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ORIGINAL ARTICLE

Performance Evaluation of a Coagulation Laboratory Using Sigma Metrics and Quality Goal Index

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SUMMARY

Background: **Sigma methodology is a statistical calculation and quality management tool that provides information about process performance. If clinical laboratories start using sigma metrics to monitor their performance, they can more easily identify gaps in their performance, thereby improve their performance and patient safety. This study aimed to calculate sigma metrics and quality target index values by using internal quality control data from coagulation tests, thus evaluating the analytical performance.**
Methods: **Sigma levels were calculated using the formula: [total allowable error (TEa) - bias]/coefficient of variation (CV). Sigma values ≥ 6, between 3 and 6, and < 3 were classified as "world-class", "good" or "unacceptable", respectively. A biological variation database (BVD) was used for TEa. The quality goal index (QGI) is the reason behind a low sigma value, that is, lower precision, lower accuracy, or both due to the combination. QGI was calculated using the formula QGI = bias/1.5 x % CV. With a QGI value of < 0.8, the measurement indicates that the accuracy of the procedure needs to be improved; QGI values > 1.2 indicate accuracy needs to be improved and values 0.8 ≤ QGI ≤ 1.2 indicate both precision and accuracy need to be improved.**
Results: **Sigma and QGI of three-monthly two-level internal quality control values were calculated by using the laboratory automation system. In the prothrombin time (PT) and activated partial thromboplastin time (APTT) tests of the coagulation parameters studied, sigma values were found to be < 3 in both levels. When the QGI value was calculated, it was PT 0.45 and APTT 0.90 for level 1 and PT 0.16 and APTT 0.6 for level 2, respectively.**
Conclusions: **It was decided that sigma values of coagulation parameters at "low quality" levels and improvement studies should be carried out for coagulation parameters in our laboratory. By evaluating sigma levels, it is possible to identify tests with a high probability of failure, and these tests should undergo strict quality control inspections. In clinical biochemistry laboratories, appropriate quality control planning should be performed for each test by using the Six Sigma methodology and by calculating the quality target index.**
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KEYWORDS

coagulation, Six Sigma, quality target index

INTRODUCTION

Laboratory data play a leading role in clinical decision-making in many aspects, such as diagnosis, treatment, evaluation of response, and recurrence. These data were collected in a three-stage process consisting of preana-

lytical, analytical, and post-analytical phases, starting with the patient's test request and ending with the conclusion and interpretation of the analysis. According to previous studies, the estimated error rates of this three-stage test process range from 30 - 75% for the pre-analytical stage, 4 - 30% for the analytical stage, and 9 - 55% for the post-analytic stage [1].

The main goal of diagnostic laboratories is to produce reliable results that accurately represent the clinical condition of patients. In recent years, much attention has been paid to optimizing the analytical quality (sensitivity and bias) of tests, partly based on methods for determining the analytical performance characteristics (APS) [1,2]. APS criteria can be defined using different approaches and may be based on clinical results, biological variation (BV), or state-of-the-art analytical performance [1]. Ideally, APS criteria should be based on clinical outcome requirements; however, high-quality data are scarce. The disadvantage of using state-of-the-art analytical performance is that it is not relevant to the clinically desired performance or what is necessary to minimize "analytical noise" compared to the biological signal. Thus, in most cases, BV is currently the best and simplest basis for defining APS criteria [3,4].

Different levels of internal and external quality control have been studied in clinical biochemistry laboratories to evaluate the precision and accuracy of laboratory tests. Westgard's rules were used to assess internal quality. Quality control materials are used to monitor the performance of analytical methods [5]. The Six Sigma method is an important quality control analysis used in the evaluation of quality and performance and is based on statistical calculations. The Six Sigma method provides a quantitative comparison of various auto analyzers, laboratories, and methods worldwide [6]. Errors can be minimized in the laboratory if six standard deviations are maintained between the mean of a test and the upper and lower limits of the test [7]. A systematic error indicator, bias, random error indicator, CV, and TEa are required to calculate the sigma level used in the determination of the analytical process [8]. The tolerance limits of the laboratory were expressed as TEa.

MATERIALS AND METHODS

This study was conducted at the clinical biochemistry laboratory of the University of Health Sciences, Haseki Training and Research Hospital. In our study, the internal and external quality control data of PT, APTT, fibrinogen, and D-dimer coagulation tests were calculated by the sigma levels of the 3 months between December 2019 and February 2020.

Innovance D-dimer (Siemens Medical Solutions Diagnostics, Deerfield, IL, USA) is a fully automated particle-enhanced immunoturbidimetric assay for the quantitative determination of D-dimer in plasma. The assay relies on the monoclonal antibody, covalently coupled to polystyrene particles, and is designed for performance on several automated coagulation analyzers from Siemens Medical Solutions Diagnostics. In this study, D-dimer testing was performed using the BCS coagulation analyzer (Siemens Medical Solutions Diagnostics) with the Innovance D-dimer kit (Bedford, MA, USA) (lot no. N0101345), and control materials (lot no. N010 1349) were used.

The internal quality control material was studied using the BCS XP (Siemens, USA) device, and the results were retrospectively obtained from the device. Microsoft office excel 2010 was used for all the calculations. The variation coefficient (% CV) was calculated by working with two levels: 72 low and 73 high levels in total. The monthly data obtained from the Randox International Quality Assessment Scheme (RIQAS) external quality control program, % bias = (target value-laboratory average)/(target value)) x 100, was calculated. The average of the three-month bias data is used in the sigma account. The Sigma value was calculated using the following formula: (% TEa - % bias)/% CV. The total permissible error rates (TEa) were included in the account, considering the recommendations of CLIA, 2019 [10]. QGI was calculated using the formula % bias/(1.5 x CV) [11]. Approval from the Non-Interventional Ethics Committee of this study (decision no. 0317) was obtained from our institution on June 24, 2021.

RESULTS

In our study, the three-month average % CV, % bias values, % TEa rates, and sigma levels of the four tests (PT, APTT, fibrinogen, and D-dimer) at two levels are shown in Table 1 and Table 2. The TEa rate for the PT and APTT tests was 15%. The sigma values of the APTT test for low and high levels were 1.7 and 1.39, respectively. For the PT test, the QGI value was < 0.8 at two levels. For the APTT test, the QGI value was > 0.8 at a low level (Table 1), yet < 0.8 at a high level (Table 2). Sigma values for low and high levels of the PT test were calculated as 2.41 and 2.25, respectively. The sigma values for low and high levels of the APTT test were calculated as 1.7 and 1.39, respectively.

DISCUSSION

In this study, we evaluated the analytical performance of coagulation parameters by calculating the sigma process and quality target index values, using the internal quality control data of coagulation tests. Six Sigma improves the quality of process outputs by analyzing and eliminating the source of defects and reducing the variability in production and business applications. In clinical laboratories, tests with low sigma values (< 3σ) indicate that precautions should be taken to improve analytical quality or that the laboratory should use alternative methods and reagents [7,8].

Since both levels of PT, APTT, fibrinogen, and D-dimer

Table 1. Quality indicators for Level 1.

Level 1	% Cv	Mean	Bias	TEa	Sigma	QGI
PT	4.85	12.7	3.31	15	2.41	0.45
APTT	4.92	26.4	6.63	15	1.70	0.90
Fibrinogen	5.96	280	1.63	20	3.08	0.18
D-dimer	5.36	0.32	12.50	30	3.26	1.55

Table 2. Quality indicators for Level 2.

Level 2	% Cv	Mean	Bias	TEa	Sigma	QGI
PT	6.03	22.8	1.45	15	2.25	0.16
APTT	6.54	50.9	5.91	15	1.39	0.60
Fibrinogen	2.3	100	5.00	20	6.52	1.45
D-dimer	8.36	2.72	1.47	30	3.41	0.12

tests are sigma values for level 1 fibrinogen, the multiple rules of Westgard should be applied. The existing QC protocol, which follows the 3S rule, does not require any change, and the test results can be published directly. We used the optimized quality control strategy for the parameters with low sigma values [9].

Good laboratory practices symbolize a set of principles that ensure the production of high-quality and reliable test results. Clinical Laboratory Improvement Changes (CLIA) regulations emphasize quality improvement at all stages of analysis. Quality indicators measure the quality and overall performance of a laboratory, leading to the identification and correction of ongoing errors [10].

Good laboratory preparation requires laboratories to design quality control (QC) procedures to ensure that conscious patient results meet the necessary quality for the intended use. Sigma metrics are based on statistical understanding: laboratory errors can be reduced by preserving six standard deviations between the parameter average and upper and lower limits. Six Sigma is related to the idea of product defects, wasted operating costs, and customer satisfaction levels. As Sigma increases, it can be concluded that the consistency and determination of the test increases, and thus, operating costs decrease. As Sigma increases, the consistency, reliability, stability, and overall performance of the test improve; thus, operating costs decrease [11].

When the method quality targets are determined as Six Sigma, tight internal quality control rules are mandatory. However, by loosening the control limits to 3 SD, the incorrect rejection rate should be maintained. On the other hand, if the method works at the sigma level below 3, even after multiple quality control cycles, the quality of the test cannot be guaranteed, and a better method will need to be applied [12].

Sigma values are useful for controlling the quality control strategy design. For a high-sigma process, it is relatively easy for the laboratory to design a quality control procedure and to detect any unrequited situation that may pose a significant risk of producing unreliable results. To facilitate the design of quality control procedures that can detect significant out-of-control conditions, a relatively major out-of-control situation should occur. Sigma metric values are useful for determining internal quality control acceptability criteria [13].

This study showed that the QGI for PT, APTT, and fibrinogen tests was less than 0.8, which suggests that there are deficiencies in the absence of the detection system. Therefore, to improve the analytical performance of these three analysts, it is necessary to improve the uncertainty of the detection system. To increase the certainty of the test, the following precautions were taken:

a) the maintenance frequency of the device was increased,

b) the control of daily reagents was strengthened to ensure that quality meets the requirements,

c) lyophilized quality control was changed with liquid quality control to reduce the experimental error caused by reconstruction of lyophilized quality control and to refine the training of laboratory personnel to ensure consistency,

d) errors caused by inappropriate operation were reduced.

In this study, a normalized method decision table was used to perform plasma protein detection.

Individualized quality control rules were developed based on the analysts' sigma metrics. Consequently, this continuous error detection reduces the false rejection

rate and orchestrates continuous improvements in analytical detection capabilities. According to our sigma values, multiple Westgard rules, such as $1^{3s}/2^{2s}/R^{4s}$, were required to ensure the accuracy and security of the test results. Our previous study also determined that Six Sigma is useful in evaluating the generation of tumor marker tests and has a potential limiting value in internal quality control.

Westgard [9] suggested that at least two concentrations of quality control products should be used daily as internal quality controls to ensure the reliability of detection results. Even the performance specification of the Milan consensus represents the opinion of its authors and is merely a 'consensus' paper from the conference, and TEa does not have universally stable quality targets, hence the need for harmony.

Declaration of Interest:

The authors declare that they have no conflicts of interest.

References:

1. Hawkins R. Managing the pre- and post-analytical phases of the total testing process. Ann Lab Med 2012;32(1):5-16. (PMID: 22259773)

2. Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing 2024. https://www.ncbi.nlm.nih.gov/books/NBK557491/

3. Braga F, Panteghini M. Performance specifications for measurement uncertainty of common biochemical measurands according to Milan models. Clin Chem Lab Med 2021;59(8). https://www.degruyter.com/document/doi/10.1515/cclm-2021-0170/html#MLA

4. Fraser CG, Petersen PH. Analytical performance characteristics should be judged against objective quality specifications. Clin Chem 1999;45(3):321-3. (PMID: 10053031)

5. "Westgard Rules" and Multirules. Westgard QC. https://westgard.com/westgard-rules.html

6. Westgard JO, Westgard SA. Six Sigma Quality Management System and Design of Risk-based Statistical Quality Control. Clin Lab Med 2017;37(1):85-96. (PMID: 28153372)

7. Kumar BV, Mohan T. Sigma metrics as a tool for evaluating the performance of internal quality control in a clinical chemistry laboratory. J Lab Physicians 2018;10(2):194-9. (PMID: 29692587)

8. Hens K, Berth M, Armbruster D, Westgard S. Sigma metrics used to assess analytical quality of clinical chemistry assays: importance of the allowable total error (TEa) target. Clin Chem Lab Med 2014;52(7):973-80. (PMID: 24615486)

9. Westgard JO, Westgard SA. The quality of laboratory testing today: an assessment of sigma metrics for analytic quality using performance data from proficiency testing surveys and the CLIA criteria for acceptable performance. Am J Clin Pathol 2006;125 (3):343-54. (PMID: 16613337)

10. Chaudhry AS, Inata Y, Nakagami-Yamaguchi E. Quality analysis of the clinical laboratory literature and its effectiveness on clinical quality improvement: a systematic review. J Clin Biochem Nutr 2023;73(2):108-15. (PMID: 37700849)

11. Kashyap A, Sampath S, Tripathi P, Sen A. Sigma Metrics: A Valuable Tool for Evaluating the Performance of Internal Quality Control in Laboratory. J Lab Physicians 2021;13(4):328-31. (PMID: 34975251)

12. Tetrault G. Evaluating laboratory performance with the six sigma scale. Arch Pathol Lab Med 2000;124(12):1748-9. (PMID: 11100045)

13. Stepman HCM, Tiikkainen U, Stockl D, et al.; Participating Laboratories. Measurements for 8 common analytes in native sera identify inadequate standardization among 6 routine laboratory assays. Clin Chem 2014;60(6):855-63. (PMID: 24687951)