EQA quantification HbA_{1c} Diabetes– Long-term and SIGMA analytical performance for Twenty one Portuguese Laboratories

Armandina Miranda[1], Susana Pereira[1], João Reguengos [1],[3], José Requeijo [3], Helena Correia[1], Ana Cardoso[1], Piet Meijer[2], Ana Faria[1]

[1] Instituto Nacional de Saúde Dr. Ricardo Jorge – Departamento de Epidemiologia – Unidade de Avaliação Externa da Qualidade, Portugal;
[2] ECAT Foundation, Netherlands;
[3] Departamento de Engenharia Mecânica e Gestão Industrial, Faculdade de Ciências e Tecnologias, Universidade Nova de Lisboa, Monte da Caparica, Portugal.

Background and Aim

Glycated hemoglobin (HbA_{1c}) plays a crucial role in the monitoring and diagnosis of diabetes. In Portugal 9,8% of the population has diabetes ($HbA_1c \geq 6,5\%$ or treatment with glucose-lowering medications)[1]. Six sigma metrics combine bias, precision, and allowable total error (Tea), and can be used for assessing the quality of the analytic phase.

The main objective of this study was to apply a linear regression model for long-term evaluation of the precision and inaccuracy, and apply the sigma metric to evaluate the performance of laboratories in HbA_{1c} quantification[2].

Methods

The long term analytical coefficient of variation (LCVa), the total analytical bias and sigma were established.

Participants were selected concerning laboratories that participated in all surveys. The assessment did not take into account the equipment used by each participant. The variables introduced to define the long-term performance in this model were the LCVa and total analytical Bias obtained by comparing the laboratory individual results with the consensus mean of each round, after outliers exclusion. The sigma value was calculate using the Tea obtained in the minimums analytical performance goals based on the biological variation[3,4]. A linear regression model was applied to quantitative HbA_{1c} results, of twelve EDTA blood samples with different HbA_{1c} concentrations, to evaluate the long-term analytical performance and the sigma value of twenty one participants in the period of 2014 to 2016 that participate in the PNAEQ (External Quality Assessment Program). Results are expressed in IFCC units (mmol/mol). Four laboratories were excluded from the analysis (outliers). We evaluate also the number of laboratories that fulfill the minimum analytical performance goals based on the biological variation (CVa and Bias).

Results

The consensus values, interlaboratory CV and number of outliers for the 12 surveys/samples used in the study are represented in **table 1**. The median LCVa was 2,4% (range 1,3%-5,2%), the median Total Bias was 2,0% (range 0,2%-6,0%) and median sigma value was 1,7 (range 0,1-4,6) (**table 2**).

The LCVa was less than 0,58 times the total biological variation (diagnostic testing) for 94 % laboratories and was less than 0,75 times the within biological variation (monitoring testing) in 29 % of the laboratories. Sixty five percent of the laboratories had a total bias less than 0,375 of the total biological variation (**table 3**).

Forty one percent of the laboratories had a sigma value less than 2,0 and fifty nine percent had a sigma value equal or higher than 2,0, when evaluated with an allowable total error of 6,72%, based on minimum performance criterions of the biological variation (**figure 1**).

Table 1: *Consensus values, interlaboratory CV and number of outliers for the 12 surveys/samples used in the study*

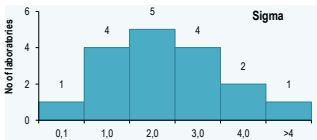
Survey/ Sample	No. of participants	Consensus value, mmol/mol	CV, %	No. of outliers
2116	38	99,7	4,72	1
2216	38	34,7	6,33	2
1116	44	59,6	4,16	2
3216	37	37,9	4,95	2
3115	52	95,7	5,37	1
3215	51	33,9	6,13	2
2115	55	101,1	4,38	1
3116	37	94,6	7,51	2
1115	51	82,7	4,37	2
1215	51	60,7	4,72	1
3114	53	85,0	2,62	12
3214	53	31,0	2,39	11

Table 2: *Descriptive analysis of Long-term analytical CV, total Bias and Sigma value results*

	LCVa, %	Bias, %	Sigma (Tea=6,72%)
Median	2,4	2,0	1,7
Range	1,3-5,2	0,2-6,0	0,1-4,6
n	17	17	17

Table 3: *"Minimum" performance goals and quality specifications for Glycated Haemoglobin. [CV_I – Total biologic variation; CV_I – Within subject variation; CV_G – Between suject variation] and percentage of laboratories in the study within the minimum performance goals*

	"Minimum" Performance goals HbA1c mmol/L	Quality specifications HbA1c mmol/L	Laboratories within the Minimum performance goals, %
Imprecision (Diagnostic) %	0,58 CVt ($\sqrt{(CVi^2 + CVb^2)}$)	5,09	**94**
Imprecision (Monitoring) %	0,75 CVb within	2,08	**29**
Total Bias%	0,375 $\sqrt{(CVi^2 + CVb^2)}$	2,52	**65**



	% of laboratories
Sigma < 2	41
Sigma ≥ 2	59

Figure 1: : *Histogram of the individual Sigma for Glycated haemoglobin for the 17 laboratories included in the study and the percentage of laboratories with sigma value inferior to 2 and superior or equal to 2.*

Conclusion

As reflected by the results the overall performance needs to be improved. Despite 94% of the laboratories evaluated accomplished the minimum quality specifications for imprecision (diagnostic), only 65% and 29% of the laboratories met the quality specifications for Total Bias and imprecision (monitoring) respectively. The median sigma (1.7) was less than 2 and only 59% of the laboratories had a sigma greater than or equal to 2.

It is a responsibility of clinical laboratories to continuously monitor the performance of the methods in use, both by the implementation of proper internal quality control, checking the daily alignment of the analytical system and evaluating the assay long-term imprecision by the participation in appropriately organized external quality assessment schemes.

Assessment of the quality on the sigma scale has the advantage of providing evidence of global laboratory performance taking into account random and systematic errors, and should be used for identifying and prioritizing improvements that are needed in the analytical quality of laboratory examinations.

References

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