ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MODIFICATION OF QUALITY CONTROL PROGRAM USING SIX SIGMA METRICS FOR EFFECTIVE ANALYTICAL PERFORMANCE

Biochemistry

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ABSTRACT

Majority of important clinical decisions are based on laboratory test results. It is thus of utmost importance that labs adopt stringent quality control measures to ensure accuracy and precision. The aim of the study was to evaluate the performance of the analytical phase of the lab by sigma metrics and use the results for modification of quality control procedure. Sigma metric analysis was done for clinical chemistry analytes, using coefficient of variation and bias from the internal and external quality control data respectively. The minimum acceptable performance was considered at 3 sigma level. Excellent performance was noted for uric acid with sigma > 6, problem analytes were urea, creatinine, sodium and potassium, while most of the other analytes showed good performance with sigma value between 3 and 6. Sigma metric analysis helps design a protocol for internal quality control, address poor performance and assess the efficiency of existing lab processes.

KEYWORDS

Quality Control, Six Sigma Metrics, Analytical Performance

INTRODUCTION

Clinical lab results are important to diagnose and manage diseases. To produce reliable results labs adopt the best quality assurance programs, inspite of which errors occasionally do occur.[1] Even though the frequency of errors are less in the analytical phase, strict monitoring of quality control is required to produce accurate results.[2] For this, running internal and external quality control alone is not enough, and an efficient approach is required to evaluate the quality control indicators.[3]

Sigma is a metric that quantifies the performance of a process as a rate of defects-per-million opportunities. It identifies the errors in quality indicators of the process and provides rectification of errors on the basis of results. [4]The six sigma scale runs from 0 to 6 with the best performers having a scale of 6. [5] Thus with the help of six sigma metrics it is possible to assess the analytical performance and formulate quality control procedure accordingly with the number of quality controls that is needed to ensure that the desired quality is achieved.[4]

The aim of the study was to evaluate the performance of the analytical phase of the lab by sigma metrics and use the results to identify the gaps and need for modification in the strategy of lab quality control procedure.

MATERIAL AND METHODS

This study was conducted in an advanced clinical chemistry lab of a tertiary care hospital in north India over a period of 6 months. Sigma metric was calculated for the evaluation of analytical quality control process of the lab.

The inclusion criteria for the analytes in the calculation of sigma metrics was all those analytes that were analyzed on the same equipment, run with the same lot of internal quality control material and undertook the external quality control program throughout the study period. On this basis Na, K, urea, creatinine, glucose, total bilirubin, AST, ALT, ALP, total protein, albumin, uric acid, cholesterol, triglycerides, HDL cholesterol, amylase, iron and Mg were included in the study.

The quality control program followed by the lab during the study period was as follows:

Internal quality control: As a routine practice 02 levels of internal quality control (normal and pathological) were run twice daily for all the parameters. Westgard rule 1_{2s} was taken as warning and 1_{3s}, 2_{2s}, R_{4s}, 4_{1s} and 10_{x} were considered as rejection for the respective run.

External Quality Control:

The lab participated in the external quality control program External Quality Assurance Scheme (EQAS) provided by CMC, Vellore during the study period. The lab and peer group results of the external quality control program were used to calculate the sigma metrics.

Sigma metric analysis was done using the coefficient of variation (CV %) and bias, calculated from internal and external quality control data respectively during the study period. [7] For each level of control, %CV was calculated from mean and standard deviation (SD) of the internal quality control data. %CV= SD/Mean x100. Bias was calculated from the data of the external quality control records. Bias%= (Lab EQAS result-Peer group mean/Peer group mean) X100. The sigma metric was calculated for each analyte by Sigma= TEa-Bias/%CV where TEa is the total allowable error of the analyte taken from the Clinical Lab Improvement Act (CLIA) guidelines. [4]

QC procedure was assessed on the sigma metric scale. The minimum acceptable performance of process was considered at 3 sigma level.[6] Performance of tests was grouped according to sigma value and quality control strategy was planned to be devised accordingly.[7]

> 6 Sigma (excellent performance): 1 level of quality control run per day (alternating levels between days) with 1_{3s} rejection rule

4-6 Sigma (suited for purpose): 2 levels of quality control runs per day with 1_{2s}rejection rule

3-4 Sigma (poor performance): 2 levels of quality control run two times a day with multiple Westgard rejection rules (1_{3s}, 2_{2s}, $R4_{s}$, 4_{1s})

Prediction of performance of quality control procedure was done by plotting the normalized method decision chart available from the Westgard website at www.westgard.com. The charts are used to judge performance on the basis of location of the operating point.

RESULTS

Sigma metrics was calculated for the analytical performance of Na, K, Urea Creatinine, Glucose, Total Bilirubin, AST, ALT, ALP, TSP, Albumin, Uric acid, Cholesterol, TG, HDL, Amylase, Iron and Mg, in an advanced clinical chemistry lab over a period of six months.

The internal quality control data during the study period was used to calculate the %CV of normal and pathological control levels, while the external quality control data was used to calculate the bias as shown in Table 1. Sigma values for each parameter for both the levels of controls were calculated using the TEa, %CV and %Bias. (Table 1)

Sigma guidelines were used to categorize the parameters based on their analytical performance. Uric acid showed a performance of ≥6 sigma level, thirteen parameters (ALP, albumin, HDL cholesterol, cholesterol, amylase, magnesium, glucose, total bilirubin, AST, ALT, total protein, cholesterol, triglycerides, iron) showed acceptable performance of 3-6 sigma levels while four parameters (Na, K, urea, creatinine) showed a poor performance of < 3 sigma level.

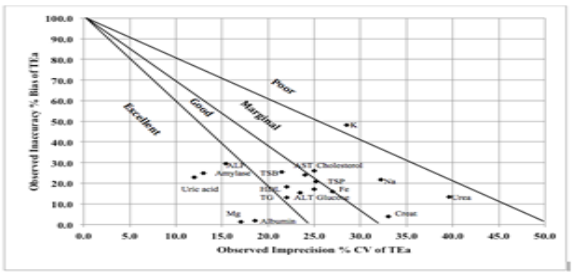
Figure 1 shows the normalized method decision chart for the normal and pathological control, showing visual inspection of excellent, marginal, good, poor and unacceptable performance of analytes.

Table 1: % CV Of Clinical Chemistry Analytes At Normal And Pathological Control Level.

Analytes	Normal Control			Pathological Control		
	Mean	SD	%CV	Mean	SD	%CV
Sodium	143.2	2.3	1.6	157.6	2.9	1.8
Potassium	4.1	0.07	1.7	6	0.1	1.3
Urea	44.9	1.6	3.6	114	3.5	3.1
Creatinine	1.5	0.07	5.0	3.9	0.2	4.9
Glucose	110.2	2.8	2.5	266.8	7.2	2.7
Totalbilirubin	1.39	0.1	4.3	4.3	0.2	4.9
AST	35.1	1.7	4.8	140.4	6.6	4.7
ALT	35	1.6	4.7	113.4	5.8	5.1
ALP	122.1	5.6	4.6	203.2	7.7	3.8
Totalprotein	5.8	0.1	2.5	4.4	0.1	2.2
Albumin	4.3	0.1	1.9	3	0.1	2.3
Uricacid	4.9	0.1	2.0	9.2	0.2	2.2
Cholesterol	156.9	4.0	2.5	264.9	6.9	2.6
Triglyceride	90.1	5.0	5.5	227.9	15.5	6.8
HDL	44.7	3.0	6.6	58.2	3.1	5.4
Amylase	85.6	3.3	3.8	263	10.2	3.9
Iron	101.4	5.5	5.4	197.3	9.0	4.6
Magnesium	2.1	0.1	4.3	3.8	0.2	5.0

Table 2: Percentage Of TEa, Bias And Sigma Metric Of Clinical Chemistry Analytes

Analytes	%Bias	%TEa	Sigma Metric	
			NormalControl	Patho Control
Sodium	1.1	5	2.4	2.1
Potassium	2.9	6	1.8	2.3
Urea	1.2	9	2.2	2.5
Creatinine	0.6	15	2.9	3.0
Glucose	1.7	10	3.3	3.1
Totalbilirubin	5.1	20	3.4	3.0
AST	4.8	20	3.2	3.2
ALT	3.1	20	3.6	3.3
ALP	8.9	30	4.6	5.5
Totalprotein	2.1	10	3.1	3.7
Albumin	0.2	10	5.3	4.2
Uricacid	3.9	17	6.4	6.0
Cholesterol	2.0	10	3.1	3.1
Triglyceride	3.3	25	3.9	3.2
HDL	5.5	30	3.7	4.6
Amylase	7.5	30	5.9	5.8
Iron	3.2	20	3.1	3.7
Magnesium	0.3	25	5.8	5.0



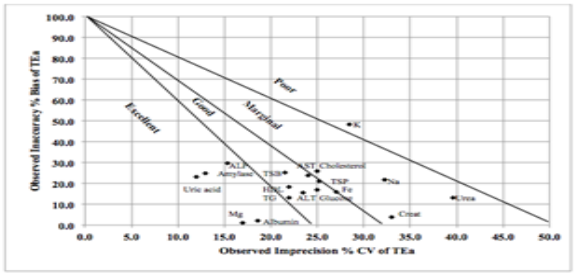


Figure 1 : Normalized Method Decision Chart For The Normal And Pathological Control

DISCUSSION

Good lab practice requires that labs design their quality control procedures to assure that reported patient results meet the quality required for the intended use. The purpose of quality control is to monitor the accuracy and precision of the analytical process and detect errors in an attempt to maintain reliability of the tests for patient care.[8]

Several statistical process control rules have been proposed by Dr James Westgard that are used to assay quality control performance, some detect random errors and others detect systematic errors.[9,10] However, one shoe fits all strategy can not be applied here, as there is no particular set of rules that is right for all the tests and methods as some methods have better precision than others and hence rules need to be selected as per the quality required and the observed performance for the tests. Most labs design the quality control protocol for the number of times and number of levels of internal quality control as per National Accreditation Board for Testing & Calibration Laboratories (NABL) protocols. However, again good lab practice requires every individual lab to design a customized individualized quality control program, which can be based on sigma values obtained from sigma metric analysis.[11]

Sigma metrics analysis is used to measure the performance of a process and identifies the errors within it.[12] Application of six sigma principles provides a scientific basis for designing an appropriate quality control strategy for improving the quality control process. It begins with specifying the quality requirements for the test ie the TEa; scrutinizing the internal and external quality control data and calculating a six sigma value (sigma= [TEa-Bias]/CV), recuperating the process based on the results of the analysis; and formulating a corrective quality control procedure wherever required.[12] Sigma value is considered as a good indicator of performance characteristics of the test in question, as it considers both bias and imprecision, which refer to the systematic error of the assay and the analytical CV of the method respectively.

Attainment of six sigma is thus envisaged as the gold standard for defining highest measure of quality, while functioning at 3-sigma level is regarded as the minimum acceptable level of quality in labs.[13] When the method sigma is more than 6, stringent internal quality control rules need not be adopted. In such cases, false rejections can be minimized by relaxing the control limits to 3s. A method below 3 sigma calls for the adoption of a newer and better method as quality of the test cannot be assured even after repeated QC runs.

In this study, sigma value was found more than 6 at both levels of quality control for uric acid. Westgard rules suggest that no rigorous procedure is needed for the quality control of such analytes with

sigma value of more than 6, and would require only a single rejection rule of 1_{3s} with control measurements of only one level once a day.[7]

The sigma levels of 4-6 were found for ALP, albumin, HDL cholesterol, amylase, magnesium and as per the sigma guidelines, the performance was found to be good. The quality control procedure for these parameters would be to run two levels of quality control once a day. [7] The sigma level for glucose, total bilirubin, AST, ALT, total protein, cholesterol, triglycerides and iron was found to be 3-4 and this would need a more extensive quality control plan with two levels of quality control twice a day and more stringent rejection rules like 1_{3s}, 2_{2s}, $R4_s$ and 4_{1s}.[7]

Although day to day quality control for urea, creatinine, sodium and potassium was always found to be within range, but was not so on sigma scale, warranting a root cause analysis on the same along with extensive quality control plans with multiple westgard rules. For these analytes revision in the daily workload division is also recommended by Westgard sigma rules ie a change in the frequency of daily runs. Number of runs need to be increased to four hourly batches instead of three. In addition 4 control measurements of each level are required in each run.[7]

Sigma metric analysis of quality control procedure for analytes has been documented by many labs, but can not be compared amongst different clinical labs as assay methodologies, precision, equipment, accuracy and QC procedures vary among different labs. [14-17]

Before the study, a single quality control procedure was being used with the same quality control rejection protocols for all analytes. However, findings from the study suggest that different analytes require focused quality control procedures ie choice of rejection rules, frequency of runs and quality control measurements, for effective and improved quality control. Customized quality control protocols will help to minimize the unnecessary quality control monitoring, hence reduce the cost for analytes with high sigma metric result on one hand and help improve the quality control of low sigma value analytes on the other hand. Labs with high sigma metric performance have been able to reduce their use of controls, reduce the number and percentage of outliers, reduce their troubleshooting, reduce recalibration, reduce even their consumption of reagent and material. [18-20]

Thus, using total allowable error, labs can calculate their sigma metrics and use tools like the method decision charts to implement changes in their consumption of control materials, reagent and calibrators, in the interpretation of control rules and in the frequency of running controls.

LIMITATIONS

One limitation of the present study was the use of commercially available controls for calculation of bias and CV, instead of reference method and material due to financial constraints. Another limitation is that, the revised sigma metric analysis has not been calculated after the modified QC procedure and frequency of runs of controls for low sigma value analytes. A result comparison of the two studies could demonstrate the reduced error rate and improved performance.

CONCLUSIONS

The need for improving the quality of the healthcare services to near zero has become the need of the hour. Clinical labs are in a constant search of methods to solve analytical problem and decrease errors to a negligible error. At the same time it is equally important to lay importance on optimal utilization of resources. Labs have to balance between decrease error, improve quality and at the same time decrease cost. This can be done by devising a QC procedure for each lab, based on the six sigma metrics. It can be used to choose an optimal westgard rule and thus can improve the reliability of the results of the diagnostic tests.

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