ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Sigma metrics application in clinical biochemistry: Practical requisite or unfeasible misadventure

Debojyoti Bhattacharjee[1], Bithika Ghosh[2], Arghya Ray Chaudhuri[3], Sebanti Chakrabarty[4], Sourav Naskar[5], Kheya Mukherjee[6]

[1]Professor and Head, [4]Senior Resident, [5]Postgraduate Trainee, Department of Biochemistry, Bankura Sammilani Medical College and Hospital, Bankura, [2]Assistant Professor, Department of Biochemistry, Burdwan Medical College, Burdwan, [3]Assistant Professor, Department of Biochemistry, Institute of Post Graduate Medical Education and Research, Kolkata, [6]Professor, Department of Microbiology, R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India

Submission: 09-03-2024 Revision: 03-05-2024 Publication: 01-06-2024

ABSTRACT

Background: The application of the Six Sigma (σ) metric in biochemical laboratories is a powerful tool for reducing the occurrence of errors and prioritizing important improvements in laboratory quality control. The National Accreditation Board for Testing and Calibration Laboratories (NABL) is an accreditation body with an accreditation system established in accordance with ISO/IEC 17011, providing specialty- or scope-based certification based on the conformance of quality indices to medical laboratories. In this context, a study has been designed that considers the quality guidelines set by NABL as well as the sigma metric rule in the assessment of analytical performance. **Aims and Objectives:** The aims of this study were to identify the gaps and need for strategy modification for quality improvement by assessing the performance of two NABL-accredited medical testing laboratories on a Sigma metric scale. **Materials and Methods:** A retrospective analytical study was conducted over 6 months (January–June 2021). Internal quality control (IQC) and EQAS data were obtained from third-party QC providers (Bio-Rad, India) and analyzed by calculating sigma (σ) values based on the coefficient of variation, bias, and total error allowable in two NABL-accredited medical testing laboratories. To identify potential problems for analytes with poor sigma values, a quality goal index (QGI) analysis was performed. **Results:** By analyzing the sigma values obtained by both NABL-accredited laboratories, we can see that laboratory 2 performed better than laboratory 1. After calculating the QGI, there was a problem of inaccuracy and imprecision in laboratory 1, and laboratory 2 had QGI values that indicated only imprecision. **Conclusion:** Diagnostic laboratories should incorporate Six Sigma metrics to identify gaps in their performance to ensure better quality control and patient safety.

Key words: External quality control; Internal quality control; National Accreditation Board for Testing and Calibration Laboratories; Quality Management; Quality goal index; Six Sigma

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i6.63624

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Six Sigma is a mathematical approach that targets to improve the work process. Sigma stands for standard deviation (SD), and Six Sigma represents the possible errors of 3.4 defects per million opportunities (DPMO). This statistically indicates deviation from the goal in any process. Since 1999, the Six Sigma method has been in use in maintaining hospital quality management.[1] In the past years, the Six Sigma method has been successfully implemented in various laboratories to assess performance. A sigma value >6 is considered excellent or real-world class quality,[2] while values >3 are considered satisfactory laboratory performance[3-6] (Table 1).

Address for Correspondence:
Dr. Sebanti Chakrabarty, Senior Resident, Department of Biochemistry, Bankura Sammilani Medical College and Hospital, Bankura West Bengal, India. **Mobile:** +91-9476293221. **E-mail:** sebanti.seven@gmail.com

Quality control management in a clinical diagnostic laboratory at the analytical level primarily involves routine performance and assessment of internal quality control (IQC) and external quality control (EQC). For this purpose, participation in quality control programs, preferably as conducted by third-party providers of analytical control materials, is required.

Individual parameter performance is expressed in terms of Westgard rules and Z scores for internal and external quality analyses, respectively. Six Sigma not only integrates IQC and EQC but also identifies existing gaps, thus improving laboratory performance. David Nevalainen, in 2001, first applied the Six Sigma metric in the biochemical laboratory and since then, a toolkit has been created that allows laboratories to apply this powerful approach.[8] With the increasing workload and a wider range of analytes, biochemical laboratories have been struggling in recent years with a constant need to provide accurate and faster reports. Six Sigma metrics allow an effective design to avoid defects and reduce analytical costs with higher quality. In this context, this study aimed to identify the gaps and needs for strategy modification for quality improvement by comparing the performance of two National Accreditation Board for Testing and Calibration Laboratories (NABL)-accredited medical testing laboratories on a sigma metric scale.

Aims and objectives

To identify the gaps and need to strategy modification for quality improvement by assessing the performance of two NABL accredited medical testing laboratories on a Sigma metric scale.

MATERIALS AND METHODS

A retrospective analytical study was designed with data from 6 months (January–June 2021). The study was done in the Department of Biochemistry, IPGME&R, Kolkata. IQC and EQAS were obtained from a third-party QC material provider (Bio-Rad, India) from two laboratories. Two levels of IQC were run in both laboratories, level 1 was normal control and level 2 was abnormal (high) level control. The instrument in Laboratory 1 was an automated biochemistry analyzer, EM- 360; Transasia India. The instrument in Laboratory 2 was an automated biochemistry analyzer, AU480; Beckman Coulter. The parameters included for comparison were urea, creatinine, glucose, amylase, uric acid, LFT, and lipid profile. The coefficient of variance (CV) was calculated from the IQC of all parameters. CV% is the SD, which is a measure of the variability of an assay expressed as a percentage, as per the equation:

CV%=(SD/mean)×(100).

The percentage bias was calculated using EQC. Bias is the systematic difference between results obtained by the laboratory test method and the results that would be obtained from an accepted reference method. Its expressed as

BIAS%=(designated mean–laboratory Mean)/(designated mean)×100.

CV% signifies the precision of IQC conducted whereas Bias% reflects the trueness of value in relation to EQC performance.

The total allowable error (TEa%) was followed as per clinical Laboratory Improvement Amendment (CLIA) Guidelines.[9] Sigma metrics were calculated using the formula:

Sigma =(TEa%) Bias %)/CV%.

For poor sigma values (below 3), root cause analysis was performed using the quality goal index (QGI). The QGI ratio indicates the extent to which both bias and precision meet their respective quality goals. QGI=Bias/1.5×CV%[5] (Table 2).

Statistical analysis was done using Microsoft Office Excel 2007.

Table 1: The correlations between sigma metric and defects[7]

Sigma value	Errors/defects per million opportunities reports
1 σ	690 000
2 σ	308 000
3 σ	66 800
4 σ	6 210
5 σ	230
6 σ	3.4

RESULTS

The summary of the performance of 16 biochemical parameters from January to June for individual laboratories was expressed in terms of CV% for level 1 (normal control) and level 2 (abnormal control) BIORAD internal controls. Bias% as derived from BIORAD EQAS program, the average bias gradation was done for both laboratories (Table 3).

Table 2: Criteria for interpreting QGI ratio[5]

QGI	Problem
<0.8	Imprecision
0.8–1.2	Imprecision and inaccuracy
>1.2	Inaccuracy

QGI: Quality goal index

Sigma levels (calculated from CV%, Bias%, and TEa%), and QGI for Laboratory 1 and 2 (Tables 4 and 5).

DISCUSSION

Six Sigma was first implemented by Motorola as an error-detection method. It defines the number of sigma which integrates within the tolerance limits.[10] Laboratory errors can be reduced using the concept of Six Sigma, maintaining the sigma value at 6.[11,12] A higher sigma value indicates lower errors, which, in turn, indicates a high level of quality at low cost.[13] This ensures a higher level of achievement of the quality level for client services and satisfaction.[11] After calculating the sigma values, it was observed that for the Level 1 control, results from laboratory 1 (Table 3) parameters such as alanine transaminase (ALT), aspartate transaminase (AST), albumin, amylase, glucose, total cholesterol, and triglyceride achieved values of 3–6 referring to the good performance.

Table 3: Average bias gradation for laboratory 1 and 2

Bias%	Laboratory 1	Laboratory 2
<3	Total protein, AST, amylase, glucose, and uric acid. (n=5)	Total protein, albumin, total bilirubin, AST, amylase, glucose, triglyceride, LDL-C, urea, and uric acid (n=10)
3–6	Albumin, ALT, cholesterol, LDL-C, urea. (n=5)	ALT, cholesterol, HDL-C, and creatinine. (n=4)
>6	Total bilirubin, direct bilirubin, ALP, triglyceride, HDL-C, and creatinine (n=6)	Direct bilirubin and ALP (n=2)

AST: Aspartate transaminase, ALT: Alanine transaminase, LDL-C: Low-density lipoprotein-cholesterol, HDL-C: High-density lipoprotein cholesterol, ALP: Alkaline phosphatase

However, all other parameters, such as total protein, total bilirubin, direct bilirubin, alkaline phosphatase (ALP), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), urea, creatinine, and uric acid, had sigma values <3, indicating poor performance. Similarly, for the level 2 control, >6 sigma values were obtained for uric acid, amylase, AST, and ALT; glucose and bilirubin had values between 3 and 6; and <3 sigma values were observed for total protein, albumin, cholesterol, triglyceride, HDL-c, LDL-c, urea, and creatinine.

Laboratory 2 results (Table 4), level 1, showed that parameters such as total protein, albumin, ALT, ALP, total cholesterol, and low-density lipoprotein cholesterol had good sigma values between 3 and 6. Parameters such as total bilirubin, AST, amylase, glucose, triglyceride, HDL-C, and uric acid had sigma values above six, indicating excellent performance. However, the direct bilirubin, urea, and creatinine levels were <3, indicating poor performance. For the level 2 control, laboratory 2 showed that parameters such as total protein, albumin, ALT, ALP, total cholesterol, LDL-C, D bilirubin, and creatinine had sigma values of 3–6 which means good performance. Only urea had a sigma value of <3. AST, triglyceride, HDL-C, bilirubin, amylase, ALT, and uric acid levels had sigma values above 6. A higher sigma value indicates fewer defects/errors.

In a retrospective study done by Nanda and Ray,[6] ALP performed the best among the parameters, with a sigma metric value of 8.4, and the least sigma metric value of 1.4 was obtained chloride. Zhou et al.,[14] in a 5 months period retrospective study, reported that sigma values of ALT, BUN, and calcium were <3 and T. Bilirubin, TG, CK, and

Table 4: Sigma values and QGI for Laboratory 1

S. No.	Parameter	TEa%	CV%		Bias%	Sigma		QGI	
			L-1	L-2		L-1	L-2	L-1	L-2
1.	Total Protein	10	3.49	2.44	2.76	2.07	2.96	0.53	0.75
2.	Albumin	10	1.36	1.77	5.57	3.26	2.5		2.1
3.	Total bilirubin	20	4.66	2.88	6.14	2.97	4.81	0.87	-
4.	Direct bilirubin	20	5.81	4.26	12.27	1.3	1.81	1.4	1.9
5.	AST	20	4.7	2.59	2.81	3.66	6.64	-	-
6.	ALT	20	3.8	2.07	5.94	3.7	6.79	-	-
7.	Alkaline phosphatase	30	7.8	8.26	11.57	2.36	2.23	0.98	0.93
8.	Amylase	30	7.03	4.61	2.26	3.94	6.01	-	-
9.	Glucose	10	2.19	2.18	0.57	4.31	4.33	-	-
10.	Cholesterol	10	1.96	3.16	3.87	3.13	1.94	-	0.81
11.	Triglyceride	25	2.22	4.05	14.78	4.6	2.52	-	2.4
12.	HDL-C	30	6.9	4.04	18.04	1.73	2.96	1.74	2.9
13.	LDL-C	12	3.21	4.41	4.33	2.38	1.74	0.89	0.65
14.	Urea	9	5.4	3.99	5.16	0.71	0.98	0.64	0.86
15.	Creatinine	15	5.6	2.74	8.56	1.15	2.35	1.02	2.08
16.	Uric acid	17	4.83	2.03	3.71	2.75	6.55	0.51	

AST: Aspartate transaminase, ALT: Alanine transaminase, LDL-C: Low-density lipoprotein-cholesterol, HDL-C: High-density lipoprotein cholesterol, QGI: Quality goal index, CV: Coefficient of variance. *TEa% as per Clinical Laboratory Improvement, and Amendment (CLIA) Guidelines. **TEa% for LDL-C as per National Cholesterol Education Program (NCEP) Guidelines

Table 5: Sigma values and QGI for laboratory 2

S. No.	Parameter	TEa%	CV%		Bias%	Sigma		QGI	
			L-1	L-2		L-1	L-2	L-1	L-2
1.	Total protein	10	2.14	2.02	2.68	3.42	3.62	-	-
2.	Albumin	10	1.79	1.59	1.6	4.69	5.28		-
3.	Total bilirubin	20	2.7	2.35	0.5	7.22	8.29		-
4.	Direct bilirubin	20	5.26	4.02	6.1	2.64	3.46	0.77	-
5.	AST	20	2.61	2.2	1.64	7.03	8.34		-
6.	ALT	20	4.85	3.55	3.46	3.41	4.65		-
7.	Alkaline phosphatase	30	5.98	5.21	6.09	3.99	4.58		-
8.	Amylase	30	2.1	2.31	1.26	13.68	12.44		-
9.	Glucose	10	1.28	1.44	2.06	6.2	5.51		-
10.	Cholesterol	10	1.42	1.7	3.12	4.84	4.05		-
11.	Triglyceride	25	1.7	1.93	0.77	14.25	12.55		-
12.	HDL-C	30	2.75	2.44	4.8	9.16	10.33		-
13.	LDL-C	12	1.55	1.68	2.76	5.96	5.55		-
14.	Urea	9	3.55	3.63	2.46	1.84	1.82	0.46	0.45
15.	Creatinine	15	4.26	2.6	4.75	2.44	3.94	0.74	-
16.	Uric acid	17	1.21	0.94	1.61	12.7	16.37		-

AST: Aspartate transaminase, ALT: Alanine transaminase, LDL-C: Low-density lipoprotein-cholesterol, HDL-C: High-density lipoprotein cholesterol, QGI: Quality goal index, CV: Coefficient of variance. *TEa% as per Clinical Laboratory Improvement Amendment (CLIA) Guidelines, **TEa% for LDL-C as per National Cholesterol Education Program (NCEP) Guidelines

ALP were >6. Various results were obtained from other studies that applied Sig Sigma metrics.[15-17]

We calculated the QGI for analytes that showed a sigma value <3. In laboratory 1, albumin (level 2), D. bilirubin, triglyceride, creatinine and HDL-C had QGI >1.2, indicating inaccuracy; ALP, cholesterol, LDL-C (level 1), and urea (level 2) QGI were between 0.8 and 1.2, which implied imprecision and inaccuracy for total protein, T. bilirubin (level 1), urea (level 1), and LDL-C (level 2), it was <0.8, suggesting imprecision only. In Laboratory 2, only a few analytes showed a sigma <3: Urea, creatinine (level 1), and direct bilirubin (level 2), which had a QGI <0.8 indicating imprecision.

Kumar and Mohan[12] calculated the QGI for analytes whose sigma values were <6; for all analytes, the QGI was <0.8, indicating imprecision, and for cholesterol, it was >1.2, which suggested that the root cause was inaccurate. In a similar study, QGI analysis was done to reflect impressions and inaccuracies in analytes with a sigma value of <4.[18] Thus, by estimating the sigma values obtained by both the NABL-accredited laboratories, we could compare and conclude that for most of the parameters, the performance of laboratory 2 was better than that of laboratory 1. Only a few analytes had a sigma value of <3 in laboratory 2. In addition, after calculating the QGI, there was a problem of inaccuracy and imprecision in laboratory 1, and laboratory 2 had a QGI value <0.8, indicating only imprecision. Another study done in Odisha, India, revealed that while the proficiency testing values were within acceptable limits, some poor performances were detected using Six Sigma metrics.[19]

According to NABL,[20] with regard to the examination process, certain guidelines were laid down to measure the uncertainty of the measured quantity values. The SD and %CV were derived from the laboratory mean; the uncertainty of the measurement was set as %CV. The uncertainty of measurement was: ±1.96×%CV approximated to ±2 %CV. A minimum of 6 months of internal QC data to calculate routine imprecision was recommended, which should be updated annually. To ensure the quality of the examination results and inter-laboratory comparisons, the NABL suggested participating in EQA/PT before gaining accreditation. Participation in an EQA program is necessary if there is a change in the methodology or equipment. The laboratory documents corrective actions based on an EQA evaluation report.

While NABL certification provides assurance and confidence in the results, it does not provide absolute accuracy of the test results. Accuracy is influenced by several factors such as human errors, sample variability, and limitations of the technology employed. Furthermore, accreditation usually covers only certain types of test. In addition, the accreditation process can be costly for smaller laboratories. Hence, by relying only on IQC and EQC, the identification of faults at the grassroots level and the gaps that exist in the quality management framework of a biochemical laboratory cannot be completely ascertained; more stringent and accurate methods should be used. Sigma scale is thus an infallible statistical tool that, when applied, provides the bonhomie between IQC and EQAS and characterizes performance at the parameter-specific level. Its implication is immense, as it can be extended for use in immunoassays and a wide variety of different routine laboratory parameters. The authors, thus, advocate that Six Sigma metrics in laboratories should be implemented for accurate and cost-effective reporting, which would lead to greater patient safety and service providers' satisfaction.

Limitations of the study

The study period was limited to 6 months. Analysis of the performance of the laboratories over a longer period of 1 year would yield more accurate results.

CONCLUSION

It can be concluded by the results of the study that the implementation of Six Sigma metrics in medical laboratories should be done for accurate and cost- effective reporting which would further lead to better quality control and patient safety.

ACKNOWLEGMENT

We are immensely grateful to all the medical technologists for the technical assistance in the compilation of raw data.

REFERENCES

1. Cano EL, Moguerza JM and Redchuk A. Six Sigma with R: Statistical Engineering for Process Improvement. New York: Springer Science and Business Media; 2012.
2. Harry M and Schroeder R. Six Sigma: The Breakthrough Management Strategy Revolutionizing the World's Top Corporations. New York: Currency Press; 2000.
3. Klee George G and Tietz WJ. Textbook of clinical chemistry and molecular diagnostics. In: Burtis AC, Ashwood ER and Brurns DE, editors. Quality Management. 5th ed. Philadelphia, PA: Saunders; 2012. p. 163-204.
4. Nevalainen D, Berte L, Kraft C, Leigh E, Picaso L and Morgan T. Evaluating laboratory performance on quality indicators with the six sigma scale. Arch Pathol Lab Med. 2000;124(4):516-519.
https://doi.org/10.5858/2000-124-0516-ELPOQI
5. Westgard JO and 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):343-354.
6. Nanda SK and Ray L. Quantitative application of sigma metrics in medical biochemistry. J Clin Diagn Res. 2013;7(12):2689-2691.
https://doi.org/10.7860/JCDR/2013/7292.3700
7. Bayat H. Expected long-term defect rate of analytical performance in the medical laboratory: Assured Sigma versus observed sigma. Biochem Med (Zagreb). 2018;28(2):020101.
8. Inal TC, Goruroglu Ozturk O, Kibar F, Cetiner S, Matyar S, Daglioglu G, et al. Lean Six Sigma methodologies improve clinical laboratory efficiency and reduce turnaround time. J Clin Lab Anal. 2018;32(1):e22180.
https://doi.org/10.1002/jcla.22180
9. CLIA Proficiency Testing Criteria. Available from: https://www.westgard.com/clia.htm [Last accessed on 2024 Jan 22].
10. Lakshman M, Reddy BR, Bhulaxmi P, Malathi K, Salma M and Prakasham SE. Evaluation of sigma metrics in a medical biochemistry lab. Int J Biol Med Res. 2015;6(3):164-171.
https://doi.org/10.7439/ijbr
11. Kanani FZ, Haider Kazmi A and Kaleem B. Sigma metrics of Alinity ci system-a study on thirty-nine clinical chemistry and immunoassay parameters. Adv Lab Med. 2021;2(2):267-285.
https://doi.org/10.1515/almed-2021-0001
12. Kumar BV and 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):194-199.
https://doi.org/10.4103/JLP.JLP_102_17
13. Ren A, Wang XY, Cheng PL, Brinc D, Berman MI and Kulasingam V. Analytical evaluation and sigma metrics of 6 next-generation chemistry assays on the Abbott architect system. Clin Chim Acta. 2023;542:117276.
https://doi.org/10.1016/j.cca.2023.117276
14. Zhou B, Wu Y, He H, Li C, Tan L, and Cao Y. Practical application of six sigma management in analytical biochemistry processes in clinical settings. J Clin Lab Dhana/12 [Take Drive] Anal. 2020;34(1):e23126.
https://doi.org/10.1002/jcla.23126
15. Ganji SB and Revupalli S. Evaluation of quality assurance in a new clinical chemistry laboratory by six sigma metrics. J Clin Diagn Res. 2019;13(3):BC04-BC07.
https://doi.org/10.7860/JCDR/2019/40658.12666
16. Medina PA, Matibag J, Datay-Lim SJ and Arcellana-Nuqui E. Pilot study on the evaluation of clinical chemistry laboratory test performance using six sigma metrics. Philipp J Pathol. 2019;4(2):31-36.
https://doi.org/10.21141/PJP.2019.13
17. Gadde R and Venkatappa H. Analysis of biochemical analytes using six sigma metrics with two analyzers at an Indian lab setting. Bioinformation. 2023;19(11):1043-1050.
https://doi.org/10.6026/973206300191043
18. Panda CR, Kumari S, Mangaraj M and Nayak S. The evaluation of the quality performance of biochemical analytes in clinical biochemistry laboratory using six sigma matrices. Cureus. 2023;15(12):e51386.
https://doi.org/10.7759/cureus.51386
19. Pradhan DP, Pandit D, Sahoo S, Rattan R and Mohanty S. Six sigma metrics: An evolving indicator of quality assurance for clinical biochemistry. J Clin Diagn Res. 2022;16(8):BC14-BC18.
https://doi.org/10.7860/JCDR/2022/56691.16718
20. National Accreditation Board for Testing and Calibration Laboratories, NABL India. Available from: https://nabl/india.org/nabl/file_download.php?filename=201905031045/NABL/112/effective/from-01.06.2019-doc.pdf [Last accessed on 2024 Jan 17].

Authors Contributions:
DB- Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, design of the study; **BG-** Concept, design, clinical protocol, manuscript editing, and manuscript revision; **ARC-** Data collection, statistical analysis, and interpretation; **SC-** Manuscript preparation and submission of article; **SN-** Review manuscript; and **KM-** Literature survey and manuscript revision.

Work attributed to:
Institute of Post Graduate Medical Education and Research, Kolkata, West Bengal, India.

Orcid ID:
Debojyoti Bhattacharjee - https://orcid.org/0000-0001-5769-5817
Bithika Ghosh - https://orcid.org/0009-0003-5029-6292
Arghya Ray Chaudhuri - https://orcid.org/0009-0001-5915-5803
Sebanti Chakrabarty - https://orcid.org/0009-0003-7637-966X
Sourav Naskar - https://orcid.org/0009-0008-8160-1209
Kheya Mukherjee- https://orcid.org/0000-0002-3319-7829

Source of Support: Nil, **Conflicts of Interest:** None declared.