Application of Sigma Metrics Analysis for the Assessment and Modification of Quality Control Program in the Clinical Chemistry Laboratory of a Tertiary Care Hospital

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Abstract Sigma is a metric that quantifies the performance of a process as a rate of Defects-Per-Million opportunities. In clinical laboratories, sigma metric analysis is used to assess the performance of laboratory process system. Sigma metric is also used as a quality management strategy for a laboratory process to improve the quality by addressing the errors after identification. The aim of this study is to evaluate the errors in quality control of analytical phase of laboratory system by sigma metric. For this purpose sigma metric analysis was done for analytes using the internal and external quality control as quality indicators. Results of sigma metric analysis were used to identify the gaps and need for modification in the strategy of laboratory quality control procedure. Sigma metric was calculated for quality control program of ten clinical chemistry analytes including glucose, chloride, cholesterol, triglyceride, HDL, albumin, direct bilirubin, total bilirubin, protein and creatinine, at two control levels. To calculate the sigma metric imprecision and bias was calculated with internal and external quality control data, respectively. The minimum acceptable performance was considered as 3 sigma. Westgard sigma rules were applied to customize the quality control procedure. Sigma level was found acceptable (≥ 3) for glucose (L2), cholesterol, triglyceride, HDL, direct bilirubin and creatinine at both levels of control. For rest of the analytes sigma metric was found <3 . The lowest value for sigma was found for chloride (1.1) at L2. The highest value of sigma was found for creatinine (10.1) at L3. HDL was found with the

highest sigma values at both control levels (8.8 and 8.0 at L2 and L3, respectively). We conclude that analytes with the sigma value <3 are required strict monitoring and modification in quality control procedure. In this study application of sigma rules provided us the practical solution for improved and focused design of QC procedure.

Keywords Bias · Laboratory proficiency testing · Quality control · Quality indicators

Introduction

Clinical laboratory results are important to diagnose and manage the disease. To produce reliable results, laboratories are aimed to adopt the best quality assurance program. Besides maintain a good compliance for required standards, errors are not uncommon within the laboratory process system [1]. Laboratory errors are more frequently seen within pre and post analytical processes. Analytical phase contains fewer incidences of errors, account approximately 10 % [2]. Even comparatively with the less frequency of errors, strict monitoring of quality control (QC) of analytical phase is required to produce valid and accurate results. Establishing the QC program and procedure for analytical phase is not sufficient. A thorough and systematic assessment of QC procedure is essential to know its effective performance [3].

In clinical laboratories, medical technologists are trained to focus on achieving the QC results within the defined acceptable limits [4]. As a routine practice, when analytical system is declared controlled after a successful attempt of QC, patient samples are allowed to run. However, besides having the controlled analytical system knowing the error rate is commendable [5]. To detect the errors in a controlled system, an efficient approach is required to evaluate the QC indicators.

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Sigma is a metric that quantifies the performance of a process as a rate of Defects-Per-Million (DPM) opportunities, graded the ideal situation as possible DPM of 3.4 at the level of six sigma [6]. Laboratory performance can be evaluated by applying Sigma metrics on any phase of laboratory process. Errors evaluation in terms of sigma metric is more meaningful than number of defects alone. For analytical process of laboratory system, sigma metric analysis identifies the errors in quality indicators of the process and provides rectification of errors on the basis of results [7].

The aim of this study is to evaluate the errors in quality control of analytical phase of laboratory system by sigma metric. For this purpose sigma metric analysis is done for analytes, using the internal and external quality control as quality indicators. Results of sigma metric analysis will be used to identify the gaps and need for modification in the strategy of laboratory quality control procedure.

Material and Method

In this cross sectional study, sigma metric was calculated for the evaluation of analytical quality control process in the section of Clinical Chemistry at Dow Diagnostic Reference and Research Laboratory (DDRRL), Karachi, Pakistan. DDRRL is providing services to Dow Hospital, a tertiary care hospital with more than 550 beds. The laboratory has 35 phlebotomy centers across the country.

The study was conducted over the period of 6 months from October 2014 till March 2015. Only those analytes were included in the study which were analyzed on Architect c8000 (Abbott Laboratories, IL, USA), run with the same lot number of internal QC material and performed on external quality control scheme throughout the study period. On the basis of inclusion criteria, plasma glucose, chloride, cholesterol, triglyceride, HDL, albumin, direct bilirubin, total bilirubin, protein and creatinine were included in the study.

As a routine practice, daily laboratory work load was divided into three shifts; each shift was comprised of 8 h. According to laboratory policy of internal quality control program, two levels (normal, L2 and pathological L3) of control material (Randox, UK) were being used in each run of 8 h. Westgard rules were applied for the interpretation of quality control results. Westgard rules of 1_3s , 2_2s , R_{4s} , 4_1s and 10_x were considered as rejection and 1_2s as warning situations for the respective run. Laboratory is also participating monthly in the external QC survey of RIQAS (Randox international quality assessment scheme, Randox Laboratories, United Kingdom). The results obtained from external QC scheme, were also considered to estimate the sigma metrics. Laboratory and peer group results of analytes were retrieved from monthly external QC program records.

Inappropriate performance of analytes on internal QC (larger % CV than target) and unacceptable performance on external QC survey were considered as quality indicators of analytical phase. Sigma metric analysis was done by using the information of assay coefficient of variation (% CV) and bias, collected from internal and external QC data, respectively.

For each level of control, CV was calculated from mean and standard deviation (SD) of internal quality control data (Eq. 1):

$$CV \% = \text{Standard deviation} / \text{mean} \times 100 \quad (1)$$

Bias was calculated from data of external quality scheme records (Eq. 2):

$$\begin{aligned} \text{Bias \%} = & \text{Mean of peer group (all laboratories using} \\ & \text{same instrument and method)} \\ & - \text{laboratory result} / \text{mean of peer group} \\ & (\text{all laboratories using same instrument and method}) \end{aligned} \quad (2)$$

The sigma metrics ($\sum \sigma$) was calculated for each analyte as shown in Eq. 3:

$$\sum \sigma = TEa - \text{Bias} / CV \quad (3)$$

where, TEa is the total allowable error of analyte taken from Clinical and Laboratory Improvement Act (CLIA) guidelines [7]. QC procedure was assessed on the sigma metric scale. The minimum acceptable performance of process was considered at 3 sigma level.

Results and Discussion

The internal quality control data was utilized to calculate the % CV at L2 and L3 of quality control material (Table 1). Mean of laboratory and peer group results were

Table 1 % CV of clinical chemistry analytes at normal (Level 2) and pathological (Level 3) control level

Analytes	Level (L) 2			Level (L) 3		
	Mean	± SD	CV	Mean	± SD	CV
Glucose (mg/dl)	107	2.8	2.6	279	9.4	3.3
Chloride (mmol/l)	98.5	2.7	2.7	115.4	2.8	2.4
Cholesterol (mg/dl)	153.4	3.8	2.5	263	6.1	2.3
Triglyceride (mg/dl)	97.6	3.3	3.3	258.3	5.9	2.3
HDL (mg/dl)	46.3	1.5	3.2	93	3.2	3.5
Albumin (g/dl)	4.2	0.1	3.3	2.9	0.1	3.5
Direct bilirubin (mg/dl)	0.9	0.1	12.1	1.7	0.1	8.6
Total bilirubin (mg/dl)	1.3	0.1	8.6	4.7	0.3	7.2
Protein (g/dl)	6.1	0.2	3.6	4.4	0.1	3.9
Creatinine (mg/dl)	1.5	0.05	3.8	4.3	0.1	2.6

taken from reports of external QC survey over the study period. Bias was calculated with the percentage difference of mean of peer group and laboratory values (Table 2). The minimum bias was observed for cholesterol (0.4 %) and maximum for direct bilirubin (7.1 %). Sigma values were calculated with TEa, bias and CV (Table 3).

Sigma level was found acceptable (≥ 3) for glucose (L2), cholesterol, triglyceride, HDL, direct bilirubin and creatinine at both levels of control. For rest of the analytes sigma metric was found < 3 (Table 3). The lowest value for sigma was found for chloride (1.1) at L2. The highest value of sigma was found for creatinine (10.1) at L3. HDL was

found with the highest sigma values at both control levels (8.8 and 8.0 at L2 and L3, respectively).

Sigma metric analysis is used to measure the performance of a process [8]. In clinical laboratories, assessment of the performance can be done separately for preanalytical, post analytical and analytical phases or as overall laboratory process system. Irrespective of process, sigma metrics covers the five universal steps including define, measure, analyze, improve and control the process. Sigma analysis also identifies errors within the process [9]. In sigma metric analysis, identified errors or defects are considered as poor outcomes which are quantified as DPM or percentage errors. In clinical laboratories, 3 sigma is the arbitrary value on the sigma scale (ranged from 1 to 6), considered acceptable for process performance. Any laboratory process with the sigma value of 3 is expected to produce 6.7 % clinically unacceptable outcomes [10].

In his study we carried out sigma metric analysis of QC procedure of analytical phase. Analysis was straightforward, as information of % CV and bias was readily available with laboratory QC record. CV is the indicator of imprecision which is the reflection of instability and fluctuation of analytical system. The higher the CV of the assay the more variation and less precision would be seen in the results. On the other hand we obtained bias from external quality control survey reports. Bias estimates the inaccuracy of results and is assessed by difference in the means of results. To reliably detect clinically significant analytic errors a systematic approach is necessary to adopt by adding up these stings to judge before allowable inherent errors. This justifies the main objective of the sigma metrics analysis; first to detect the errors more than allowed and then to minimize the identified defects to guarantee compliance with the significant specifications.

For QC procedure, sigma metric analysis is found helpful to evaluate the performance and to optimize the protocol for improvement and cost effectiveness [11]. Westgard sigma rules are intended to support laboratory efforts to select statistical QC procedures that are accurate for the specific clinical use and the method performance [10, 12].

In this study, Sigma value was found > 6 at both levels of control for triglyceride, HDL and creatinine. Westgard rules suggest that no rigorous exercise is needed for the quality control of such analytes with the sigma value of > 6 . According to the Westgard sigma rules these analytes are required only a single rejection rule of 1_3s , with 2 control measurements of each level in a run.

We found sigma value of < 4 for glucose, chloride, albumin, total bilirubin and protein at both levels and for cholesterol and direct bilirubin at L2 (Table 3). Similarly for cholesterol and direct bilirubin, sigma value was found approximate equal to 4 (4.1 and 4.3 respectively).

Table 2 Bias of clinical chemistry analytes calculated from external quality control (QC) program

Analytes	Mean of results obtained from external QC program (6 months data)		% Bias
	Laboratory result	Peer group results	
Glucose (mg/dl)	165	163	1.2
Chloride (mmol/l)	107	105	1.8
Cholesterol (mg/dl)	225	217	0.4
Triglyceride (mg/dl)	176	175	0.5
HDL (mg/dl)	76	77.5	1.9
Albumin (g/dl)	3.4	3.5	2.8
Direct bilirubin (mg/dl)	1.3	1.4	7.1
Total bilirubin (mg/dl)	3.2	3.3	3.0
Protein (g/dl)	5.1	5.3	3.7
Creatinine (mg/dl)	2.9	2.8	3.5

Table 3 Percentage of total allowable error (TEa), bias, CV [at level (L) 2 and level (L) 3] and sigma metric ($\sum\sigma$) of analytes

Analytes	TEa	Bias	CV (L2)	CV (L3)	$\sum\sigma$ at L2	$\sum\sigma$ at L3
Glucose (mg/dl)	10	1.2	2.6	3.3	3.3	2.6
Chloride (mmol/l)	5	1.8	2.7	2.4	1.1	1.3
Cholesterol (mg/dl)	10	0.4	2.5	2.3	3.8	4.1
Triglyceride (mg/dl)	25	0.5	3.3	2.3	7.4	10.6
HDL (mg/dl)	30	1.8	3.2	3.5	8.8	8.0
Albumin (g/dl)	10	2.8	3.3	3.5	2.1	2.0
Direct bilirubin (mg/dl)	44.5	7.1	12.1	8.6	3.0	4.3
Total bilirubin (mg/dl)	20	3.0	8.6	7.2	1.9	2.3
Protein (g/dl)	10	3.7	3.6	3.9	1.7	1.6
Creatinine (mg/dl)	30	3.5	3.8	2.6	6.9	10.1

Considering these results, these analytes require 8_x instead of 10_x , along with 1_{3s} , 2_{2s} , R_{4s} and 4_{1s} Westgard rules to apply on internal QC to achieve the improved sigma value.

For analytes having less than three sigma value, revision in the daily work load division is also recommended by “Westgard sigma rules”, Along with the modification in QC procedure strategy (Table 3). We are also required to adopt the changes in our protocol of number of shifts in a day. For analytes with the outcome of sigma values <3 , a change in the frequency of daily run is also required in our laboratory. The frequency would be required to change as 2 (12 hourly) or 4 (6 hourly) runs per day (instead of 3). In addition, 4 or 2 control measurements of each level (L2 and L3) are required in each run respectively, if runs are 2 or 4 in numbers per day [13–16].

Before this study, we were using a single QC procedure for all analytes with the same QC rejection protocol for all analytes. However, findings from this study suggest that analytes are required focused procedures (choice of rejection rules and frequency of runs and quality control material measurements) for effective and improved quality control. The focused QC protocols will help to minimize the unnecessary QC monitoring hence reducing the cost for analytes with the high sigma metric result and to improve the QC of low sigma value analytes. Assay methodologies, precisions, accuracy and QC procedures may vary among different laboratories. Hence, sigma metrics analysis of QC procedures for analytes could not be compared amongst different clinical laboratories [17, 18].

This study presented the sigma metric of analytical process observed in our clinical chemistry laboratory. Results obtained from this study are helpful to minimize the variance and get the optimal quality control procedures for improved quality assurance. With the help of “Westgard sigma rules”, QC protocol could be customized for better outcome. Each laboratory should monitor the quality control procedures and strategies in a structured manner using sigma metric for improvement of various laboratory processes.

The one of the big limitation of this study is to use the external quality scheme and commercially available controls for calculation of bias and imprecision, respectively. Financial constraints could explain the inability for using reference method and material to calculate the bias and imprecision. Another limitation of this study is to not conduct a pilot study of revised sigma metric analysis with modified strategy of quality control procedure and frequency of runs for the same low sigma value analytes, which were included in this study. A result comparison of two studies could demonstrate the reduced defect rate and improved performance.

Compliance with Ethical Standards

Conflict of interest Authors declare that they have no conflict of interest and financial support for this study.

References

- Sciacovelli L, O’Kane M, Skaik YA, Caciagli P, Pellegrini C, Da Rin G, et al. Quality indicators in laboratory medicine: from theory to practice. Preliminary data from the IFCC working group project “Laboratory Errors and Patient Safety”. *Clin Chem Lab Med*. 2011;49(5):835–44.
- Plebani M. Errors in clinical laboratories or errors in laboratory medicine? *Clin Chem Lab Med*. 2006;44(6):750–9.
- Westgard JO, Burnett RW, Bowers GN. Quality management science in clinical chemistry: a dynamic framework for continuous improvement of quality. *Clin Chem*. 1990;36(10):1712–6.
- Westgard JO, Seehafer JJ, Barry PL. Allowable imprecision for laboratory tests based on clinical and analytical test outcome criteria. *Clin Chem*. 1994;40(10):1909–14.
- Westgard JO, Seehafer JJ, Barry PL. European specifications for imprecision and inaccuracy compared with operating specifications that assure the quality required by US CLIA proficiency-testing criteria. *Clin Chem*. 1994;40(7 Pt 1):1228–32.
- Coskun A. Six sigma and laboratory consultation. *Clin Chem Lab Med*. 2007;45(1):121–3.
- 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.
- Afrifa J, Gyekye SA, Owiredu WK, Ephraim RK, Essien-Baidoo S, Amoah S, et al. Application of sigma metrics for the assessment of quality control in clinical chemistry laboratory in Ghana: a pilot study. *Niger Med J*. 2015;56(1):54–8.
- Klee GG. Establishment of outcome-related analytic performance goals. *Clin Chem*. 2010;56(5):714–22.
- Westgard JO. Statistical quality control procedures. *Clin Lab Med*. 2013;33(1):111–24.
- Nevalainen D, Berte L, Kraft C, Leigh E, Picaso L, Morgan T. Evaluating laboratory performance on quality indicators with the six sigma scale. *Arch Pathol Lab Med*. 2000;124(4):516–9.
- Jones GR. Reevaluation of the power of error detection of Westgard multirules. *Clin Chem*. 2004;50(4):762–4.
- Eggert AA, Westgard JO, Barry PL, Emmerich KA. Implementation of a multirule, multistage quality control program in a clinical laboratory computer system. *J Med Syst*. 1987;11(6):391–411.
- Lunetzky ES, Cembrowski GS. Performance characteristics of Bull’s multirule algorithm for the quality control of multichannel hematology analyzers. *Am J Clin Pathol*. 1987;88(5):634–8.
- Menendez GR, Cabrera CO. Selection of an optimal combination of decision criteria for the internal quality control in an automatic analyzer. *Clin Chim Acta*. 2000;292(1–2):139–47.
- Coskun A. Westgard multirule for calculated laboratory tests. *Clin Chem Lab Med*. 2006;44(10):1183–7.
- Westgard JO. Internal quality control: planning and implementation strategies. *Ann Clin Biochem*. 2003;40(Pt 6):593–611.
- Fokkens AS, Wiegersma PA, Reijneveld SA. A structured registration program can be validly used for quality assessment in general practice. *BMC Health Serv Res*. 2009;9:241.