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Assessment of analytical performance of Internal QC and External QC of HbA1c By 6 Sigma Using Total Allowable Error (TEa) calculated by CLIA 88, and NGSP

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Abstract

Objective:

To determine Six sigma score of BioRad D-10 HbA1c analyzer using different Total Allowable error (TEa) taken from CLIA and NGSP 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 using TEa taken from CLIA and NGSP guidelines and plot on Method decision chart (Operator Specific 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 and RIQAS data, TEa taken from CLIA and NGSP guidelines. Sigma metrics for each parameter was calculated.

Result:

Six Sigma score was calculated for both levels of QC and RIQAS with TEa 10 and 6 from CLIA and NGSP guidelines respectively. Mean sigma for level 1 at TEa 10% (CLIA) was 5.42 and at TEa 6% (NGSP) was 3.3 while for level 2 TEa 10% (CLIA) was 5.5 and TEa 6% (NGSP), was 3.12. Mean six sigma for our RIQAS over 5 month period was 4.42 at a TEa of 10% (CLIA) and 2.46 at a TEa 6% (NGSP)

Conclusion:

Since our lowest sigma score at TEa 6% was 2.46 (RIQAS), it shows that our lab is with acceptable quality six sigma for diagnostic labs, however we will strive to achieve a higher sigma score and keep improving our laboratory quality.

Keywords: HbA1c, Six Sigma Metrics, Diabetes Mellitus, Quality Control, Operator specific chart

Introduction

As laboratories improve and progress, there is a need to assess and improve methods of measurement and analysis. HbA1c is an important biomarker, needed to evaluate long term outcomes of diabetes [1]. There is a need of analytical reliability of HbA1c to be obtained by clinical laboratories. This reliability is obtained by Internal Quality Control (IQC) and External Quality Control (EQC) using analysis of data using statistical methods. Six sigma is one of method by which we can analyse the analytical performance of HbA1c [2].

Six sigma comprises of 5 steps, DMAIC which stands for Define, Measure, Analyse, Improve and Control. DMAIC shows degree of how much of the process deviates from perfection. In this methodology, sources of errors come from variables. High Sigma denotes a well-functioning lab with low errors and acceptable test results. Low sigma levels denote error in analyses [2]. When calculating Sigma

scores, Total Allowable Error [TEa] is used alongside Bias and CV % (Coefficient of variation). Total Error or TE is a representation of overall/total error which may occur as a result of both imprecision (random error) and inaccuracy (systemic error) of said measurement/test procedure [3]. Total Allowable Error or TEa refers to error that is allowed without invalidating the interpretation of a test result [4-6].

Recommendations of TEa are often taken from many national and international Proficiency and External quality control tests [4-5]. Everybody has a calculated TEa for a parameter, eg, College of American association of Pathologists or CAP uses 7% as Total allowable error for HbA1C while National Glycohemoglobin Standardization Program (NGSP) utilises 6% and CLIA 88 guidelines give 10% as its criteria [6]. Usually the criteria are closed based on the appropriate method used by the laboratory which is stable in terms of precision and bias. The TEa also helps evaluating the performance and acceptance of the laboratory methodology using Method decision chart [2-7].

In this study, we apply the various TEa criteria put forward by various bodies like Clinical Laboratories Improvement Act (CLIA) and NGSP to apply the best criteria suited for our laboratory.

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)

Analyser: BioRad D-10 Glycated Hemoglobin program. 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) value was taken from CLIA and NGSP.

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

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

Sigma metrics for each parameter was calculated using below formula

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

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

Using CV%, bias and SD, Method decision chart was plotted for each month to evaluate the imprecision and inaccuracy [8].

Results:

We calculated internal QC level 1 and 2 and RIQAS using TEa values from CLIA and NGSP. The mean sigma for level 1 at TEa 10% (CLIA) was 5.42 and at TEa 6% (NGSP) the mean was 3.3 (Table 01). As the TEa is decreasing, i.e. the tolerance level of error was reduced, the sigma value also decreased accordingly.

The Internal QC level 2 was also calculated with above mentioned TEa values. The mean sigma was at TEa 10% (CLIA) was 5.5 and TEa 6% (NGSP), the mean was 3.12 (Table 02).

Since our internal quality control sigma is within acceptable limits, we decided to calculate the sigma of our RIQAS values to see if it was also within acceptable limits. The mean sigma was 4.42 at a TEa of 10% (CLIA) and 2.46 at a TEa 6% (NGSP).

We plotted these values on a method decision chart to see how much of the sigma values fell within the acceptable limits. The charts were plotted for both levels of IQC and RIQAS at both TEa's of 10% and 6% (Figure 1 and Figure 2).

Discussion

Earlier, laboratory often used precision and accuracy as separate sources of error, however it was established that the analytical quality of the lab

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depended on the overall affect both precision and accuracy of the method. A quality target consisting of values were assigned by an approved reference measurement procedure with tolerance levels which is derived from quality concept of total allowable error (TEa/TEA). Now the recommendations for TEa can be found from various national and international bodies such as CLIA, NGSP etc [5-7].

Every lab follows a different set of guidelines and based on those guidelines the TEa is used in order to calculate the sigma and assess laboratory performance. This is same when assess or calculating sigma for HbA1c analysers. As standardisation of the method is either done based on CLIA, NGSP or DCCT guidelines, the Total allowable error should also be used accordingly when calculating sigma. In our lab, while we follow CLIA guidelines, our BIORAD D-10 programme for HbA1c is standardised according to NGSP/DCCT and thus use the same unit (%) as recommended by NGSP. Thus, we have used the TEa provided by CLIA and NGSP to assess the analytical quality of BIORAD D 10. Just as with Huysal et al, we used the bias values from out external quality control programme, RIQAS and calculated the sigma used both TEa from CLIA and NGSP [9].

We did not use Biological Variation (BV) in our study as we are not sure if the data, we currently have will be applicable for our population. Weykamp et al mentions that it is not known if biological variation data for a young healthy Caucasian population would be applicable to other age, sex and races or populations with uncontrolled glucose levels [10]. Another issue of using biological variation is state of art as it may vary from country to country and city to city to follow the minimum criterion of BV model.

Weykamp et al suggest that HbA1c performance sigma of 2 for routine laboratories was acceptable [9]. When using TEa of 10% (CLIA Guidelines), we had a mean sigma of 5.42 for level 1, 5.5 for level 2 and a sigma of 4.42 for RIQAS. This showed that our lab has good analytical quality at a TEa of 10%. We then used 6% (NGSP) as our TEa and recalculated our sigma levels to see how our analytical performance was at a tighter acceptable level. Our mean sigma for level 1 was 2.86, for level 2 was 3.12 and RIQAS was 2.46. Even at a lower TEa, our HbA1c was able to show a sigma of more than 2 which is acceptable for routine lab.

Klonoff et al stressed that while CLIA has loosened the acceptable limits for proficiency testing from 6% to 10% for HbA1c, it is best to asses our accuracy and precision at a TEa of 6, hence the need to calculate the sigma of our lab on these tighter values [11]. This tighter value was proposed as HbA1c is an important marker in the monitoring of diabetic treatment and prognosis and thus needs to be as precise and accurate as possible. Both DCCT and United Kingdom Prospective Diabetes study (UKPDS) had determined that an HbA1c level of ≤ 7% resulted in reduction of all micro vascular complications. This was further accepted by the NGSP. Thus, the need to maintain a good sigma score even at a lower TEa level [9-10].

While having a sigma of 2 at a TEa of 6% (NGSP)[10] is acceptable, we are aiming to achieve a higher sigma by working more towards quality performances and setting a higher and tighter quality target, allowing a better sigma and thus better patient care.

Conclusion

Our BIORAD D-10 from above data seems to have shown to have an acceptable mean sigma level at both TEa of 10% (CLIA) and 6% (NGSP) creates a confidence on our HbA1c and we thus aim for a higher and better sigma level.

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References:

1. Glycemic Targets: standards of medical care in diabetes: Diabetes care 2021; 44: S73-84
2. Emekli DI, Guclu K, Nar R, Avci E. Assesment of analytical performance of HbA1c testing by six sigma medthodology. J Basic Clin Test 2020;4:104-7
3. Westgard, J., 2007. The Meaning and Application of Total Error - Westgard. [online] Westgard.com. Available at:

<https://www.westgard.com/essay111.htm> [Accessed 11 March 2022].

4. Westgard, S., 2013. Total Analytic Error: from Concept to Application - Westgard. [online] Westgard.com. Available at: <https://www.westgard.com/ate-tea.htm> [Accessed 11 March 2022].
5. 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
6. 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
7. 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
8. Aggarwal K, Patra S, acharya V, Agrawal M, Mahapatra SK et al. Application of sigma metrics and method decision charts in improvising clinical chemistry laboratory performance enhancement. Int J Adv Med. 2019; 6: 1524-30
9. 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
10. 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
11. Klonoff, D., Aron, D., Cohen, R., Home, P., John, W., Little, R., Nathan, D. and Sacks, D. The Need for Accuracy in Hemoglobin A1c Proficiency Testing: Why the Proposed CLIA Rule of 2019 Is a Step Backward. Journal of Diabetes Science and Technology. 2019; 13(3), pp.424-27

Figures and Tables

Table 01: Calculating Sigma for different TEa for IQC level 01

	November 2020	**December 2020**	**January 2021**	**February 2021**	**March 2021**
TEa (CLIA-88)	10	10	10	10	10
Sigma (CLIA-88)	6.2	4.8	5.7	4.4	6
TEa (NGSP)	6	6	6	6	6
Sigma (NGSP)	3.3	2.2	3.2	2.6	3

Table 02: Calculating Sigma for different TEa for IQC level 02

	November 2020	**December 2020**	**January 2021**	**February 2021**	**March 2021**
TEa (CLIA-88)	10	10	10	10	10

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Sigma (CLIA-88)	3.3	9	6.3	4.2	4.7
TEa (NGSP)	6	6	6	6	6
Sigma (NGSP)	2	5.1	3.7	2.4	2.4

Table 03: Calculating sigma for different TEa for RIQAS

	November 2020	**December 2020**	**January 2021**	**February 2021**	**March 2021**
TEa (CLIA-88)	10	10	10	10	10
Sigma (CLIA-88)	4.1	4.6	5.4	4.5	3.5
TEa (NGSP)	6	6	6	6	6
Sigma (NGSP)	2.2	2.3	3.2	2.6	2

Figure 01: Quality control levels 1 and 2 plotted on method decision chart (Operator specific chart) with TEa, taken as 6

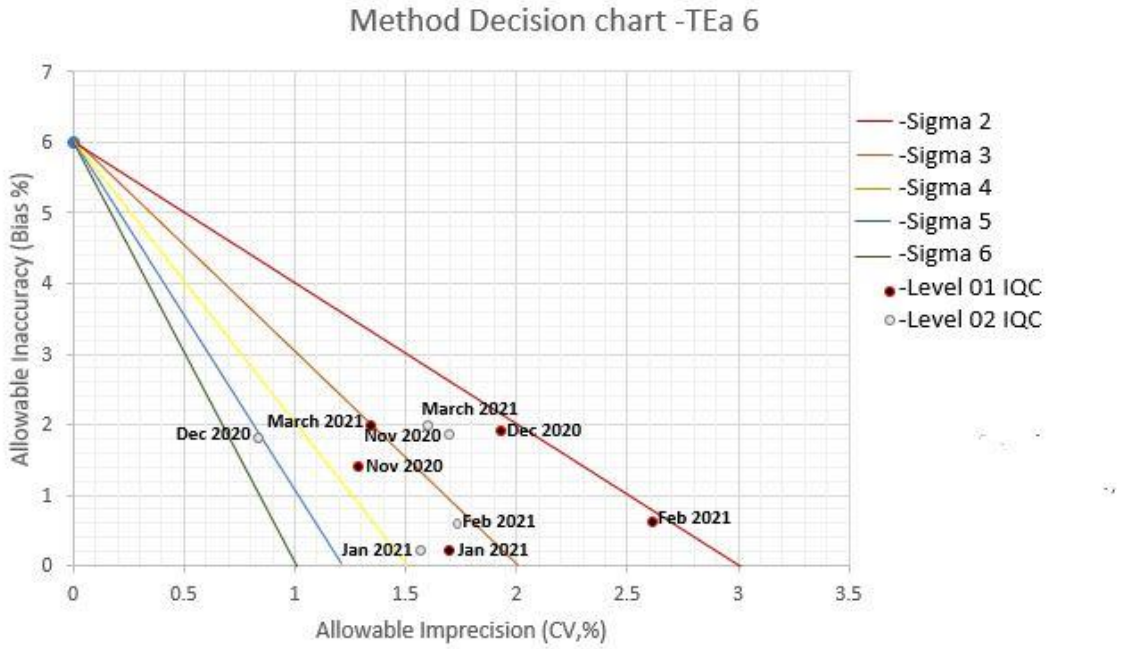

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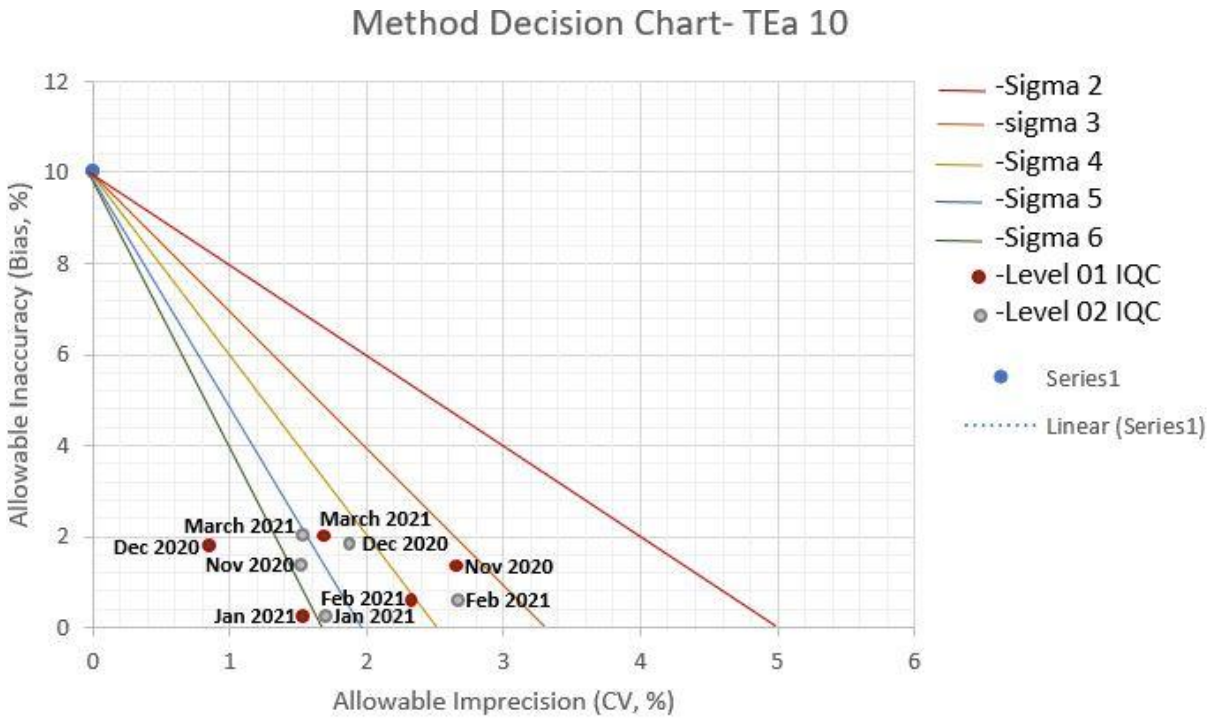
Figure 02: Quality control levels 1 and 2 plotted on Method Decision Chart (Operator Specific Chart) with TEa as 10



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