(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 5, Issue 2, Page No: 465-469
March-April 2022

IJMSCR

Application of sigma metrics and method decision charts for assessment of quality assurance in BioRad D-10 HbA1c analyzer

Dr. Anisha Mathew, Dr. Ekta Debnath, Dr. Preeti Chauhan, Dr. Sanjukta Naik, Dr. Ritu Singh
Department of Biochemistry, Lady Hardinge Medical college, New Delhi, India

***Corresponding Author:**
Dr. Preeti Chauhan
Department of Biochemistry, Lady Hardinge Medical college, New Delhi, India

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Objective:

To determine the Six sigma score and quality of BioRad D-10 HbA1c analyzer over a period of 5 months

Methods and Materials:

Retrospective study conducted using Internal Quality Control data and EQAS (RIQAS) data from November 2020 to March 2021 to calculate Six sigma score and plot lab performance on Method decision chart

Statistical analysis

Mean and SD was calculated using SPSS. CV, Coefficient of Variation was determined from calculated laboratory mean and calculated standard deviation, obtained from 5 months of IQC data and sigma metrics for each parameter was calculated.

Result:

Six Sigma score was calculated for both levels of QC. The lowest was 3 in month of November 2020 and highest was 9 in month of December 2020 in Quality control Level 2. The average Six Sigma score for Quality Control level 1 was 5.4 (total of 5 months) and for Quality Control level 2 was 5.2

Conclusion:

Six Sigma metrics should be added as an additional tool for periodical assessment of quality for HbA1c results to achieve better laboratory results in diabetic patient care.

Keywords: HbA1c, Six Sigma Metrics, Method Decision Chart, Diabetes Mellitus, Quality Control

Introduction

Glycated Hb (HbA1c) testing is an important parameter for the long term control of glycemia in diabetic patients. The American Diabetes Association (ADA), International Expert Committee (IEC), and the World Health Organisation (WHO) recommend the use of HbA1c to diagnose diabetes, using a threshold of 6.5%. The threshold is based upon sensitivity and specificity data from several studies. Patients who have an HbA1c between 5.7 and 6.4 are considered at increased risk for developing diabetes in the future[1]. Often there are differences reported values in inter laboratory HbA1c levels from different laboratories, making it difficult to compare values. That is why reproducibility in analysis is important for monitoring diabetic patients as changes in results also reflect change in response to treatment. For HbA1c's high analytical quality, it is recommended to use commercial dedicated High Pressure Liquid Chromatography (HPLC) with use of appropriate Quality Control (QC) materials to increase operation confidence and monitor performance and efficiency of analytic process allowing room for improvement [2-3].

Mainstay testing process in every laboratory consists of Pre-analytical phase, Analytical Phase and Post-

analytical phase with each phase being prone to error and must be closely monitored. These errors, also known as laboratory errors, are any defect or deviation of result from true value. It is for these reasons, that QC is used for to identify and correct said errors[4]. The Internal QC (IQC) helps to show amount of variation occurring in our results while External QC (EQC) helps to evaluate accuracy or imprecision. Both make use of Levy-Jennings (LJ) chart. However, using only IQC and EQC does not help in quantification of error needing the use of stronger performance characteristics such as Six Sigma[5].

Sigma metrics is about measuring or counting the number of defects. Six sigma (6σ) is a mathematical symbol for Standard Deviation (SD) which is derived from Defects-per-Million (DPM). Defects or laboratory errors can be counted and converted to defects-per-million (DPM).This DPM is converted into Sigma metrics by appropriate calculation[4]. Six sigma, originated at Motorola in 1987[3], measures quality in an objective and quantitative manner, providing a more quantitative framework to evaluate process performance[6]. Six Sigma utilises 3 traditional elements to evaluate assay performance: Allowable total error (TEa), Bias and Precision.

International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Task Force on implementation of HbA1c standardisation (TF-HbA1c) has suggested quality target for HbA1c with respect to a metric model[2]. Thus, aim of this study is to evaluate that sigma metrics can be used as quality control tool which can impact in maintaining efficiency of BioRad D-10 HbA1c program analyser.

Materials and Methods

Study was conducted in Hormone lab of Lady Hardinge Medical College, New Delhi

Study Design: Retrospective Study

Study Period: Five months (November 2020-March 2021)

Analyte to study**:** Glycated Hemoglobin (HbA1c) Internal quality control data and External quality control data.

Analyser**:** BioRad D-10 Glycated Hemoglobin program. The manufacturer directions were followed regarding maintenance of machine, reconstitution of Primer, Calibrator and Quality control materials, after which QC and Calibrator were stored according to said instructions.

Statistical Analysis

Two levels of internal quality controls (Provided by BioRad QC materials) results over 5 months were compiled and mean was calculated to establish CV%. BIAS% was taken from External Quality scheme of Randox (RIQAS) and Total Allowable Error (TEa)[7]value was taken from Clinical Laboratories Improvement Act (CLIA).

Mean and SD was calculated using SPSS

CV, Coefficient of Variation was determined from calculated laboratory mean and calculated standard deviation, obtained from 5 months of IQC data

$$\text{CV\%} = \frac{\text{Standard Deviation}}{\text{Laboratory mean}} \times 100$$

Sigma metrics for each parameter was calculated using below formula

$$\text{Sigma} = \frac{\text{TEa} - \text{Bias}}{\text{CV}}$$

The minimum acceptable performance of process was a sigma of 3 and world class performance is sigma of 6 or higher.

Using CV%, bias and SD, Method decision chart was plotted for each month to evaluate the impression and inaccuracy

Results

Present Study analysed 5 months of Quality Control Data of HbA1c run on Bio Rad-D10 analyser and laboratory mean was calculated for each month. The Laboratory mean, kit insert QC mean and External Quality control data (RIQAS) was used to calculate the sigma score to assess laboratory quality. Both levels of IQC values for 5 months were compiled and calculated. The Laboratory mean for level 1 and level 2 was 5.2% and 9.7% in months of November 2020, December 2020, January 2020 and 5.7% and 11.1 % in February 2021 and November 2021. CV% for each month was <5% (Table 1) as they had different lot numbers. External Quality control values (RIQAS) was studied for this period of 5 months. The results are shown in table 2

Sigma score was calculated for both levels of QC. The lowest was 3 and highest 9 in Level 2. The average Sigma score for level 1 was 5.4 (total of 5 months) and for level 2 was 5.2. The results of sigma score for each month for both levels of QC are shown in Table 3

CV% and Bias% of Quality control level 1and level 2 were plotted on a method decision chart (Figure 01& Fig 2) Level 1 was more than a sigma of 6 in November 2020 (6.2 Sigma) and March 2021 (6.2 sigma) while remaining was more than a sigma of 3 but less than a sigma of 6. Level 2 was more than 6 sigma in December 2020 (10.3 sigma) and Jan 2021 (6.1 sigma).

Discussion

Employing of Six Sigma helps in quantifying and appraising in laboratory functions as Six Sigma combines bias, precision and TEa to asses laboratory quality, allowing is to assess the exact errors quantitatively and analyse analytical methods while comparing analytical quality of instruments and optimise QC plans[2,4]. Initial sigma of HbA1c implanted by IFCC task force is 2 for routine laboratory and 4 for clinical trail laboratory[8]. Weykamp et al. demonstrated biological variation and sigma metric model which would be suitable to set and evaluate quality targets within and between laboratories in their HbA1c study. In their study also, they suggested a sigma of 2 is sufficient for routine laboratories to estimate the quality status of HbA1c of a single laboratory and manufacturer[8-9]. The sigma achieved for our machine, BioRad D-10 HbA1c programme, for level 1 was 5.4 and level 2 was 5.2.

TEa was taken in accordance with total error criteria as it may vary with biological variability (3%), CLIA 88 guidelines (10% TEa) and ecole such as Rilibak and NGSP (6%)[9]. Huysal et al[2] study took TEa of 10% while Emekli et al used 6% from NGSP guideline as in USA. BioRad D-10 ion-exchange HPLC is used for HbA1c estimation according to National standardisation (NGSP,DCCT trails).In scientific circles, HbA1c units are in mmol/ml while NGSP guidelines express HbA1c in percentage (%). As IFCC accepts both units, in our laboratory, we use NGSP units and thus these units were also used during the evaluation with Six Sigma methodology[9].

The sigma metrics for a single number that estimates quality based on traditional parameters used in clinical laboratories via TEa, Precision and bias. Receiving a high Six Sigma result means that 99.9996% of our results are error free corresponding to 3.4 defects per million and indicates that reports of false test results are very low[4]. So this has lead in maximising efficiency and reduce control cost through fewer re-run and recheck.

We usually use control $\pm$ 2SD approach by which all assays are assured to be equal quality and same rule applies to all analytes despite the fact the assay are clearly more robust and some are typically more problematic[4-5]. Our lab HbA1c on D-10 is meeting the optimum, desirable and minimum criterion. The Sigma Metric model which we followed is in which TE(a) ranged from 1-10 mmol/mol (0.09-0.9) and sigma from 2,4,6[8]. We used TEa of 10 and sigma metric ranged from 4-9 except for the month of Nov 2020 in which sigma was 3.

Advantage- we have taken precision estimates for period of 5 months by using long term QC data. So our sigma metrics is not only high but also optimistic

Drawback- Taken TEa from CLIA and distinct sigma metric can be obtained depending on TEa value selected and using same bias and precision value in sigma metrics model.

ii) We have not taken biological variation in consideration when calculating sigma score as Biological Variation error window is very tight and narrow and difficult to follow in day to day laboratory practise.

Conclusion

HbA1c performance also depend on biological variation as well as change in lot for control and reagents but Six Sigma metrics should be used as an additional tool for periodically assaying quality of results for better results of diabetic patient care.

Acknowledgements

We would like to acknowledge all the authors for their contribution and would also like to acknowledge out laboratory technical staff for ensuring good quality control practises

Conflicts of Interest

There are no conflicts of interest.

References

1. Glycemic Targets: standards of medical care in diabetes: Diabetes care 2021; 44: S73-84
2. Huysal K, Budak UY. Application of sigma metrics for assessment of quality assurance using MQ 2000 PT HbA1c analyser. Biochemia Medica 2015;25:416-20
3. Rohlfing CL, Parvin CA, Sacks DB, Little RR; NSGP steering committee. Comparing analytical performance criteria: evaluation of HbA1c certification criteria as an example. Clin chem acts 2014; 10: 259-63
4. Aggarwal K, Patra S, acharya V, Agrawal M, Mahapatra SK. Application of sigma metrics and method decision charts in improvising clinical chemistry laboratory performance enhancement. Int J Adv Med. 2019; 6: 1524-30
5. Westgard JO, Barry PL, Hunt MR, Groth T. A multi-rule Shewhart chart for quality control in clinical chemistry. Clin Chem. 1981; 27: 493-501
6. Hens K, Berth M, Armbruster D, Westgard S. Sigma metrics used to assess analytical Quality of clinical chemistry assays: Importance of allowable Total Error (Tea) target. Clinchem lab med 2014; 52: 973-80
7. Westgard JO, Westgard SA. The quality of laboratory testing today. An assessment of sigma metric for analytic quality using performance data from proficiency testing surgery and the CLIA criteria for acceptable performance. AMJ Clin Pathol 2006; 125: 343-54
8. Weycamp C, John Garry, Grillery P, English E, Ji L, Lenters-westera E et al. Investigation of 2 models to set and evaluate quality targets for HbA1c: Biological variation and sigma metrics. Clin chem. 2015 May; 61:752-9
9. Emekli DI, Guclu K, Nar R, AvciE. Assesment of analytical performance of HbA1c Test by Six Sigma Methodology. J Basic Clin health Sci 2020; 4:104-7.

Figures and Tables

	QC-1					QC-2				
	Nov-20	**Dec-20**	**Jan-21**	**Feb-21**	**Mar-21**	**Nov-20**	**Dec-20**	**Jan-21**	**Feb-21**	**Mar-21**
Calculated mean	5.41	5.4	5.422	5.48	5.64	9.5	9.56	9.97	9.77	9.71
Laboratory mean	5.2	5.2	5.2	5.7	5.7	9.7	9.7	9.7	11.1	11.1

Table 01: Internal quality data and calculated mean

	Nov-20	**Dec-20**	**Jan-21**	**Feb-21**	**Mar-21**
Lab result	**8.30**	**5.50**	**5.70**	**11.10**	**7.30**
Group mean	**8.19**	**5.60**	**5.69**	**11.03**	**7.26**
Bias %	**1.4**	**1.8**	**0.2**	**0.6**	**2.0**
MU(measurement of uncertainity)	**0.02**	**0.01**	**0.01**	**0.03**	**0.02**

Table 02: External Quality control data

	QC-1					QC-2				
	Nov-20	Dec-20	Jan-21	Feb-21	Mar-21	Nov-20	Dec-20	Jan-21	Feb-21	Mar-21
SD	0.072	0.098	0.089	0.12	0.076	0.25	0.079	0.15	0.25	0.19
CV%	1.39	1.88	1.71	2.16	1.33	2.61	0.82	1.56	2.23	1.69
Sigma	6	6	5	4	6	3	9	6	4	4

Table 3: Sigma values for both QC levels.

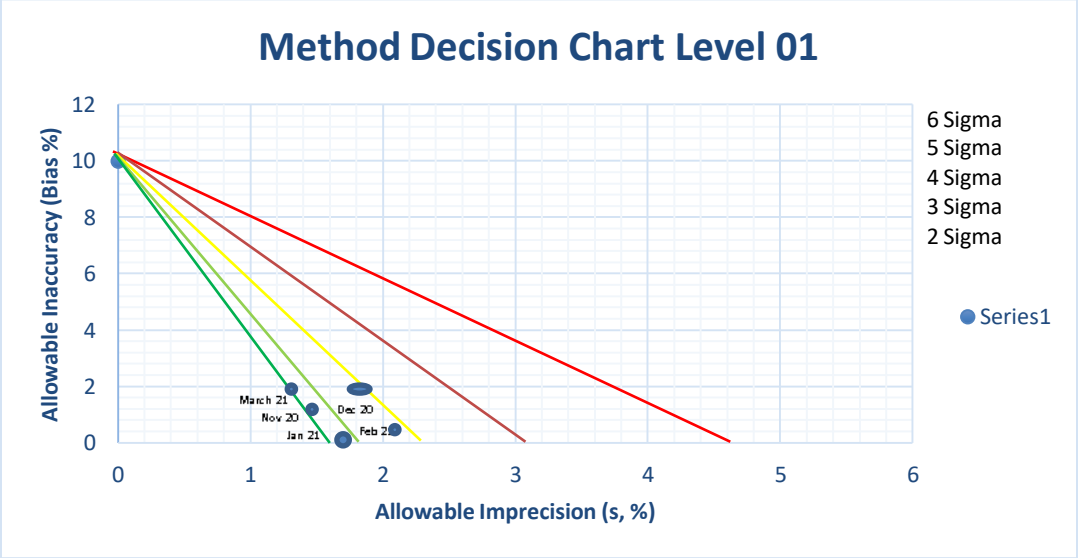

Figure 01: Quality Control Level 01 plotted on Method Decision Chart

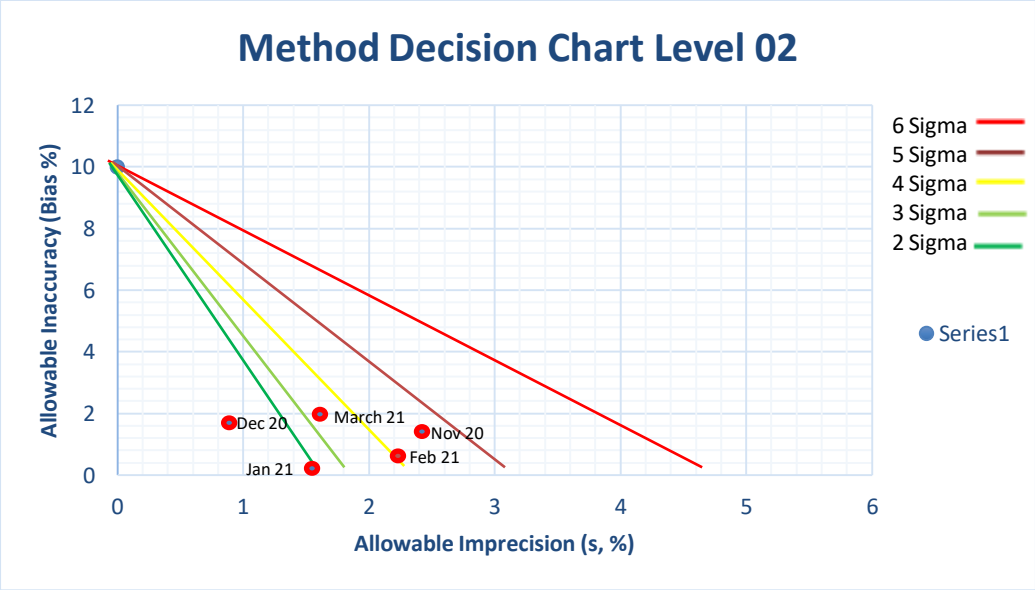

Figure 02: Quality Control Level 2 Plotted on Method Decision Chart