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Application of Sigma Metric Analysis to Evaluate the Performance of the Biochemistry Analytical System in a Medical Biology Laboratory in Côte d'Ivoire

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Abstract

Introduction: The Six Sigma methodology is an opportunity for a better understanding of the performance of analytical methods and for a better adaptation of the quality control management policy of the medical biology laboratory. Using the sigma metric, this study assessed the performance of the Biochemistry analytical system of a medical biology laboratory in Côte d'Ivoire. **Methods**: Six Sigma methodology was applied to 3 analytes (alanine aminotransferase, glucose and creatinine). Performance indicators such as measurement imprecision and bias were determined based on the results of internal and external quality controls. The sigma number was calculated using the total allowable error values proposed by Ricos *et al*. **Results**: For both control levels, ALT had a sigma number greater than 6 (7.6 for normal control and 7.9 for pathological control). However, low sigma numbers, less than or equal to 2 for creatinine (1.4 for normal control and 2 for pathological control) and less than 1 for glucose were found. **Conclusion**: This study revealed good analytical performance of ALT from the point of view of 6 sigma analysis. However, modifications to the overall quality control procedure for glucose and creatinine are needed to improve their analytical performance. The study should be extended to the entire laboratory's analytes in order to modify the strategies of quality control procedures based on metric analysis for an overall improvement in analytical performance.

Keywords

Six Sigma, Qualities Controls, Bias, Imprecision, Total Allowable Error

1. Introduction

Obtaining reliable results from medical analyses requires quality control of the activities involved in the sample handling and analysis processes. Quality control is the implementation of control steps at logical and strategic points of each process in the laboratory to verify its proper execution and the quality of results [1]. The incidence of errors is around 10% in the per-analytical phase [2]. It is therefore necessary to establish and strictly monitor quality control (QC) in order to produce reliable results. However, establishing a QC program (internal or external) and following the procedure in the per-analytical phase is not enough [3]. The entire quality assurance procedure of the per-analytical phase should be evaluated systematically and thoroughly to know the effectiveness of its performance [3] [4].

To control their analytical system, most medical biology laboratories focus on obtaining internal and external quality control results within defined acceptable limits [3] [5]. However, knowing the error rate of an analytical system under control would be an opportunity to improve the quality assurance system of the analytical phase [3] [6]. An effective approach is needed to evaluate the performance of the analytical phase to detect errors in a controlled analytical system. The Six Sigma methodology represents an evolution in quality management widely used in industry, but increasingly used in medical biology laboratories. It uses the DMAIC (Definition, Measurement, Analysis, Improvement, and Control Steps) strategy [7] [8]. The Six Sigma strategy is, therefore, a management tool that allows for a better understanding of the performance of techniques and to adapt the laboratory's quality control management policy (frequency, number of controls per day, choice of alarm rules, and rejection) [9].

The objective of our study was to assess, using the Sigma metric, the performance of the biochemistry analytical system of a medical biology laboratory in Côte d'Ivoire.

2. Materials and Methods

2.1. Materials

Our study was retrospective. The data was collected over the period from January to June 2023. They concerned the results of IQC (internal quality control) and EQA (external quality assessment) carried out on the Roche® Cobas C 311 automated analyzer at a medical biology laboratory in Ivory Coast. Glucose (GLUC) and alanine aminotransferase (ALT) and creatinine (CREAT) are the three biochemical analytes used in the biological monitoring of people living with HIV (Human Immunodeficiency Virus) in Ivory Coast. For better control of these analytes, their normal and pathological CQI are carried out and validated daily. External quality controls were available and satisfying during the study period. We therefore had enough values for the calculations of our analytical performance indicators. Analytical performance indicators was determined these biochemicals analytes (GLUC, ALT and CREAT). Two levels of internal

quality control values were used: the normal value level: PreciControl ClinChem Multi 1® (PCCC1) and the pathological value level: PreciControl ClinChem Multi 2® (PCCC2).

2.2. Methods

At the start of each working day, two CQI levels (PCCC1 and PCCC2) are used for each of the biological analyte of the study. Westgard rules were applied for the interpretation of quality control results. Westgard's rules of 1_{3s}, 2_{2s}, R_{4s}, were considered a rejection. The laboratory also participates international external quality control assessment from. The results obtained from the external quality control system were also taken into account to estimate the sigma metrics. Laboratory and peer group results were extracted from monthly external QC program records.

Using the CQI values obtained daily, we calculated the monthly mean (M) and standard deviation (S) of the measurements of each level of control sera (pathological and normal) for each of the analyte studied. Then, the analytical performance indicators were determined: intermediate precision expressed in terms of imprecision (CV%) and the bias % compared to the group average (GA) (all laboratories participating in the EQA). The sigma metrics (Σσ) were calculated for each analyte. The Equation (1), Equation (2) and Equation (3) were used.

$$\%\mathrm{CV} = \left(\frac{\mathrm{M}}{\mathrm{S}}\right) \times 100 \tag{1}$$

$$\%\mathrm{Bias} = \left(\frac{\left(\mathrm{M} - \mathrm{GA}\right)}{\mathrm{GA}}\right) \times 100 \tag{2}$$

$$\sum \sigma = \frac{\left(\%\mathrm{TEa} - \|\%\mathrm{Bias}\|\right)}{\%\mathrm{CV}} \tag{3}$$

TEa % is the total allowable error taking into account the biological variation of the biological analyte considered. A % TEa database established by Ricos *et al*. for more than 321 analytes is regularly updated on the Westgard site [10] [11]. QC procedure was assessed on the sigma metric scale. The minimum acceptable performance of process was considered at 6sigma level.

3. Results

The % CV of the different levels of internal quality control was calculated for the 6-month period and was recorded in Table 1. The majority of % CV were less than 3 % with the exception of the normal creatinine control (3.6%).

The average of our laboratory results and of those participating laboratory groups during the EQA, are recorded in Table 2. The minimum bias was observed for creatinine (3.8%) and maximum for alanine aminotransferase (7.0%).

Sigma values calculated with % TEa, % bias and % CV are reported in Table 3. The Sigma level was found to be acceptable only for alanine aminotransferase

Table 1. % CV of analytes at normal (PCCC1) and pathological (PCCC2) control level.

	PCCC1			PCCC2		
ANALYTES	**M**	**± SD**	**% CV**	**M**	**± SD**	**% CV**
ALT	46.3 UI/l	1.2	2.7	128.4 UI/l	3.3	2.6
GLUC	1.0 g/l	0.0	2.5	2.4 g/l	0.1	2.4
CREAT	9.8 mg/l	0.3	3.6	38.9 mg/l	1.0	2.5

PCCC1: normal control; PCCC2 : pathological control; SD: standard deviation.

Table 2. % bias of measurements obtained from an external quality control program (6-month data).

	Mean of results obtained from external QC program (6 months data)		**% Bias**
Analytes	**Laboratory results**	**Peer group results**	
ALT (UI/l)	61.7	66.3	7.0
GLUC (mmol/L)	8.6	9.1	5.6
CREAT (µmol/l)	249.5	240.4	3.8

QC: quality control.

Table 3. Percentage of total allowable error (TEa), bias, CV [at normal (PCCC1) and pathological (PCCC2) control level] and sigma metric (Σσ) of analytes.

Analytes	**% TEa (Ricos *et al.*)**	**% Bias**	**% CV (PCCC1)**	**% CV (PCCC2)**	**Σσ (PCCC1)**	**Σσ (PCCC2)**	**Interpretation sigma acceptable Σσ > 6**
ALT	27.48	7.0	2.7	2.6	7.6	7.9	acceptable
GLUC	6.96	5.6	2.5	2.4	0.5	0.6	low
CREAT	8.87	3.8	3.6	2.5	1.4	2.0	low

PCCC1: normal control, PCCC2: pathological control.

(PCCC1 and PCCC2). The lowest sigma values were found for glucose (0.5 for normal control and 0.6 for pathological control).

4. Discussion

Internal and external quality controls are important tools to ensure the quality of results produced in medical analysis laboratories. Long used alone to guarantee the stability of analytical performances in the medical biology laboratory, they are increasingly supplemented by the sigma metric methodology. This methodological approach makes it possible to measure the performance of a process by evaluating its quality control indicators in order to detect errors in an analytical system under control [3] [12] [13]. The objective of this study was to evaluate the performances of biochemistry analytical system of a medical biology laboratory in Ivory Coast in the determination of three analytes (ALT, GLUC and CREAT) using the sigma metric.

In the medical biology laboratory, in the sigma metric analysis, the errors or defects identified correspond to poor results gave to the client. These poor results are quantified in number of defects per million (DPM) or percentage of errors. A method is analytically robust when it has a high sigma number (greater than 6). We can then define more flexible alarm and rejection rules, and also adapt the frequency of passage of the CQI. However, for methods presenting a sigma between 3 and 6 (average performance), the frequency of passage and the number of internal quality controls will be adjusted according to the sigma value [14] [15]. Performances is said to be insufficient when the sigma value is less than 3. A link has been established between the number of sigma and programs for managing internal quality controls [16]. In our study we arbitrarily chose the value 6 sigma on the sigma scale (ranging from 1 to 6) to evaluate the performances of our analytical system [2] [3]. With the 6 sigma metric, according to this scale, the probability of detecting errors in the analytical process should be 98% with a probability of rejection of 1% [9] [17]. We therefore used the 6sigma metric in our study. A method with a sigma value greater than 6 was considered to have acceptable performance. The measurement imprecision (expressed in %CV) of each analyte was determined over 6 months. The % CV of the pathological level of all analytes (ALT = 2.7/GLUC = 2.5%/CREAT = 3.6%) were all acceptable according to the desirable analytical objectives of Ricos *et al*. (ALT = 9.7%/GLUC = 2.8%/CREAT = 2.98%) [10] [11]. Imprecision is a reflection of the instability and fluctuation of the analytical system. Acording to the analytical objectives of Ricos, for the pathology control of all our analytes the fluctuation of our analysis system was acceptable. It was the same for the normal control of the analytes ALT AND GLUC (ALAT = 2.6%/GLUC = 2.4%). However, the imprecision of the normal control of creatinine (CREAT = 3.8%) was not acceptable according to the analytical objectives of Ricos *et al*. The bias was acceptable for ALT and CREAT (ALT = 7%/CREAT = 3.8%) but unacceptable for glucose (GLUC = 5.6%), still according to the analytical objectives of Ricos *et al*. (ALT = 11.48%/GLUC = 2.34%/CREAT = 3.96%). Thus, despite the establishment of a quality control program defined, validated by Westgard rules with good performances of extenal quality control, we note variability in the performance of our methods. Consequently, it was necessary to detect clinically significant analytical errors by adopting a more holistic approach (sigma methodology) to anticipate and reduce errors [3] [9] [17]. The evaluation of the analytical performance of the analytes of biological monitoring of people living with HIV by the sigma metric, revealed that the performance of ALT had for his two levels of controls a sigma greater than 6 (7.6 for the normal control and 7.9 for pathological control). Hens *et al*. (2014), in a similar study (using the TEa of Ricos *et al*. for the calculation of the sigma number), found a sigma number for ALT reaching 12 (normal control) and up to 21 (pathological control) for their analytical systems [17]. We found low sigma values, either less than or equal to 2 for creatinine (1.4 for the normal control and 2 for the pathological control) or less than 1 for glu-

cose. In the same study by Hens *et al*., sigma values was low but reaching 3 was found for creatinine, and sigma values varied from 3 to 8 for glucose [17].

Westgard has defined sigma rules, intended to select precise statistical quality control procedures, for specific clinical use and for method performance indicators [2] [3] [18]. According to these Westgard sigma rules, for sigma values greater than 6, no rigorous quality control procedure is necessary for the analytes. Only one rejection rule, that of 1_{3S} with 1 control measurements for each of the control levels in a series of analyses is necessary. This would detect 98 % of errors. This rule could apply to ALT in the case of our study. Thus, this shows that the application of all the Wesgard CQI rejection rules is not necessary for ALT. According to Westgard's sigma rules, for analytes having a value less than three sigma, in addition to the adaptation of the rejection rules and the frequency of passing the CQI, a revision of the division of the daily workload is also recommended, as well as modification of the quality control procedure strategy. Improving the performance of the glucose and creatinine will require the adoption of changes both in the work protocol daly and in the quality control procedure strategy.

The application of the sigma metric to these 3 analytes reveals the efforts to be undertaken to continuously improve the analytical performance of our analysis system. It would be advantageous for the laboratory to extend this sigma metric analysis to all analytes in the laboratory. This would allow targeted quality control protocols to be defined based on sigma number with the aim of minimizing unnecessary quality control monitoring, thereby reducing the cost of analytes with a high sigma metric result and improving quality control of analytes at low sigma value.

The sigma metric is strongly linked to the choice of the value of the total allowable error (TEa) [17]. This value varies depending on whether it concerns the recommendations of CLIA(Clinical Laboratory Improvements Amendments) or RiliBÄK (German Medical Council for the Quality Assessment of Quantitative Analyses in Medical Laboratories, 2008 version) or those base on Ricos's biological variability data base (desirable target values). These three sources are regularly updated and can be freely accessed through http://www.westgard.com. The laboratory must then, after analysis, choose the TEa benchmark that it will adopt for these next sigma metric analyses.

5. Conclusion

The 6 sigma methodology is a holistic approach to the management of quality control processes widely used in industry, however, increasingly recommended and even applied in medical biology laboratories. This study that we undertook, with the 3 analytes for biological monitoring of people living with HIV, reveals the good analytical performance of ALT from the point of view of 6 sigma analysis. However, modifications to the entire quality control procedure for glucose and creatinine are necessary to improve their analytical performance. This pre-

liminary study should extend to all analytes in the laboratory in order to modify our quality control procedure strategies based on metric analysis for an overall improvement in our analytical performance.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] OMS (2023) Laboratory Quality Stepwise Implementation Tool. https://extranet.who.int/lqsi/fr/node/1055

[2] Westgard, J.O. (2013) Statistical Quality Control Procedures. *Clinics in Laboratory Medicine*, **33**, 111-124. https://doi.org/10.1016/j.cll.2012.10.004

[3] Iqbal, S. and Mustansar, T. (2017) Application of Sigma Metrics Analysis for the Assessment and Modification of Quality Control Program in the Clinical Chemistry Laboratory of a Tertiary Care Hospital. *Indian Journal of Clinical Biochemistry*, **32**, 106-109. https://doi.org/10.1007/s12291-016-0565-x

[4] Westgard, J.O., Burnett, R.W. and Bowers, G.N. (1990) Quality Management Science in Clinical Chemistry: A Dynamic Framework for Continuous Improvement of Quality. *Clinical Chemistry*, **36**, 1712-1716. https://doi.org/10.1093/clinchem/36.10.1712

[5] Westgard, J.O., Seehafer, J.J. and Barry, P.L. (1994) Allowable Imprecision for Laboratory Tests Based on Clinical and Analytical Test Outcome Criteria. *Clinical Chemistry*, **40**, 1909-1914. https://doi.org/10.1093/clinchem/40.10.1909

[6] Westgard, J.O., Seehafer, J.J. and Barry, P.L. (1994) European Specifications for Imprecision and Inaccuracy Compared with Operating Specifications That Assure the Quality Required by US CLIA Proficiency-Testing Criteria. *Clinical Chemistry*, **40**, 1228-1232. https://doi.org/10.1093/clinchem/40.7.1228

[7] Coskun, A. (2007) Six Sigma and Laboratory Consultation. *Clinical Chemistry and Laboratory Medicine*, **45**, 121-123. https://www.degruyter.com/document/doi/10.1515/CCLM.2007.023/html

[8] Mhone, A.O. and Jin, J. (2021) Deployment of Lean Six Sigma and KAIZEN Techniques: A Case Study of the Concrete Production Plant for the 750 MW (5 * 150 MW) Kafue Gorge Lower Hydro Power Project. *American Journal of Industrial and Business Management*, **11**, 1052-1069. https://doi.org/10.4236/ajibm.2021.1110064

[9] Scherrer, F., Bouilloux, J.P., Calendini, O., Chamard, D. and Cornu, F. (2017) Interest and Limits of the Six Sigma Methodology in Medical Laboratory. *Annales de Biologie Clinique* (*Paris*), **75**, 107-113. https://doi.org/10.1684/abc.2016.1216

[10] Ricós, C., Alvarez, V. and Cava, F.J.V. (1999) Current Databases on Biological Variation: Pros, Cons and Progress. *Scandinavian Journal of Clinical and Laboratory Investigation*, **59**, 491-500. https://doi.org/10.1080/00365519950185229

[11] Westgard, Q.C. (2012) Biologic Variation and Desirable Specifications for QC—Westgard. https://www.westgard.com/guest17.htm

[12] Afrifa, J., Gyekye, S.A., Owiredu, W.K.B.A., Ephraim, R.K.D., Essien-Baidoo, S., Amoah, S., *et al*. (2015) Application of Sigma Metrics for the Assessment of Quality Control in Clinical Chemistry Laboratory in Ghana: A Pilot Study. *Journal of the*

Nigeria Medical Association, **56**, 54-58. https://doi.org/10.4103/0300-1652.149172

[13] Klee, G.G. (2010) Establishment of Outcome-Related Analytic Performance Goals. *Clinical Chemistry*, **56**, 714-722. https://doi.org/10.1373/clinchem.2009.133660

[14] Westgard, J.O. (2011) Six Sigma Risk Analysis. Westgard QC Inc Edition, Madison.

[15] Westgard, J.O. (2006) Six Sigma Quality Design and Control.

[16] Westgard, J.O. and Stein, B. (1997) Automated Selection of Statistical Quality-Control Procedures to Assure Meeting Clinical or Analytical Quality Requirements. *Clinical Chemistry*, **43**, 400-403. https://doi.org/10.1093/clinchem/43.2.400

[17] Hens, K., Berth, M., Armbruster, D. and Westgard, S. (2014) Sigma Metrics Used to Assess Analytical Quality of Clinical Chemistry Assays: Importance of the Allowable Total Error (TEa) Target. *Clinical Chemistry and Laboratory Medicine*, **52**, 973-980. https://www.degruyter.com/document/doi/10.1515/cclm-2013-1090/html

[18] Jones, G.R.D. (2004) Reevaluation of the Power of Error Detection of Westgard Multirules. *Clinical Chemistry*, **50**, 762-764. https://doi.org/10.1373/clinchem.2003.025585