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Original Article

Evaluation of Performance of Biochemistry Analytes Using Six Sigma Metrics in Clinical Laboratory of Nobel Medical College Teaching Hospital

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Abstract

Background

Six sigma metrics is a tool used in clinical laboratories that helps to quantitate the approximate number of analytical errors and provide an objective assessment of quality. This study aims to evaluate the performance of various biochemistry analytes using six-sigma metrics to identify areas for improvement and enhance overall quality control.

Materials and Methods

This study is a cross sectional study conducted at the Clinical Chemistry Laboratory of Naya Lab, Nobel Medical College Teaching Hospital, Biratnagar that evaluated internal quality control and external quality control data of 18 routine biochemistry tests for a period of four months to calculate sigma value. The analysis was performed using a Beckmann Coulter automated biochemistry analyzer. Quality goal index values were calculated to find the reason behind lower sigma values <3.

Results

Out of the 18 analytes, four for level 1 quality control and six for level 2 quality control were found to have a sigma value of more than 6. Similarly, five analytes, namely, urea, creatinine, calcium, potassium, and total protein, were found to have a sigma value of less than 3. Most of the analytes fell between 3 and 6. The quality goal index of the analytes for whose sigma value was less than 3, found that imprecision was the major problem.

Conclusion

This study highlighted the critical role of six sigma metrics in enhancing the quality control processes within clinical laboratories. We identified significant variability in the sigma values of 18 analytes, with some analytes demonstrating excellent performance while others revealed areas needing improvement.

Keywords: *Biochemistry, Sigma Metrics, Quality control*

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Introduction

Laboratory results are crucial for healthcare, with approximately 70% of clinical decisions relying on diagnostic tests. Ensuring the quality of these reports is essential for effective decision-making [1, 2]. Sigma metrics, a key quality control tool, assess laboratory performance by measuring defects per million opportunities, help for accurate evaluation, problem-solving and process improvement [3, 4].

Six Sigma metrics have been adopted by various clinical laboratories in the world and various authors have elucidated its application in all aspects of clinical laboratories [5-7]. Several studies have showcased its utility, few in our region as well [8], at the same time identified challenges in implementing the same. In Nepal, research on Six Sigma metrics in biochemistry laboratories is scant, with the majority of laboratories relying on conventional quality control methods. This gap in understanding the application and impact of Six Sigma metrics in our setting calls for further study.

The performance of 18 biochemistry tests was appraised in this study using Six Sigma metrics, analyzing internal quality control (IQC) and external quality assessment (EQA) data. For the poor performance views, the quality goal index (QGI) calculation was done to address the issues of inaccuracy and imprecision. The findings are expected to bring out ways of implementing Six Sigma metrics in resource-limited settings, improve laboratory performance, and support evidence-based clinical decisions within Nepal.

Materials and Methods

This cross sectional study was conducted at the Clinical Chemistry Laboratory of Nobel Medical College Teaching Hospital, Biratnagar. The ethical clearance was obtained from institutional review committee, Nobel Medical College Teaching Hospital (IRC-NMCTH 7171022) prior to obtaining data from laboratory. The study period was from January 2024 to December 2024 in which the quality control data was collected for four months (April 2024 to July 2024). Analytes for which regular internal quality control was conducted and had external quality assurance (EQA) data for the specified time frame were included in the study. Total of 18 analytes of routine biochemistry, viz. aspartate transaminase (AST), glucose, cholesterol, triglyceride (TG), urea, albumin, alkaline phosphatase (ALP), total bilirubin, amylase, total creatine kinase (Total CK), sodium, potassium, total protein, iron, calcium, uric acid (UA), alanine transaminase (ALT), and creatinine were included in the study.

The analysis was performed using a Beckmann Coulter automated biochemistry analyzer (AU480). The analyzer was regularly calibrated according to the manufacturer's guidelines to ensure the accuracy of results. Two levels of QC materials L1 (normal concentration, lot no. 1049H, Beckman Coulter) and L2 (abnormal concentration, lot no.1050G, Beckman Coulter) were tested daily before patient sample analysis to monitor precision and reliability. IQC data were collected for all 18 analytes. The obtained internal QC data for all 18 analytes were plotted on Levy-Jennings chart and Westgard rules were followed to monitor quality of each analytes individually that were under study. External quality control data were collected through the External Quality Assurance Services (EQAS) provided by RANDOX.

The data was collected, entered and analyzed in MS-excel 2013.

The Sigma metrics was calculated with following formula: [9]

$$\text{Sigma metrics} = \frac{(\text{TEa} - \text{Bias}\%)}{\text{CV}\%}$$

The total allowable error (TEa) values were referenced from the American Clinical Laboratory Improvement Amendment (CLIA) 2024 criteria [10].

Bias is the systematic error or deviation in measurement, where the results from a test method consistently differ from the true value or an accepted reference method. Bias in our study was calculated from external quality assurance records using the formula:

$$\text{Bias } \% = \frac{(\text{Laboratory mean} - \text{Group mean})}{\text{Group mean}} \times 100$$

The mean bias was used in formula of sigma metrics.

The coefficient of variance (CV%) was determined from the calculated laboratory mean and calculated standard deviation procured from four months of IQC data and calculated as:

$$\text{CV } \% = \frac{\text{Standard deviation}}{\text{Laboratory mean}} \times 100$$

The Six Sigma metrics were calculated for each analyte using the above formula. The performance of each analyte was assessed by comparing the calculated sigma values to standard benchmarks.

Analytes were classified according to their performance as follows: >6: excellent, 4-6: suited for purpose, 3-4: poor performer, <3: problematic.

The number of defects associated with specific Sigma values and their corresponding accuracy percentages are:
6 - 99.9997% accuracy and 3.4 DPM
5 - 99.98% accuracy and 233 DPM
4 - 99.4% accuracy and 6210 DPM
3 - 93.3% accuracy and 66,807 DPM
2 - 69.1% accuracy and 308,537 DPM
1 - 31% accuracy and 698,000 DPM
Quality goal index (QGI) values were calculated to find the reason behind lower sigma values <3.
QGI = Bias /1.5
QGI values were interpreted as:
QGI ratio of <0.8 indicates imprecision, a ratio >1.2 indicates inaccuracy, and a QGI ratio between 0.8 and 1.2 indicates both imprecision and inaccuracy.

Results

In this study, a total of 18 biochemical analytes were evaluated for their performance using Six Sigma metrics. CV% was calculated for each analytes using level 1 quality control and level 2 internal quality control. Bias for each of them was calculated from data obtained from external quality control (RANDOX) using laboratory mean and group mean. The total allowable error (TEa) values were sourced from CLIA 2024, providing a benchmark for evaluating the quality of laboratory results.
Six sigma values for level 1 IQC is shown in table 1. The average Bias% and CV% of four months data were used for calculation of sigma metrics. ALT, total bilirubin, total creatine kinase and potassium showed the superior performance with sigma level greater than 6. Four analytes showed the poor performance with sigma value lying below 3.

Table 1: Sigma metrics for level 1 internal quality control for analytes

Table 2 shows the sigma metrics for level 2 IQC.

Parameter	TEa	Bias %	CV %	SIGMA
Albumin	8	3.09	1.12	4.38
ALP	20	0.25	4.84	4.08
ALT	15	2.19	1.66	7.71
Amylase	20	4.96	2.61	5.76
AST	15	4.64	2.14	4.83
Total Bilirubin	20	1.51	2.83	6.53
Calcium	10	0.41	3.37	2.84
Cholesterol	10	6.16	0.89	4.3
CK total	20	5.72	1.94	7.35
Creatinine	10	0.23	4.17	2.34
Glucose	8	0.59	1.44	5.14
Iron	15	4.55	3.48	3.00
Potassium	5.6	2.01	0.51	7.03
Total protein	8	3.10	1.39	3.52
Sodium	3.6	0.98	0.52	5.04
TG	15	3.19	3.21	3.67
Urea	9	1.07	2.68	2.95
Uric acid	10	0.64	2.40	3.90

Result shows the performance of analytes were slightly better for pathological control materials with five analytes performing well with sigma metrics greater than 6 and only three analytes, viz. iron, potassium, total protein had sigma level below three.

Table 2: Sigma metrics for level 2 internal quality control for analytes

Table 3 shows the tabulation of analytes on basis of four sigma grades in both level of IQC. Analytes like urea, creatinine and calcium in L1 IQC and potassium and total protein in L2 IQC was found to have <3 sigma and classified as problematic performance. Total CK was an excellent performer in both level of QC. Most of the other analytes were in the acceptable range coupled with more stringent quality control.

Parameter	TEa	Bias	CV	SIGMA
Albumin	8	3.09	0.78	6.27
ALP	20	0.25	3.44	5.73
ALT	15	2.19	2.80	4.57
Amylase	20	4.96	2.11	7.12
AST	15	4.64	1.42	7.28
Bilirubin, T	20	1.51	3.51	5.26
Calcium	10	0.42	2.27	4.21
Cholesterol	10	6.16	0.53	7.19
CK, total	20	5.73	1.79	7.97
Creatinine	10	0.23	1.66	5.86
Glucose	8	0.59	1.46	5.07
Iron	15	4.55	3.03	3.44
Potassium	5.6	2.01	1.30	2.76
Protein, T	8	3.10	1.73	2.83
Sodium	3.6	0.98	0.44	5.89
TG	15	3.19	2.01	5.87
Urea	9	1.07	1.97	4.01
Uric acid	10	0.64	2.75	3.40

Table 3: Analytes classified according to sigma grades for IQC L1 and L2

Sigma grades	L1	L2
>6	ALT, Total Bilirubin, CK total, Potassium	Albumin, Amylase, CK total, Creatinine, AST, Cholesterol,
4-6	Albumin, ALP, AST, Amylase, Cholesterol, Sodium, Glucose	ALP, ALT, Total Bilirubin, Glucose, Sodium, TG, Urea, Calcium
3-4	Iron, Total Protein, TG, UA	Iron, UA
<3	Urea, Creatinine, Calcium	Potassium, Total Protein

Quality goal index (QGI) was calculated for five analytes with σ < 3. Table 4 shows QGI values for level 1 and level 2 IQC runs. It was found that out of five analytes, three analytes, viz. urea, creatinine and calcium had problem in precision,

one had problem with accuracy in the results and potassium was found to have problem in both imprecision and accuracy.

Table 4: Quality goal index and interpretation of problem for analytes with σ < 3

Analytes	QC level	Bias%	CV%	Sigma	QGI	Problem
Urea	L1	1.07	2.68	2.95	0.27	Imprecision
Creatinine	L1	0.23	4.17	2.34	0.04	Imprecision
Calcium	L1	0.41	3.37	2.84	0.08	Imprecision
Potassium	L2	2.01	1.3	2.76	1.03	Imprecision and Inaccuracy
Total protein	L2	3.10	1.73	2.83	1.2	Inaccuracy

Discussion

Originally developed by Motorola, Six sigma focuses on reducing defects to 3.4 per million opportunities through statistical analysis and process optimization. Widely accepted globally, it enhances clinical laboratory quality, which is crucial as 70% of clinical decisions rely on diagnostics. However, its application in Nepal's Biochemistry laboratories remains limited, requiring further exploration [5, 8, 11, 12].

In the present study, we have included 4 months period of IQC and EQA data bias%, CV% and sigma value of 18 routinely performed biochemistry analytes. Table 1 shows that certain analytes at level 1 IQC like ALT, total bilirubin, potassium, and CK total, perform exceptionally well with high sigma values, reflecting reliable and consistent testing processes in clinical labs. On the other hand, analytes such as calcium, creatinine, and urea have lower sigma values, pointing to greater variability and potential inaccuracies. These findings highlight the need for further investigation and process improvements to ensure better accuracy and overall lab performance.

Similarly, sigma value for pathologic control level is shown in table 2. At level 2 IQC, amylase, AST, cholesterol, total CK showed excellent performance, while potassium and total protein were low performers.

Numerous recent studies have shown different sigma metrics for different analytes at two levels of quality control. Study by Cevlik et al. showed amylase and CK had sigma value above 6 and glucose, calcium, creatinine, total cholesterol and total protein had sigma value below 3 at level 1 control [13]. Similarly a study done in Nepal by Mishra et al. found AST and ALT had higher sigma value above 6 and urea, creatinine, albumin, triglyceride, total-cholesterol, alkaline phosphatase (ALP) and magnesium for both levels of control had lower sigma value less than three [8]. Ganji et al. found only two (direct bilirubin and HDL-C) out of 16 tests they evaluated achieved a sigma value of six [14]. In contrast, Gadde et al. in their study found larger number of analytes achieving sigma value greater than 6 in two different analyzers at two level of control [15]. The reason for sigma value less than six (14 analytes in our cases out of 18) and for other researchers in their study is due to low precision and bias% nearing total allowable error. The variations in the result of different studies might be due to difference in analytical techniques, sample size (total months enrolled in study), quality control protocols, personnel training and environmental factors.

In our study there was also the variation in results like some analytes performed well in one level of QC and not performed well in another level. In our study, the low performers were Urea, Creatinine, Calcium at level 1 QC and Potassium, Total Protein at level 2 QC. While creatinine was found to be a excellent performer in level 1 QC. Similarly potassium has sigma value greater than 6 at level 1 QC. Similar types of variation in results have been found in study by various authors [8,16,17]. The difference in sigma values at various control levels for the same analyte might be due to factors like variations in test precision, the stability of the control material, or slight biases at certain concentration ranges.

Quality goal index (QGI) provides a balanced assessment of both precision and accuracy. It is a crucial tool for evaluating laboratory analyte performance within the six sigma framework. QGI was calculated for those analytes whose sigma values were less than 3 to find the problem whether the poor performance is due to imprecision or inaccuracy. Imprecision was the major finding in our case. This insight allowed us to implement precise corrective actions and refining the testing protocols [18].

This study has some limitations worth noting. First, it relies on quality control data from just one laboratory, which may not reflect the diverse practices found in laboratories throughout Nepal. Additionally, the analysis covers only a four-month period, the picture might be different from average values of longer duration. Lastly, while the focus is on routine biochemistry analytes, other important areas of clinical testing are not addressed in this research.

Conclusion

This study aimed to evaluate the performance of various biochemistry analytes through six sigma metrics to enhance quality control in clinical laboratories. This study demonstrated the sigma values of various analytes at two level of IQC and found some analytes can be relied upon for clinical decision and some needs to be stringently monitored. While this study provides valuable insights, it is limited by its focus on a single laboratory over a four-month period, which may not capture broader trends across different settings. This study underscores the necessity of implementing six sigma metrics in their quality assessment processes. By integrating six sigma methodologies into routine laboratory practices, we can significantly enhance diagnostic accuracy and ultimately improve patient care outcomes.

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Conflict of interest: None

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