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A Clinical Laboratory Assessment of Sigma Metrics of Frequently Assayed Biochemical Parameters

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Abstract
Introduction: Six Sigma is a quality management method that emphasizes the detection and elimination of flaws in order to enhance the quality of operations. Six Sigma implementation in laboratory procedures enables mistake detection and the adoption of cutting-edge ways to cost reduction without compromising quality. With this in mind, the study biochemical laboratory set out to evaluate the process performance of frequently assessed parameters on a sigma scale, which would aid in evaluating the laboratory's performance and would allow for the development and selection of the best strategy for improving the performance of problem analytes.
Objectives: Recognize the value of Six Sigma and use it to calculate Sigma metrics for frequently measured biochemical parameters, improving laboratory quality control.
Methods: Retrospective data collection for quality control was conducted between June and September 2022. Sigma metrics were derived using Total Allowable Error (TEa), Coefficient of Variation (CV), and Average Bias for six biochemical parameters measured on Analyser following Clinical Laboratories Improvement Act (CLIA). To determine the root of the fault, Quality Goal Index (QGI) of the problematic analytes were generated.
Results: The first three of the following parameters—cholesterol, amylase, HDL, triglycerides, SGOT, and SGPT—produced good sigma values, while triglycerides, SGOT, and SGPT fared badly. Finally Quality Goal index were determined for the parameters if the issue is brought on by imprecision, inaccuracy, or both.
Conclusion: According to the study's findings, sigma metrics are a valuable tool for evaluating the analytical performance of a clinical biochemistry laboratory, and for parameters with sigma between 3-6, strict internal Quality Control (IQC) guidelines are not necessary. However, prior to routine usage, root cause investigation and technique performance improvement should be carried out for a problem analyte with a sigma metric below 3.
Keywords: Six sigma; Total allowable error; Bias; Coefficient of variation; Quality goal index

1. Introduction

Clinical labs are intricate and dynamic companies that continuously strive to lower costs while maintaining high standards for testing quality[1]. These days, laboratories must manage growing workloads including a wider range of parameters with constrained staffing, provide findings of the highest calibre within the allotted turnaround time, and do it in an economical manner[2]. The most recent management trend, Six Sigma, has been described as a repackaging of traditional quality management ideas, methods, and tools/techniques. The sigma number, which is expressed as defects per million (DPM), indicates the likelihood that mistakes or defects may occur. By using six sigma in the lab, the amount of mistakes or defects produced by the lab may be measured. Application of six sigma to laboratory operations can be used to evaluate laboratory performance[3]. In addition to offering a dispassionate evaluation of analytical techniques and equipment, sigma metric analysis also makes vital design data accessible for practical application. QC processes that are suitable for identifying deviations are essential for the clinical interpretation of the test[4]. Each analyte has a very different quality requirement. Because blood electrolyte levels, for instance, are tightly controlled physiologically, even slight variations are likely to have a clinically significant impact. For a clinically relevant shift that justifies further research or therapy, liver enzymatic activity, in contrast, exhibit substantially wider changes. As a result, much greater increases are necessary. With evidence for process improvement and a description of how many sigma fit inside the tolerance limits, six sigma offers a more quantitative framework for assessing process performance[5]. So, the sigma scale is used to rate quality, with 3 sigma serving as the least acceptable

sigma for ordinary performance and 6 sigma serving as the target for world-class quality. When six sigma is used in a clinical laboratory, the test method's performance is calculated using normal QC processes, and the test's quality standards are specified in terms of the total allowable error. Additionally, it calls for ongoing data analysis, computing a six-sigma value [Sigma value = TEa - bias)/CV], improvising a procedure based on the analysis of the data, and long-term follow-up[6].The 3-sigma level of process performance is regarded as the minimally acceptable level of quality. The association between the amount of product defects, wasted operational expenses, and customer satisfaction is represented by the sigma metrics. Utilizing Six Sigma in a laboratory entails quantifying test performance using conventional quality control techniques, outlining the test's quality requirements, analysing the data, and computing a sigma value, then recovering the process based on the analysis's findings and closely monitoring it. It may be concluded that when the sigma value rises, the test's reliability and consistency improve, lowering operational expenses. Keeping in view the above, we aimed to gauge the process performance of some routinely assayed parameters on sigma scale in assessing the laboratory's performance on sigma scale which will enable in working out and choosing the correct approach towards improvement of target analyte performance[7,8].

2. Aims and objectives

To comprehend the significance of Six Sigma performance and use it to calculate the performance of frequently used biochemical parameters using Sigma metrics.

3. Materials and methods

Our goal is to give the sigma metrics that were recorded during a four-month period (June 2022-September 2022) in our clinical biochemistry laboratory. For a period of 4 months, internal statistical Quality Control data were collected using automated chemical analyser from the Instrumentation Laboratory. Materials for internal quality control were purchased from Bio-Rad and information for external quality control was received by signing up for Bio-Rad External Quality Assurance Scheme (EQAS). Prior to running patient samples, both levels of QC material level I and level II were analysed. SGPT, SGOT, Triglyceride, Cholesterol, HDL and Amylase were among the analytes examined with the use of the Total Allowable Error, Coefficient of Variation and Average Bias, Sigma metric value applying CLIA criteria[9,10]. By establishing the CV and bias for each analyte using data from 4 months of internal QC and the EQAS, the lab's quality control was validated. The statistical analysis was performed using the updated version of Microsoft Office Excel. The following equation were used to determine the sigma metrics for the different analytes.

$$QGI = Bias / 1.5 \times CV\%$$

3.1 Measurement Variables

3.1.1 Total Allowable Error: The maximum permitted deviation from the acceptable reference value is what may be noticed in the departure of a single measurement from the desired value. Guidelines under the CLIA were used to determine the TEa values for various parameters.

3.1.2 Bias: Bias is the systematic discrepancy between the findings that would be achieved using a recognized reference technique and the expected results from the laboratory's test procedure. Testing for proficiency led to bias (Bio-Rad EQAS)

Bias (%) = (Mean of all laboratories using same instrument and method – Our mean) X 100 / Mean of all laboratories using same instrument and method.

3.1.3 Coefficient of Variance: It is an analytical coefficient of variation of the test method. CV was calculated from internal QC material data for all the parameters.

CV (%) = (Standard deviation X 100) / Our laboratory mean.

The following formula was used to derive sigma metrics from CV%, average bias, and total permissible error for all parameters:

Process Sigma Σ (σ) = (TEa - bias) / CV%

3.1.4 Quality Goal Index: The QGI Ratio indicates how closely bias and accuracy adhere to the respective quality objectives. Analyzing the cause of lower sigma values in the problematic analytes is meant to determine if the issue is brought on by imprecision, inaccuracy, or both[11].

The following are the requirements for interpreting QGI of the issue analytes with poor sigma performance: - A QGI of 0.8 or less indicates imprecision, a QGI of 0.8 to 1.2 indicates both imprecision and inaccuracy, and a QGI of 1.2 or more indicates inaccuracy.

4. Results

HDL, Cholesterol and Amylase all generated satisfactory sigma values but SGPT, SGOT, and Triglycerides fared poorly (**Table 1, 2, 3).** The attainment of six sigma is referred to be the gold standard for identifying a top-notch quality metric.Application of six sigma to laboratory operations can be used to evaluate laboratory performance. It is not necessary to establish strict internal QC guidelines when the process sigma value is in between 3-6 or more than 6. For less than 3 it is necessary to follow guidelines.

Table1: Month wise bias for the parameters between June and September 2022

Parameter	**June**	**July**	**August**	**September**	**Average**
SGPT	12	10	12	13	11.75
SGOT	4.19	12.31	4.12	16.31	9.23
Cholesterol	5.1	3.15	4.02	3.52	3.94
Triglyceride	16.09	4.10	2.17	3.11	6.36
HDL	23.49	21.87	12.11	9.02	16.62
Amylase	4.09	4.01	5.94	5.07	4.77

Table 2: Average Bias, TEa, CV and Sigma value for quality control level 1 and 2

Parameter	**Total Allowable Error [TEa (%)]**	**Average Bias**	**Level 1**		**Level 2**	
			Coefficient of variance (CV)	Sigma value(σ)	Coefficient of variance (CV)	Sigma value (σ)
SGPT	25	11.25	4.82	2.85	3.88	3.54
SGOT	20	9.29	4.98	2.15	4.96	2.16
Cholesterol	15	3.9	2.15	5.16	2.08	5.34
Triglyceride	20	6.39	4.74	2.87	4.69	2.9
HDL	30	16.79	2.26	5.84	2.57	5.14
Amylase	30	4.78	4.51	5.59	4.58	5.51

Table 3: Sigma Values of Biochemical Parameters

Parameter	Sigma-level 1	Sigma- level 2
SGPT	2.85	3.54
SGOT	2.15	2.16
Cholesterol	5.16	5.34
Triglyceride	2.87	2.9
HDL	5.84	5.14
Amylase	5.59	5.51

Table 4: Displaying the issue analytes' CV%, Average Bias, and Sigma values as well as calculating the QGI ratio to identify the problem

Analyte	CV%		Average Bias	Sigma		QGI Ratio		Problem	
	L1	L2		L1	L2	L1	L2	L1	L2
SGPT	4.82	3.88	11.25	2.85	3.54	1.55	1.93	Inaccuracy	Inaccuracy
SGOT	4.98	4.96	9.29	2.15	2.16	1.24	1.24	Inaccuracy	Inaccuracy
Triglyceride	4.74	4.69	6.39	2.87	2.9	0.89	0.9	Imprecision and Inaccuracy	Imprecision and Inaccuracy

5. Data Interpretation and Discussion

Three analytes (SGPT, SGOT, and Triglycerides) with an average sigma value less than 3 were found to have errors in the current study's retrospective review of sigma metrics during the analytical phase. The difference in the instruments, the quality control material employed, and various pre and post analysis variables may be responsible for variations in the sigma values achieved. To identify the root of mistakes, the QGI ratio was determined for each of the six. For SGPT and SGOT, the issue was determined to be inaccuracy, whereas imprecision and inaccuracy were both the root of the mistake for triglycerides. Similar studies have been conducted, and total allowable error is the maximum amount of mistake that can occur without undermining the value of the test results for medical purposes. It is used to define acceptable analytical performance for the evaluation of the analytical performance of a specific instrument, for the validation of quality control, and as a way to gauge the consistency or comparability of findings for analytes measured on various systems[12]. To guarantee clinical value, TEa establishes the upper limit for combined imprecision (random error) and bias/inaccuracy (systematic error) that is allowed in a single test result. A predetermined quality criterion also assures consistency across various laboratory analyzers. The total allowable error for the analytes in the current investigation was derived from several industry standards. This established permissible error levels that are neither too lax to overlook the underlying mistakes nor too strict to cause erroneous outlier alerts. The many sources of total permissible error limitations for the study's parameters are shown in **Table 2.** As a result of our research, we have shown that sigma metrics are a reliable instrument for evaluating the analytical performance of a clinical chemistry laboratory and that strict internal QC guidelines are not necessary for methods with sigma 3-6[13]. Prior to routine usage, root cause investigation and technique performance improvement should be carried out for a problem analyte with a sigma metric below 3. Poor sigma performance (less than 3) also necessitates the implementation of a newer and better procedure since in these circumstances, even after several QC runs, the test's quality cannot be guaranteed.

6. Conclusion

The use of six sigma concepts will help to improve IQC processes and offer the scientific foundation for recommendations for the quantity of QC that is really required. The best option for resolving analytical and management issues in laboratory medicine and reducing mistakes to a minimal level is the Six Sigma approach. We used a sigma scale to evaluate six clinical chemistry analytes at two levels. Cholesterol, HDL and Amylase a sigma value of 3-6 was discovered, indicating that these substances do not require strict quality control. For SGOT, SGPT and Triglyceride sigma was found to be lower than 3, necessitating the adoption of a better procedure as well as stricter QC checks and the implementation of guidelines. The diagnostic and healthcare industries are constantly challenged to improve diagnosis, raise quality standards, and reduce costs. The budget for the laboratory as well as the quality of reports may be significantly impacted by operational inefficiencies. Therefore, identifying the bottlenecks is essential for increasing operational productivity. Six Sigma implementation in laboratory procedures enables mistake detection and the adoption of cutting-edge ways to cost reduction without compromising quality. Generally speaking, laboratories base their QC protocol design for frequency and the quantity of daily IQC runs on the rules set out by accrediting authorities. However, according to Good Laboratory Practice, each laboratory must create its own Individual Quality Control Plan based on Sigma metric analysis. By doing this, needless recurring QC runs that result in waste and increase the institution's operational expenses are avoided.

7. References

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