ORIGINAL RESEARCH ARTICLE

Sigma Metrics Assessment as Quality Improvement Methodology in a Clinical Chemistry Laboratory

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Abstract

Background: The concept of sigma metrics and lean six sigma is well known in the field of health care. However, not many labs utilize the six-sigma metrics for the maintenance of high-quality laboratory performance. A minimum value of 3 σ is desired in any clinical laboratory and a value of σ ≥6 is regarded as the gold standard for obtaining high-quality lab reports.

Objective: To calculate bias, Coefficient of variation (CV) and sigma metrics from the internal quality control (IQC) and external quality control (EQC) data to ascertain the extent of quality management.

Materials and methods: An extensive study of sample processing and quality practices was carried out in the Central Laboratory of Department of Biochemistry, PGIMER and Dr. RML Hospital, New Delhi; from February 2020 to July 2020. The IQC used (both Level I and II) was from Biorad Laboratories India (Lyphochek assayed chemistry control) and the EQC used was from Randox Laboratories, UK. All the controls were run on Beckman Coulter clinical chemistry analyzer AU 680. A total of 14 clinical parameters were analyzed and subsequently, mean SD, CV, bias and σ were calculated through their respective formulas.

Results: Amylase showed σ >6 for both levels of IQC. It indicates world-class performance. Total bilirubin, AST, triglyceride and HDL depicted σ values between 3.1 and 6 for both L_1 and L_2. Iron showed an σ value of 5.5 in L_1 whereas it was 3.78 in L_2. The remaining parameters had σ <3 in L_1. As far as L_2 is concerned, besides ALT which had σ value of 4.24; the rest of all analytes had σ <3.

Conclusion: Sigma metrics in the clinical laboratory are an essential technique to ascertain poor assay performance, along with the assessment of the efficiency of the existing laboratory process.

Keywords: Bias, Biochemistry, Clinical Biochemistry, Coefficient of variation, External quality control, Internal quality control, Laboratory, Quality control, Six sigma, Total allowable error.

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Introduction

In any Health care Laboratory, the term "quality" is defined as conformance to the requirements of users (nurses and physicians) or customers (patients or other parties who pay the bills) and the satisfaction of their needs and expectations.[1]

Certain good quality indicators like reduced number of repeats and reruns; reduced time for sample transportation and storage ultimately leading to decreased turnaround time (TAT), etc., signify the good quality of lab reports.[2,3] A good quality laboratory performance is depicted in the test reports it generates and is also equally reflected in the quality controls performed as its performance checks. Besides internal quality control (IQC) and external quality control (EQC), their exhaustive interpretation has become quite indispensable in the present scenario. This can be carried out by using the concept of "Six Sigma" and "Lean Six Sigma". Although the "Six Sigma" methodology was introduced in Motorola in 1986, in order to reduce the defects in the manufacturing process, this concept was adopted in laboratory medicine in the year 2000. A process having sigma metrics ≥6 signifies only 3.4 defects per million opportunities.[4,5]

Sigma (σ) reflects the defects or errors per million opportunities (DPMO). The "Sigma" refers to the "number of SDs from the mean a process can be before it is outside the acceptable limits". The process having 6 σ is considered extremely precise, having only 3.4 DPMO.

The present study aims to calculate bias, CV and sigma metrics from the IQC and EQC data in order to ascertain the extent of quality management in our lab.

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Materials and Methods

An exhaustive retrospective study of sample processing and quality control procedures was carried out in the Central Laboratory of Department of Biochemistry, ABVIMS and Dr RML Hospital (Atal Bihari Vajpayee Institute of Medical Sciences and Dr. Ram Manohar Lohiya Hospital), New Delhi; from February 2020 to July 2020. The corresponding data was collected and analyzed subsequently. Since this study is a preliminary retrospective study of quality controls, only 6 months of data is being taken. The ethical clearance waiver for the study was obtained from the "Institutional Ethics Committee" ABVIMS and Dr. RML Hospital. The study approval number is 524 (60/2021)/IEC/ABVIMS/RMLH/636. This study was carried out using

quality control materials and no human or animal blood or tissue was used in this study.

The IQC used (both Level I and II) were from Biorad Laboratories India (Lyphochek assayed chemistry control) and the EQC used was from Randox Laboratories, UK. All the controls were run on Beckman Coulter clinical chemistry analyzer AU 680. On each day, both levels of IQC were run and analyzed. The patients' samples were run and reported only if the IQC came within the acceptable range following the Westgard rules.

The parameters which were analyzed include glucose, urea, total bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), total protein, albumin, cholesterol, triglyceride, high-density lipoprotein (HDL), sodium, potassium, amylase and iron.

By using IQC data; Mean and SD were determined. Subsequently, CV% (coefficient of variation) was calculated using the following formula:

$$CV\% = SD \times 100/\text{Lab mean}$$

Further; Bias was ascertained by employing RIQAS with the following formula:

Bias (%) = | (Mean of all laboratories using same instrument and method – Our laboratory mean) |/(Mean of all laboratories using same instrument and method) × 100

Values for TE_a (total allowable error) were taken from CLIA (Clinical Laboratories Improvement Act) guidelines

Finally, Sigma metrics (σ) was determined using the following equation:

$$\text{Sigma metrics } (\sigma) = (TE_a - \text{Bias})/CV$$

The methodology employed to implement lean six sigma in our Central Laboratory was DMAIC, i.e., define, measure, analyze, improve, and control. It means "defining" the problem due to which our results are deviating from the range of established standards. It also includes defining the resources which may be required to solve the problem.[6]

Subsequently, to solve the problem, its extent was "measured", through the collection of pertinent data and retained in a more presentable form, e.g., collection of IQC and EQC data and calculating CV% and Bias% respectively from it.[6,7]

Further, the data was "analyzed" to ascertain the root causes of the defect or problem. In this phase; the differences between our results and the target values are estimated along with the determination of their possible causes.[8]

After that, the root causes were eliminated by implementing certain corrective measures following Westgard sigma rules to "improve" the process performance.[9] Once the defect is rectified; certain preventive measures are also taken to "control" or check that such a problem or defect should not occur in the future.

To eliminate any errors and wasteful steps during sample processing; every step of sample processing was carefully reviewed and monitored. Many corrective measures were taken to reduce errors at the preanalytical; analytical and post-analytical phases to reduce TAT and improve the quality of sample processing.

Results and Observations

In the present study, IQC and EQC data for 6 months (February–July 2020) was collected and compiled in Excel sheets to calculate mean, SD, CV%, Bias, and Sigma Metrics for 14 different parameters. While evaluating IQC, it can be observed that only total bilirubin, ALT and HDL had CV% >5 in L_1 and the rest of all parameters showed CV% <5 (Table 1).

As far as L_2 is concerned, except for HDL (CV% >5), the rest of all parameters had CV% <5.

Now considering EQC, out of all the measured parameters, the average bias of sodium was minimum (0.85) whereas triglyceride and HDL had a bias >5 (Table 2).

As seen in Table 3, the average σ value for amylase is maximum for both levels of IQC.

According to Table 4; σ >6 for both levels of IQC was observed for amylase. It indicates the world-class performance of this analyte.

Table 1: The division of sigma scores for selection of QC rules

Sigma scores	*Description*	*QC rules*
>6	"World class"	1_{3s}
4–6	Suitable for purpose	$1_{3s}/2_{2s}/R_{4s}$
≥3–4	Suitable for purpose but higher QC frequency and more rules needed	$1_{3s}/2_{2s}/R_{4s}/4_{1s}$
<3	"Problem test"	$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$

Table 2: CV% calculated from internal quality control L_1 and L_2 from February 2020 to July 2020 (6 months)

	L_1							L_2						
Parameter	*Feb*	*March*	*April*	*May*	*June*	*July*	*Average*	*Feb*	*March*	*April*	*May*	*June*	*July*	*Average*
Glucose	2.43	1.78	2.18	3.76	4.81	4.29	**3.21**	2.46	1.63	2.68	4.54	5.51	3.78	**3.43**
Urea	2.86	4.22	3.77	1.52	3.26	4.32	**3.32**	3.08	2.77	3.5	2.64	3.35	4.8	**3.36**
Total bilirubin	4.83	3.88	5.36	2.04	5.63	9.03	5.13	2.22	4.44	4.54	2.94	4.09	6.79	**4.17**
AST	3.28	4.16	3.88	2.62	4.27	4.75	**3.83**	2.14	2.01	3.12	2.87	3.48	4.39	**3.0**
ALT	8.09	9.19	7.12	3.75	5.06	5.24	6.41	2.94	2.93	5.91	3.09	3.26	4.64	**3.8**
Total protein	3.12	2.27	3.15	4.01	3.79	3.35	**3.28**	3.39	2.55	4.21	5.17	4.05	3.43	**3.8**
Albumin	2.16	1.96	2.27	1.7	3.85	5.59	**2.92**	2.55	1.74	2.89	3	3.36	5.49	**3.17**
Cholesterol	2.43	4.36	3.29	2.31	2.31	3.59	**3.05**	2.03	2.42	2.86	2.6	2.14	4.67	**2.79**
Triglyceride	6	2.35	4.14	2.66	4.06	5.03	**4.04**	5.52	2.68	3.04	3.67	5.8	6.21	**4.49**
HDL	4.48	5.98	6.42	5.25	6.49	5.14	5.63	3.53	4.09	5.67	6.14	6.78	6.25	5.41
Sodium	1.34	1.19	1.72	1.31	1.31	2.19	**1.51**	1.16	1.31	2.52	1.56	1.18	2.25	**1.66**
Potassium	1.53	1.71	2.08	1.87	1.53	2.46	**1.86**	1.28	1.33	2.77	1.51	1.58	2.54	**1.84**
Amylase	2.22	3.15	2.92	2.45	2.01	3.47	**2.7**	1.91	1.34	4.29	2.98	2.58	4.48	**2.93**
Iron	2.86	3.59	3.75	2.63	2.24	3.44	**3.08**	3.63	4.73	4.29	5.6	3.88	4.76	**4.48**

All the bold values show CV% <5%. This shows very good performance & precision of the method used

Table 3: Bias% calculated from RIQAS for 6 months (February–July 2020)

Parameter	*Feb*	*March*	*April*	*May*	*June*	*July*	*Average*
Glucose	1.36	3.98	1.32	6.17	3.14	3.61	3.26
Urea	0.07	0.9	4.9	0.68	3.65	3.15	2.22
Total bilirubin	0	1.79	5.67	0	1.79	0.59	1.64
AST	2.78	0.76	3.3	2.44	3.57	10.08	3.82
ALT	0.83	2.9	2.2	9.09	2.24	6	3.87
Total protein	2.63	1.72	9.09	3.45	0	0.87	2.96
Albumin	0.48	2.6	3.7	0	1.96	2.25	1.83
Cholesterol	5.24	6.01	2.75	2.09	4.56	3.49	4.02
Triglyceride	7.8	0.39	3.2	6.5	10.04	3.59	5.25
HDL	6.2	3.84	3.92	0	13.50	3.39	5.14
Sodium	1.29	0.97	0.06	1.05	0.8	0.98	0.85
Potassium	2.44	2.24	0.17	2.56	1.59	0.51	1.58
Amylase	5.06	1.28	0.64	0.61	1.54	0.12	1.54
Iron	4.09	4.04	3.01	2.74	2.09	2.48	3.07

Table 4: Sigma metrics calculated from internal quality control L_1 and L_2 from February 2020 to July 2020 (6 months)

	L_1							*L_2*						
Parameter	*Feb*	*March*	*April*	*May*	*June*	*July*	*Average*	*Feb*	*March*	*April*	*May*	*June*	*July*	*Average*
Glucose	3.54	3.4	3.9	1	1.42	1.5	2.46	3.5	3.7	3.23	3.5	1.2	1.7	2.8
Urea	3.11	1.9	1.1	5.4	1.64	1.3	2.4	2.9	2.9	1.17	3.1	1.6	1.2	2.1
Total bilirubin	4.3	4.7	2.7	9.7	3.2	2.1	4.45	8.9	4.1	3.1	6.7	5.3	3	5.18
AST	5.2	4.6	4.3	6.7	3.8	2.1	4.45	8.01	9.5	5.3	6.1	4.7	2.3	5.98
ALT	2.3	1.8	2.5	2.9	3.5	2.7	2.61	6.5	5.8	3	3.5	5.4	3	4.53
Total protein	2.35	3.6	0.3	1.6	2.6	2.7	2.19	2.1	3.2	0.2	1.3	2.4	2.6	1.96
Albumin	4.4	3.8	2.8	5.8	2.1	1.4	3.38	3.7	4.3	2.2	3.3	3.6	1.4	3.08
Cholesterol	1.9	0.9	2.2	3.4	2.3	1.8	2.08	2.3	1.6	2.5	3	6.8	1.4	2.93
Triglyceride	2.8	10.4	5.3	6.9	3.7	4.2	5.55	3.1	9.1	7.1	8.6	6	4.6	6.41
HDL	5.2	4.4	4	5.7	2.5	5.2	4.5	6.7	6.4	4.6	4.9	2.4	4.2	4.86
Sodium	2.7	3.3	2.8	3	3.2	1.8	2.8	3.2	3.1	1.9	3.8	4.9	1.8	3.11
Potassium	2.3	2.2	2.8	1.8	2.8	2.2	2.35	2.8	2.8	2.1	5.6	4.8	2.1	3.36
Amylase	11.2	9.1	10	11.9	14.1	8.6	**10.81**	13.1	21.4	6.8	9.8	11	6.7	**11.46**
Iron	5.5	4.4	4.5	6.5	7.9	5.1	5.65	4.4	3.4	3.9	4	5.7	3.7	4.18

All the bold values show average sigma metrics value of serum amylase, which is more than 6 and depicts its excellent performance

Further, four parameters namely total bilirubin, AST, triglyceride and HDL depicted σ values between 3.1 and 6 for both L_1 and L_2. Iron showed an σ value of 5.5 in L_1 but 3.78 in L_2. The remaining parameters had σ <3 in L_1. As far as L_2 is concerned, besides ALT which had σ value of 4.24; the rest of all analytes had σ <3.

Discussion

In the process of maintaining high laboratory quality standards, six sigma is regarded as an indispensable tool. The concept of Lean six sigma aims at reducing wasteful activities during sample processing. When sigma metrics is ≥6, then the process is said to have only 3.4 DPMO and it is regarded as the "World Class Quality".

Although the achievement of sigma metrics value of 6 or more is not easy, with appropriate precautions to minimize the errors associated with sample processing (at preanalytical, analytical and post-analytical phases), this goal can be approached.

In the present study, IQC and EQC data from 6 months (February–July 2020) was used to calculate the mean, SD, CV%, bias, and sigma metrics of 14 analytes. The two entities, SD and CV% are used to measure the extent of deviation and variation respectively of IQC test results concerning its mean. In general, CV% is the favored mode of presentation. If the CV is less than 5%, then the particular method used for the determination of an analyte's concentration is said to have a very good performance and precise.[10] It can be visualized between Tables 1 and 2 that except for HDL, (CV% >5 in both L_1 and L_2) along with total bilirubin and ALT (having CV% >5 in L_1), rest all parameters depicted CV <5%. This indicates that our lab has achieved a high level of precision in the remaining 11 analytes.

Another important calculated index in the present study is bias% by using the EQC data. As per the definition, the term "bias" implies any discrepancy between the results of our lab and the peer group labs employing the same instrument and methodology.[11] This means that we should try to minimize the bias, to decrease the differences between the lab results. Out of all the parameters measured in the present study, Sodium had a minimum bias of 0.85 (Table 2) while the rest analytes had a bias of <5% (except HDL and Triglyceride). This shows a high degree of accuracy in our lab results.

Table 5: Average bias, average CV% and sigma metrics calculated for 6 months for both levels of IQC (L_1 and L_2)

Parameter	*TE_a%*	*Average bias%*	*Average CV% (L_1)*	*σ (L_1)*	*Average CV% (L_2)*	*σ (L_2)*
Glucose	10	3.26	3.21	2.09	3.43	1.96
Urea	9	2.22	3.32	2.04	3.36	2.01
Total bilirubin	20	1.64	5.13	3.58	4.17	4.4
AST	20	3.82	3.83	4.22	3.0	5.39
ALT	20	3.87	6.41	2.51	3.8	4.24
Total protein	10	2.96	3.28	2.14	3.8	1.85
Albumin	10	1.83	2.92	2.79	3.17	2.58
Cholesterol	10	4.02	3.05	1.95	2.79	2.14
Triglyceride	25	5.25	4.04	4.88	4.49	4.39
HDL	30	5.14	5.63	4.41	5.41	4.59
Sodium	5	0.85	**1.51**	2.74	**1.66**	2.5
Potassium	6	1.58	**1.86**	2.36	**1.84**	2.4
Amylase	30	1.54	2.7	10.5	2.93	9.71
Iron	20	3.07	3.08	5.5	4.48	3.78

All the bold values show CV% <2% in serum sodium and potassium. This is again an indication of highly precise results

TE_a is the sum of random error (imprecision) and systematic error (bias or inaccuracy).[12,13] Also, this term encompasses the pre-analytical variations, biologic variations, etc., that lead to variability in patients' results.

In the present study; σ >6 for both levels of IQC was observed for amylase (Tables 4 and 5). Hence it required only the 1_{3s} Westgard sigma rule to be followed since it was showing excellent performance. Among others, total bilirubin, AST, triglyceride and HDL depicted σ values between 3.1 and 6 for both L_1 and L_2 with Iron showing σ value of 5.5 in L_1 and 3.78 in L_2. It implies that Westgard sigma multirole application is needed for such parameters. For parameters having σ values from 5 to 6; three rules namely 1_{3s}, 2_{2s}, and R_{4s} are needed. 4-sigma quality requires the addition of a 4th rule and implementation of a $1_{3s}/2_{2s}/R_{4s}/4_{1s}$ multirole. Those parameters having σ <3 require extensive evaluation in terms of reducing analytical bias and imprecision.[14,15]

Limitations

One major limitation of the present study is that this study included data of only 6 months. Such a study may provide much more implicative results if it is carried out for a longer duration.

Conclusion

Sigma metrics in the clinical laboratory is a vital methodology to identify and correct any deviation of lab results from the prescribed standards. It can help us ascertain poor assay performance along with the assessment of the efficiency of the existing laboratory process. The unnecessary and time-consuming wasteful additional steps can be eliminated using the concept of sigma metrics and lean six sigma. This will decrease the TAT and help in dispatching good-quality reports for better patient management. Further, sigma metrics can help in devising appropriate strategies for the judicious utilization of IQC and EQC in a large-sized clinical laboratory.

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Ethical Approval

The ethical clearance waiver for the study was obtained from the "Institutional Ethics Committee", ABVIMS and DR. RML Hospital. The study approval number is 524 (60/2021)/IEC/ABVIMS/RMLH/636. This study was carried out using quality control materials and no human or animal blood or tissue was used in this study.

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