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International Journal of Clinical Biochemistry and Research

Journal homepage: https://www.ijcbr.in/

Original Research Article

Effectiveness of six sigma score analysis of clinical biochemistry parameters in a newly installed automated analyser– Retrospective analysis in a tertiary cancer care centre

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ARTICLE INFO

Article history:
Received 16-02-2023
Accepted 27-03-2023
Available online 05-04-2023

Keywords:
Quality assurance
Bias
Six sigma

ABSTRACT

Background: Quality assurance is need of the hour in a laboratory. Clinician's decision regarding treatment modality is based on the laboratory results on most occasions. So to ensure accuracy of results reported periodic evaluation as per standard criteria and audit is necessary. Six sigma is one such tool to apply in day to day practice for monitoring and enhancing performance of a laboratory. A new machine is a new challenge for a laboratory from validation to reporting of quality result with assurance for which six sigma is invariably a necessary method. So this study was taken up to check for month wise status of six sigma and performance of clinical chemistry analyser for 20 different analytes.

Materials and Methods: It was a retrospective study and data required for the study were collected from March 2020 to November 2020 in clinical biochemistry laboratory of Tata Medical Centre Kolkata, West Bengal. Test parameters were analysed on Vitros 7600 automated analyser. Data collected were IQC-coefficient of variation percent (CV %) and proficiency test -Bias%. Six sigma score were analysed monthly using standard formula applicable.

Result: We obtained an excellent performance (> 6 sigma) for test parameters CK, Urea, Creatinine, Uric acid, albumin, Calcium, Phosphorus, Magnesium, AST, ALTV, ALKP, GGT, Lipase, LDH in both level of IQC and for sodium and amylase in level 2 IQC. However we noticed poor performance (<3 sigma) for test parameters Glucose, potassium, chloride, TP in both level IQC and for sodium and amylase in level 2 IQC.QGI score analysed to find out root cause and corrective action.

Conclusion: Monitoring IQC and EQAS with six sigma method helps evaluation and improvement of performance of a laboratory even with a new machine. It supports root cause analysis and necessary corrective and preventive action.

1. Introduction

Six sigma is a process of quality measurement and improvement program developed by Motorola in the early 1980s. Sigma methodology can be applied wherever an outcome of a process is be measured. A poor outcome is counted as an error or defect. This is quantified as defects per million (DPM). Six sigma provides a more quantitative frame work for evaluating process performance with evidence for process improvement and describes how many sigma fit within the tolerance limits.[1] Quality is assessed on the sigma scale with a criterion of 3 σ as the minimum allowable sigma for routine performance and a sigma of 6 being the goal for world-class quality.[2] In 2001, David Nevelainen did a first study which bench marked the laboratory quality in six sigma scale.[3]

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https://doi.org/10.18231/j.ijcbr.2023.013

Six sigma is a powerful tool which can be used by laboratories for assessing the method quality, optimizing QC procedure, change the number of rules applied, number of controls run and change the frequency of QC run. Even to assess the quality of instrument sigma metrics can be effectively used.

Clinical laboratories are now the major pillars of diagnostic testing across all healthcare specialities. It is not feasible for the clinicians to diagnose, prognosticate, initiate appropriate interventions, and make future predictions without the valuable inputs from these laboratories.

The laboratory represents a small percentage of medical costs, but it leverages 60-70% of all major clinical decisions including critical ones. The most important costs to consider in the laboratory are related to total episode of care and the effects of unnecessary or inappropriate testing on subsequent procedures.[4]

Quality control in medical laboratory is a statistical or non-statistical process to monitor and evaluate the analytical process. Quality control results are used to validate whether the system is working properly within the pre-defined conditions and whether the patients' tests results are reliable or not. There are two types of assessment for quality in laboratory viz. internal quality control (IQC) and Proficiency testing. IQC ensures continuous monitoring of the analytical system, so as to check whether the results are reliable enough to be released for clinical decision-making. Levey Jennings chart and Westgard's rules are applied on daily quality control data to evaluate reliability.

"The main objective of internal quality control is to ensure day to day consistency." as per WHO 1981 guidelines.[5]

Proficiency testing involves analyzing and reporting of control samples supplied by an external agency, at a predefined time interval usually being one month for Clinical biochemistry parameters. Proficiency test is interpreted by either Z-score or standard deviation index.

To calculate the sigma level of a laboratory, we have to determine the errors or defects first and then measure the performance process. Coskun et al. have found that if we do not measure, we do not know, and if we do not know, we cannot manage. So Six Sigma helps us how to measure and, consequently, how to manage the laboratory.[6]

In resource-poor settings, it becomes imperative to implement measures that avoid wastage while maintaining the desired level of quality. Hence, practising the use of sigma metric to design quality control can prove useful.

Cooper et al.[7] suggested the use of sigma to decide quality control frequency. They suggested that the tests should be divided into three groups as follows:

1. >6σ (excellent tests)—evaluate with one QC per day (alternating levels between days) and a 1:3.5 s rule.
2. 4σ–6σ (suited for purpose)—evaluate with two levels of QC per day and the 1:2.5 s rule.
3. 3σ–4σ (poor performers)—use a combination of rules with two levels of QC twice per day.
4. <3σ (problems)— maximum QC, three levels, three times a day.

Through sigma metrics, it is easy to identify high-risk and low risk test methods.[8]

Irrespective of process, sigma metrics covers the five universal steps that includes 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 defects per million (DPM) or percentage errors. In clinical laboratories, 3 sigma is the arbitrary value on the sigma scale considered acceptable for process performance. Any laboratory process with the sigma value of 3 is expected to produce 6.7% clinically unacceptable outcomes.[10]

The aim of our study was to evaluate the month wise performance of individual parameters of clinical biochemistry by calculating the sigma metrics for each parameter unlike most of the studies done till date which are concerned with overall six sigma assessment for a certain duration like months or years.

2. Materials and Methods

This was a retrospective study, and data required for the study were collected from March 2020 to November 2020 in clinical biochemistry laboratory of Tata Medical Centre Kolkata, West Bengal. The data was collected after the new vitros7600 machine validation was done after installation. Data collected were IQC-coefficient of variation percent (CV %) and proficiency test -Bias%.

2.1. Inclusion criteria

IQC data of two levels that were accepted for analytical run in the laboratory from March to November 2020 without any reagent and/or quality control lot change during the period were included in the study.

2.2. Exclusion criteria

Any data point that have been rejected or excluded by the laboratory owing to flagged with errors during QC run, gross mistakes while preparing QC (pipetting errors, wrong lot number) that were not accepted for analytical runs, QC runs just before or at the time of equipment breakdown, and multirule criteria applied for QC run were excluded from the study.

Altogether twenty parameters were included viz. glucose, urea, creatinine, sodium, potassium, chloride, calcium, phosphorus, magnesium, alkaline phosphatase, aspartate transaminase, alanine transaminase, gamma glutamyl transferase, lipase, amylase, uric acid, total

protein, albumin, lactate dehydrogenase and creatine kinase . Mean, standard deviation (SD), and coefficient of variance (CV) were calculated for each month for both levels.

For internal quality control program, two levels (low, QC1 and high QC2) of control material (BioRad) are being used in each run of 12 hours. Westgard rules are applied daily for the interpretation of quality control results. Westgard rules of 1_{3s}, 2_{2s}, R_{4s}, 4_{1s} and 10_{x} are considered as rejection and 1_{2s} as warning sign for the respective run. Laboratory is participating monthly in the proficiency testing survey of BioRad along with monthly proficiency test with lyophilized sample obtained from Christian Medical College, Vellore. The results obtained from internal quality control and proficiency testing scheme, were used to calculate the sigma metrics in the present study. Laboratory and peer group mean result of analyte's were retrieved from monthly proficiency test program records.

This study was done to assess the performance of 20 biochemical parameters run on VITROS 7600 fully automated biochemistry analyzer on a Sigma Scale by calculating the sigma metrics for each parameter every month. Sigma metrics was calculated with the formula:

Sigma metric= {(TEa − Bias)/CV} x 100

Where, TEa denotes total allowable error. Bias and CV indicates systematic and random errors, respectively.

TE_a values of various parameters are taken from the Clinical Laboratory Improvement Amendment (CLIA) - 88 Proficiency Testing Criteria in terms of total allowable error "TE_a" (or more correctly "total allowable variation") for acceptable performance for each analyte.[11]

Bias percentage for each parameter was calculated from the commercially available proficiency testing system using the formula

Bias %= (Lab mean – Peer group mean) x 100 / Peer group mean

CV percentage was determined from the calculated laboratory mean and calculated standard deviation obtained from the internal QC data over the period of 9 months:

CV% = Standard deviation x 100 / Laboratory mean

The quality goal index (QGI) ratio represents the relative extent to which both bias and precision meet their respective quality goals.[12] It was used to analyze the reason for the lower sigma in analytes, i.e., the problem is due to imprecision or inaccuracy or both. The QGI ratio is calculated using the formula given below.

QGI = Bias/1.5 × CV%.

For analytes which fall short of Six Sigma quality, a QGI score of <0.8 indicates imprecision, QGI >1.2 indicates inaccuracy, and QGI score 0.8-1.2 suggestive of both imprecision and inaccuracy.

3. Results

Cause of the low sigma score obtained is analysed for each month individually and each level separately using QGI score Table 3.

4. Discussion

Six sigma is a powerful tool which can be used in various areas of quality assurance in a medical Biochemistry laboratory. Importantly, sigma metrics are an important self-assessment tool to guide QC strategy design. It helps to improve the process of quality by removing defects.

We have analysed 20 analytes on sigma metrics. In this study, performance for CK, Urea, Creat, Uric acid, albumin, Ca, Phos, Mg, AST, ALTV, ALKP, GGT, LDH, Lipase are varying from world-class quality to acceptable sigma metrics for both level 1 and 2 over 9 months analysis; the exception being amylase which in level 1 showed a low sigma score owing to imprecission in the month of June.

Analytes with low sigma scores are glucose, sodium, potassium, chloride, amylase and total protein with sigma score less than 3.0 in our analysis. Imprecission as well as inaccuracy were found as the major causes as shown in Table 3.

In this study potassium found to be poor performer for five of the nine months analysis in level 1 and three of the nine months analysis in level 2 cause of which found to be inaccuracy on most occasions along with imprecision. On root cause analysis fluctuations in the electrolyte qality control results more specifically for potassium repeatedly found to be due to contamination or deterioration of the reference electrode. So we rectified the issue by changing the reference fluid and performing electrode maintenance more often. Similar studies done by Aggarwal K et al[13] found six sigma score to be lowest for potassium. So stringent monitoring of electrolyte reporting in laboratory is very vital for patient's being monitored for electrolyte disturbances for which six sigma assessment plays a vital role.

As a practice, for parameters showing lower sigma values, root cause analysis is done and corrective action taken to reduce the occurrence of defects in measurement in future.

There are certain limitations in the sigma metrics system too because we have observed no issues in the CV % and bias % of potassium in both levels of internal quality control but sigma is showing a lesser value.

A systematic approach is needed to reliably detect clinically significant analytic errors that are beyond allowable inherent errors. This justifies the main objective of the sigma metrics analysis; first, to detect the errors that are more than allowed and then to minimize the identified defects.[14–16]

Selection of appropriate QC procedures for detecting errors can help to improve test methods. However, it would be a good practice to choose a test method with a six sigma performance to avoid wastage in repeating tests and troubleshooting and to reduce the cost of quality control.

Table 1: Showing six sigma metrics for 20 biochemical parameters for level 1 and 2 internal quality control (parameter having less than 3 sigma score even in one level are highlighted

S. No.	Parameter		Mar 2020	Apr 2020	May 2020	Jun 2020	Jul 2020	Aug 2020	Sep 2020	Oct 2020	Nov 2020
1	Glucose	L1	3.8	5.5	9.7	8.3	9.7	**2.4**	**2**	7.3	7.3
		L2	6.7	6.4	10.8	9.1	9.7	**2.2**	**4.9**	6	5.3
2	Sodium	L1	**2.9**	6.2	4.4	4.6	3.9	4.4	4	7.5	5.8
		L2	3.8	5.4	5.2	4	3.9	4.9	4.5	5.6	5.8
3	Potassium	L1	**1.1**	**1.7**	**2.9**	**2.6**	3.3	4.3	**2.3**	5.5	5.3
		L2	**1.6**	**2.1**	3.3	3.3	3.3	4.3	**2.9**	4.9	5.3
4	Chloride	L1	3.3	4.4	3.4	4.4	1.7	3.6	4.2	6.8	5.1
		L2	5.5	4.4	**2.1**	3.9	1.7	3.9	4.5	5.3	3.3
5	Creatine Kinase	L1	5.7	6.3	6.9	5.9	7.3	5.7	4.8	8.3	7.1
		L2	5.9	6.4	6.7	6.9	8.7	6.8	6.4	7.9	104
6	Urea	L1	3.8	4.4	5.1	10.5	9.4	3.3	7.2	6.3	7.8
		L2	8.9	8.3	8.8	6.3	5.6	4.1	11	12.6	13.8
7	Creatinine	L1	4.9	4.2	10	6.7	8.9	4.33	7.7	4.7	6.9
		L2	10.2	10.2	9.3	9.3	7.0	4.1	6.4	6.7	5.4
8	Uric	L1	10.6	17.2	21.1	16.8	15	6.4	11.2	12.8	14.6
		L2	13.5	11.0	16.9	16.8	16.7	6.8	9.9	12.8	12.1
9	TP	L1	4.9	3.8	4.6	5.9	6.1	4.4	8.9	7.6	**2.6**
		L2	3.8	5.4	5.8	7.4	4.9	4.9	6.9	7.6	**2.4**
10	ALB	L1	6.4	3.3	3.3	6.8	6.2	4.5	6.1	4.3	4.1
		L2	10.7	3.8	5.5	7.4	6.2	5.6	7.6	5.2	5.0
11	Calcium	L1	9.2	5.7	7.8	10.7	12.6	7.97	7.5	9.6	10.5
		L2	8.7	5.0	6.3	9.6	9.1	5.7	5.2	6.9	10.5
12	PHOS	L1	7.7	7.1	4.3	8.7	8.9	8.0	10.6	7.4	4.4
		L2	8.4	6.3	4.3	6.7	6.4	5.7	5.3	5.8	5.1
13	Mg	L1	7.6	10.7	11.9	10.1	12.2	10.3	11	9.9	8.9
		L2	11.8	10.7	13.3	13.9	13.7	12.4	11	11.5	12.2
14	AST	L1	10.2	10.6	8.3	12.3	9.4	11.7	8.6	12.3	11.2
		L2	9.6	8.9	7.2	7.4	7.7	10.4	8.2	9.9	9.6
15	ALTV	L1	3.1	6.4	9.9	7.1	5.8	4.9	5.1	6.9	5.4
		L2	6.5	7.0	11.7	11.1	8.2	6.2	6.3	12.0	12.1
16	ALKP	L1	7.2	6.1	6.5	4.9	13.2	5.3	16.2	11.2	5.02
		L2	9.8	6.5	6.5	7.1	12.6	7.9	17.1	12.7	7.4
17	GGT	L1	10.7	11.6	12.6	8.1	11.2	6.5	19.1	16.6	10.8
		L2	21.4	17.9	25.1	20.3	23.8	17.9	19.1	26.1	13.1
18	LDH	L1	7.2	6.8	4.7	5.5	5.6	5.4	6.6	7.3	6.9
		L2	10.1	8.0	6.1	9.4	8.3	9.4	7.9	11.4	11.1
19	Amylase	L1	3.7	3.3	4.3	**2.8**	4.8	3.5	**1.6**	5	4.4
		L2	15.8	12.8	10.6	10.7	11.1	12.4	4	10.9	13
20	Lipase	L1	8.6	12.1	8.6	9.7	10.6	8.9	12.3	11.9	8.3
		L2	18.1	10.1	10.4	9.7	12.9	11.5	15.4	13.8	18.2

Table 2: Performance of the analytes on sigma metrics over 9 months retrospective analysis

Six sigma level	Level 1	Level 2
Acceptable six sigma score above 3	CK, Urea, Creat, Uric acid, albumin, Ca, Phos, Mg, AST, ALTV, ALKP, GGT, Lipase, LDH	Sodium, CK, Urea, Creat, Uric acid, albumin, Ca, Phos, Mg, AST, ALTV, ALKP, GGT, Lipase, LDH, Amylase
Below 3 sigma	Glucose, sodium, potassium, chloride, amylase, TP	Glucose, Potassium, TP, Chloride

Table 3: QGI score of problem analytes (i.e those with sigma metric score <3 in level 1 and 2 analysed on month of low score) with cause

		March	April	May	Jun	Jul	Aug	Sep	Oct	Nov
Glucose	L1	N/A	N/A	N/A	N/A	N/A	N/A	**QGI=2.2 inaccuracy**	N/A	N/A
	L2	N/A	N/A	N/A	N/A	N/A	**QGI=3.3 inaccuracy**	N/A	N/A	N/A
Sodium	L1	**QGI=2.3 Inaccuracy**	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	L2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Potassium	L1	**QGI=1.6 inaccuracy**	**QGI=2.2 imprecission and inaccuracy both**	**QGI=2.3 imprecission and inaccuracy both**	**QGI=0.7 imprecission**	N/A	N/A	**QGI=1.7 inaccuracy**	N/A	N/A
	L2	**QGI=2.3 inaccuracy**	**QGI=2.8 inaccuracy**	N/A	N/A	N/A	N/A	**QGI=1.8 inaccuracy**	N/A	N/A
Chloride	L1	N/A	N/A	N/A	N/A	**QGI=2.2 inaccuracy**	N/A	N/A	N/A	N/A
	L2	N/A	N/A	**QGI=2.5 inaccuracy**	N/A	**QGI=2.2 inaccuracy**	N/A	N/A	N/A	N/A
TP	L1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	**QGI=2.2 inaccuracy**
	L2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	**QGI=1.2 inaccuracy and imprecission both**
Amylase	L1	N/A	N/A	N/A	**QGI=0.1 imprecission**	N/A	N/A	**QGI=2.6 inaccuracy**	N/A	N/A
	L2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Laboratories must also try to control precision through proper training of laboratory technologist, instrument maintenance, etc. [17]

There is still a wide scope of improvement in the quality of laboratory processes, and there is an utmost need to follow the right strategies for doing so to avoid wastage and delivery of wrong results. [18]

5. Conclusion

The concept of implementing six sigma to assess the quality of laboratory reporting in itself is a novel process which is helpful in the healthcare sector for the long term benefit of patient care provided in integrity with clinical and nonclinical departments together. On the basis of sigma metrics and quality goal index, it may be concluded that the clinical biochemistry laboratory taken for this study is able to achieve quality results required as per six sigma methodology and hence six sigma is a useful tool to assess performance of clinical chemistry parameters if implemented for overall improvement of performance of laboratory along with added advantage of validating the efficacy of a newly installed machine. The data collected by us represents month wise performance which is advantageous in the sense corrective action can be implemented for improving performance on the same go while dispatching patient reports with accuracy which may otherwise vary time to time due to lot changes, machine maintenance and alteration of instrument handling technologist. So it can be said that periodic evaluation is must to assess laboratory performance through six sigma.

6. Declaration of Authors

1. Conception and design, acquisition of data, or analysis and interpretation of data has been done by the 1^{st} author
2. Drafting the article and revising it critically for important intellectual content done by the 2^{nd} author
3. Final scrutiny of the article being done by 1^{st} author as supervised by Prof Dr.Kalyan Goswami for necessary correction.
4. The final approval of the version to be published has been given by all the authors. Each contributor has participated sufficiently in the work to be allowed to take public responsibility for suitable portions of the content.

7. Source of Funding

None.

8. Conflict of Interest

None.

Acknowledgments

The authors would like to thank the technical manager Mr. Ranjan Bhattacharya and associate scientific officer Mr. S Sugumar for their technical help and valuable inputs provided time to time .Authors would like to thank Prof. Dr. Kalyan Goswami, H.O.D. Deptt. of Biochemistry, AIIMS, Kalyani for supervising the manuscript.

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Cite this article: Sarma N, Chakraborty S. Effectiveness of six sigma score analysis of clinical biochemistry parameters in a newly installed automated analyser– Retrospective analysis in a tertiary cancer care centre. *Int J Clin Biochem Res* 2023;10(1):81-86.