSP-traceable methods could easily be compared to the globally accepted clinical goals for glycaemic control (3).

In the meantime, International Federation of Clinical Chemistry (IFCC) developed primary reference standard and reference method, which has been accepted as the only valid anchor to calibrate hemoglobin A_{1c} methods worldwide (4). However, due to its specificity, IFCC reference method managed to produce significantly lower hemoglobin A_{1c} results than DCCT-HPLC method (5). This was found to be unacceptably confusing for the medical diabetology community, mostly because of the evidence that lowering the hemoglobin A_{1c} range and, consequently, glycaemic goals, could have psychological impact to the patients and lead to the worsening of glycaemic control (6).

In order to overcome this problem, IFCC proposed to switch reporting units from conventional (%) to the SI units (mmol/mol) (6), which finally resulted into „2010 Consensus Statement on the Worldwide Standarization of the Hemoglobin A_{1c} Measurement" (7). The consensus was agreed between American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), International Diabates Federation (IDF), IFCC and International Society for the Pediatric and Adolescent Diabetes (ISPAD) during the IDF-World Diabetes Congress in Montreal, Canada, October 2009.

Consensus statement implicates global standardization of hemoglobin A_{1c} according to the IFCC reference system, and proposes dual system of hemoglobin A_{1c} reporting by clinical laboratories worldwide: SI (mmol/mol, no decimals) and conventional (%, NGSP-derived, one decimal). Conversion between units should be done by using IFCC-NGSP master-equation, and conversion tables should be available to the medical and lay parts of diabetic community. The reportable term is HbA_{1c}. As regards publishing, there is a strong recommendation to the editors of medical journals to require dual system of reporting in all manuscripts reporting HbA_{1c} results.

The consensus should be implemented as soon as possible worldwide, with concerted efforts of laboratory and medical professionals in transferring all necessary information within the diabetes community. Further steps in global standardization of hemoglobin A_{1c} shall be proposed on the next consensus meeting, at the IDF World Diabetes Congres in Dubai, December 2011.

The implementation of the global consensus in Croatia is planned as a 4-step process:

1. Croatian Chamber of Medical Biochemists has announced on its web-pages activities regarding consensus implementation, together with translated consensus summary (October 2010).
2. Croatian Society of Medical Biochemistry, as the national EQAS-organizer, has prepared necessary modifications in the HbA_{1c} part of the scheme, which shall be executed with the 3rd annual EQA-cycle in November 2010. Briefly, all the participants shall be asked to provide results expressed in dual reporting system, and make all the necessary arrangements for the routine consensus implementation (December 2010). It should be mentioned that consensus implementation requires only a mathematical operation, and no additional expenses to the HbA_{1c} testing are to be expected. Reagent manufacturers have already prepared all the necessary NGSP-conversion formula details.
3. Dual reporting of HbA_{1c} results from all laboratories in Croatia should be operative as from January 1st 2011. Croatian Chambers of Medical Biochemists shall prepare a letter of information, addressed to all relevant partners in the diabetes community (January 2011).
4. A special report covering this issue will be published in relevant scientific journals: *Biochemia Medica, Diabetologia Croatica*, and translated version in *Liječnički vjesnik.*

We hope that this process will ensure necessary conditions for successful implementation of the global consensus to the Croatian medical and laboratory community involved in diabetes care.

Considering rising prevalence of diabetes mellitus in Croatia (8), compliance to the global consensus not only provides harmonization of hemoglobin A_{1c} reporting, but also assures the continuity of implementation of the highest standards of medical care for diabetic patients in Croatia.

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