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Quality improvement in clinical biochemistry laboratory using six sigma metrics and quality goal index

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Abstract

Introduction: One of the most popular quality management system tackle employed for process perfection is six sigma. When the process outcome is measurable, six sigma can be used to assess the quality.

Aim: Present study was conducted with the objective to apply six sigma matrices and quality goal index for the assessment of quality assurance in a clinical biochemistry laboratory.

Materials and methods: Present study is a retrospective study. Internal and external quality control data were analyzed retrospectively during July 2020 to December 2020. Descriptive statistics like laboratory mean ± standard deviation; bias and coefficient of variation (CV) were calculated for the parameters glucose, urea, creatinine, ALT (SGPT), AST (SGOT), cholesterol, triglyceride and HDL. Sigma value was calculated for both level I & level II of internal quality control (IQC).

Results: Satisfactory sigma values (≥3) were elicited for blood glucose, cholesterol, triglyceride, HDL, urea and creatinine, while ALT (SGPT) and AST (SGOT) performed poorly (<3) on the sigma scale. The quality goal index (QGI) ratio was found (> 1.2) for only 2 parameters SGPT and SGOT (with sigma value <3) for both levels 1 and 2, indicating inaccuracy.

Conclusion: Results of present study focuses on meticulous appraisal and execution of quality measures to improve sigma standards of all the analytical processes. Even though six sigma provides benefits over former approaches to quality assurance, it also opens newer challenges for laboratory practitioners. Therefore, sigma metric analysis provides a point of reference to design a protocol for IQC for the laboratory; address poor assess performance, and assess the existing laboratory process efficiency.

Keywords: six sigma; bias; internal quality control; quality goal index; coefficient of variation

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Introduction

Laboratory services may make up 5% of a hospital's budget but they are the mainstay in 60-70% of all critical decision-making such as admittance, discharge and medication [1]. The testing process in a clinical chemistry laboratory consists of three phases namely pre-analytical phase, analytical phase and post-analytical phase. All the three phases are prone to error.

Laboratory error can be defined as any defect or deviation of result from true value. Internal Quality Control (IQC) and External Quality Assurance Service (EQAS) are presently the procedures that are being used for quality control in the analytical phase. The IQC shows the amount of variation that occurs in our results in the form of imprecision while EQAS helps in evaluating the accuracy or trueness of our results. For a lab the result generated is a form of product. All Production processes always have a certain tendency for error generation. In 1981, Dr. James O. Westguard proposed several statistical process control rules used with Levey-Jennings chart for evaluating Quality Control (QC) performance [2]. However the quantification of error in the analytical process cannot be expressed through IQC or EQAS procedures. Here comes the role (response of question one of six sigma which can help us in expressing our quality goals.

Sigma metrics is about measuring or counting the number of defects. Sigma is denoted by a Greek letter "σ" and used to measure the standard deviation. Defects or laboratory errors can be counted and converted to defects-per-million (DPM). This DPM can then be converted into a sigma metrics. Six sigma is the ideal goal or world class quality equivalent to 3.4 defects per million. Six-sigma originated at Motorola in 1987 which was meant to mainly focus on defect reduction and improved yield. Bill Smith started it in the pager making unit to reduce defects and got breakthrough results. This was later modified and adapted by many companies [3, 5].

In 2001, Nevelainen et al. did a first study which benchmarked the laboratory quality in six sigma scale [6]. Since then six sigma tool have been used by laboratories to check method quality, QC optimization, change the number of rules and controls run and to change the frequency of QC. Mao et al., used Six sigma to assess quality of an instrument and Xia et al., utilized six sigma for risk assessments connecting test results to patient care [7, 8].

So, six-sigma can be used as a tool not only to count defects but also to assess analytical methods, optimize QC plans and compare analytical quality of instruments and so on. Laboratories face quality challenges and need to continually improve their processes and work cultures, six-sigma would be an added tool in the quality process which will help laboratories in their self-improvement.

Materials and methods

Study type: Retrospective study

Data collection

Study data were extracted during July 2020 to December 2020 from Clinical Biochemistry Laboratory, GAIMS and G.K General Hospital, Bhuj after taking ethical approval from GAIMS, IEC committee. The data obtained for the study are coefficient of variation percent (CV%) from internal quality data and Bias (%) for parameters glucose (Hexokinase method), urea (Urease method), creatinine (Enzymatic Creatinine method), alanine aminotransferase (ALT or SGPT) (IFCC Kinetic method), aspartate aminotransferase (AST or SGOT) (IFCC Kinetic method), cholesterol total (Cholesterol oxidase and peroxidase method), triglyceride (GPO - TOPS endpoint method) and HDL (Direct method) (response of question two from EQAS. This study was done to assess the performance of these 08 biochemical parameters run on fully automated biochemistry analyzer on a sigma scale by calculating the sigma metrics for each parameter.

Formulas used for statistical analysis

Sigma: Sigma metrics was calculated with the following formula:

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

Where, TEa: Total Error Allowable,
Bias: Indicator of systematic error and
CV: Coefficient of variation is the indicator of random error.

Total allowable error: Analytical quality requirements are defined by Clinical Laboratory Improvement Amendment (CLIA) -88, Proficiency Testing Criteria in terms of total allowable error "TEa" (or more correctly "total allowable variation") for acceptable performance for each parameter [5].

Bias: The systematic difference between the expected results obtained by the lab's test method and the results obtained from peer group mean is called Bias.

Bias percentage for each parameter was calculated from the Biorad-EQAS.

$$\text{Bias\%} = \frac{\text{mean of all laboratories using same instrument and method - our mean)}}{\text{mean of all laboratories using same instrument and method}} \times 100$$

The average bias of six months period (July 2020 to December 2020) was used for sigma value calculation.

Coefficient of variation (CV): CV is called the coefficient of variation of the analytical test method. CV was obtained from the calculated laboratory mean and calculated standard deviation, obtained from 6 months of IQC data.

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

Quality Goal Index (QGI) ratio: QGI ratio represents the relative extent to which both bias and precision meet their respective quality goals [5]. This was used to analyze the reason for the lower sigma in parameter, i.e., the problem is due to imprecision or inaccuracy or both.

The QGI ratio was calculated using the following formula:

QGI = Bias/1.5 × CV% [5].

The criteria used for interpreting QGI when test parameters fall short of Six-Sigma quality is shown in Table 2.

Results

Table 1, Table 2 and Table 3 shows TEa for some of the common biochemical investigations as per CLIA recommendation, level of sigma metrics and the corresponding defects per million tests, and criteria for interpreting QGI ratio respectively.

Table 1: Shows TEa for some of the common biochemical and other investigations as per CLIA recommendation.

Parameter or test	*CLIA criteria for Acceptable performance*
Blood glucose	Target value ±10% or 6mg/dl (greater)
Blood urea	Target value ±9 % or 2 mg% (greater)
Creatinine	Target value ±15% or ± 0.3 mg/dl/ (greater)
ALT (SGPT)	±20%
AST (SGOT)	±20%
Cholesterol total	±10%
Triglyceride	± 25%
HDL	±30%

Table 2: Level of sigma metrics and the corresponding defects per million tests.

Six sigma level	*Percentage accuracy*	*Defects per million*
1	99.9997	3.4
2	99.98	233
3	99.4	6210
4	93.3	66,807
5	69.1	308,537
6	31	698,000

Table 3: Criteria for interpreting Quality Goal Index ratio.

QGI	*Problem*
<0.8	Imprecision
0.8-1.2	Imprecision and inaccuracy
>1.2	Inaccuracy

Table 4 summarizes the CV% of level 1 IQC for 8 biochemical parameters from July 2020 to December 2020 and their average.

Table 4: Month wise Coefficient of variation percentage of level 1 IQC (response of question three of parameters during July 2020 – December 2020.

Parameter	*CV percentage level 1 IQC (response of question three)*						*Average*
	July	*August*	*September*	*October*	*November*	*December*	
Glucose	1.69	2.23	2.02	1.88	1.96	2.12	1.98
Urea	1.98	1.67	1.96	1.87	1.54	1.62	1.77
Creatinine	2.58	2.59	2.54	2.52	2.49	2.51	2.54
ALT (SGPT)	3.64	3.26	3.35	3.44	3.33	3.4	3.40
AST (SGOT)	4.02	3.98	4.21	4.16	3.97	4.12	4.08
Cholesterol	1.76	2.14	1.89	1.87	2.03	1.74	1.91
Triglyceride	4.7	4.23	4.23	4.67	4.97	4.4	4.53
HDL	2.97	3.32	2.89	2.96	3.04	3.19	3.06

Table 5 summarizes the CV% of Level 2 IQC for 8 biochemical parameters from July 2020 to December 2020 and their average.

Table 5: Month wise coefficient of variation percentage of level 2 IQC of parameters during July 2020 – December 2020.

Parameter	*CV Percentage level 2 IQC*						*Average*
	July	*August*	*September*	*October*	*November*	*December*	
Glucose	1.70	1.56	2.10	1.90	2.19	2.00	1.90
Urea	1.67	1.78	2.02	1.95	2.01	1.87	1.88
Creatinine	2.29	2.59	2.42	2.2	2.12	2.35	2.32
ALT (SGPT)	3.59	4.22	3.35	3.89	4.02	3.95	3.84
AST (SGOT)	4.39	4.67	4.02	3.89	4.35	4.24	4.26
Cholesterol	1.57	1.67	2.20	2.17	2.21	2.24	2.01
Triglyceride	4.78	4.90	4.91	4.70	5.12	4.64	4.84
HDL	3.13	3.12	3.20	3.33	2.90	3.30	3.16

Table 6 summarizes the Bias% obtained from Bio-Rad EQAS for 8 biochemical parameters from July 2020 to December 2020 and their average.

Table 6: Month wise Bias of parameters during July 2020 – December 2020.

Parameter	*Bias percentage*						*Average*
	July	*August*	*September*	*October*	*November*	*December*	
Glucose	3.49	3.63	3.5	3.45	3.61	3.45	3.52
Urea	3.04	2.97	3.09	3.05	3.01	3	3.03
Creatinine	2.34	2.31	2.36	2.31	2.29	2.31	2.32
ALT (SGPT)	9.97	10.02	10.1	9.97	10.01	10.1	10.03
AST (SGOT)	9.1	8.97	8.99	9.06	9.07	9.05	9.04
Cholesterol	2.69	2.57	2.72	2.65	2.68	2.69	2.67
Triglyceride	5.71	5.62	5.69	5.63	5.72	5.64	5.67
HDL	18.28	18.26	18.19	18.27	18.39	18.37	18.29

Table 7 shows that, the sigma metrics of both level 1 and level 2 shows that 2 parameter (ALT and AST) failed to meet minimum sigma quality performance with sigma metrics < 3 and another 6 parameter (glucose, urea, creatinine, cholesterol, triglyceride and HDL) performance with sigma metrics was between 3 and 6.

Table 7: The sigma metrics from Tea (%), average CV(%), and Bias (%).

Parameter	*TEa (%)*	*Average Bias*	*Level 1*		*Level 2*	
			CV	*Sigma value*	*CV*	*Sigma value*
Glucose	10	3.52	1.98	3.27	1.90	3.41
Urea	09	3.03	1.77	3.31	1.88	3.17
Creatinine	15	2.32	2.54	4.99	2.32	5.46
ALT (SGPT)	20	10.02	3.4	2.93	3.84	2.59
AST (SGOT)	20	9.04	4.08	2.67	4.26	2.57
Cholesterol	10	2.67	1.91	3.85	2.01	3.64
Triglyceride	25	5.67	4.53	4.29	4.84	3.99
HDL	30	18.29	3.06	3.77	3.16	3.70

Table 8 shows the QGI ratio of both level 1 and level 2, for ALT and AST, with < 3 sigma value; QGI was >1.2 indicating inaccuracy.

Table 8: Biochemical parameters performing low on sigma metrics (below 3 and QGI ratios for the cause for the low sigma values.

Parameter	*Level 1*			*Level 2*		
	Sigma value	*QGI*	*Cause*	*Sigma value*	*QGI*	*Cause*
ALT (SGPT)	2.93	1.96	Inaccuracy	2.59	1.74	Inaccuracy
AST (SGOT)	2.67	1.48	Inaccuracy	2.57	1.41	Inaccuracy

Discussion

Most of the laboratories design the Quality Control protocol for the number of times and number of levels of IQC is scheduled per day according to the guidelines of National Accreditation Bodies. However, as per good laboratory practice (GLP), every individual laboratory requires to design a personalized Individualized Quality Control Plan (IQCP) protocol based on Sigma(values obtained from Sigma metric [9]. The sigma metrics integration reduce laboratory errors by maintaining six standard deviations between the parameter upper and lower limits and its average [10].

Achievement of six-sigma is considered as the gold standard to define world class measurement of quality. In clinical laboratory, six sigma methodology give attention on regulating a process within 6 standard deviations which represents 3.4 defects per million opportunities [11]. Process performance at the 3-sigma level is considered as the minimum acceptable level of quality. The sigma metrics represent the association among the numbers of wasted operating costs, product defects, and customer satisfaction. Therefore, as sigma increases, the consistency, reliability, steadiness and overall performance of the test improves, thereby decreasing the operating costs [12]. When the method quality goals are set at six sigma, stringent internal QC rules are mandatory. Though, on the bases of study done by Chaudhary et al., keeping in mind the false rejections rate, this can be minimized by relaxing control limits up to 3 standard deviation(SD) [13]. On other hand, according to the study done by Chaudhary et al., if method is performing at sigma level < 3, it will require to execute a newer and better methodology because quality of the test cannot be assured even after multiple Quality Control cycles

[3, 13]. Application of six sigma in clinical laboratory involves calculating the performance of the test method using standard QC procedures and also specifying the quality requirements for the test in term of total allowable error (TEa) [13]. It also require continuous scrutiny of the data, computing a six sigma value, lateral thinking of process based on the data analysis and long term follow up [13, 14].

The quality requirements, expressed as total allowable error. (TEa), should indicate the degree of change that needs to be detected in a parameter for a clinically important decision to be made with regard to further investigation or treatment. Internal and external Quality Control materials are used for monitoring the performance and outcome of analytical methods [13]. When process performance is validated in opposition to Westgard rules or any other QC criteria for acceptability of control data, chances for rejection and probability of error detection are of paramount importance [15].

In present study, we obtained values of six sigma for glucose, urea, creatinine, ALT (SGPT), AST (SGOT), cholesterol, triglyceride and HDL for both the levels of IQC.

Present study observes that 2 parameters (ALT and AST) failed to meet minimum sigma quality performance with sigma metrics < 3 and another 6 parameters (glucose, urea, creatinine, cholesterol, triglyceride, and HDL) performance with sigma metrics was between 3 and 6. A similar result was observed in a study done by Kumar et.al. that sigma value of ALT for level 1 was 2.56 and sigma values of glucose, creatinine, AST, cholesterol, triglyceride and HDL was between 3and 6 [16]. This result contradict with the studies given by Singh et al., Nanda et al., and Garber [17-19].

Different methodology, QC material, traceability calibrators, instruments, and other analytical/ pre-analytical conditions can create the variations in sigma values for few parameter between present study and others.

QGI ratio was calculated for the parameters whose sigma value was observed below 3 to determine the cause of errors. The problem was identified to be inaccuracy for ALT and AST for both level 1 and level 2 with QGI was >1.2. However in studies done by Kumar et al, QGI values for ALT and AST were recorded below 1.2, indicating imprecision [16, 20]. Hence, on the bases of a study done by Westgardet al. 2006, a very stringent IQC protocol needs to be followed, frequent IQC are required, and remedial actions are required for these parameters [10].

According to current study, sigma metrics founds as a good quality tool to assess the analytical performance of a clinical biochemistry laboratory.

Conclusion

In our laboratory , on applying sigma value metrics for the analytical phase, the good performance was noted for glucose, urea, creatinine, cholesterol, triglyceride, HDL, whose sigma was between 3 to 6 and the problem parameters were noted to be ALT and AST with sigma value <3. A method sigma below 3 calls for the adoption of a newer and better method as quality of the test cannot be assured even after repeated QC runs. Employing six sigma metric methods in laboratory involves quantifying the performance of the test using standard Quality Control methods. The application of six-sigma method is necessary to minimize both variance and QC processes to improve the compliance with the vital condition. Sigma value metrics will also assist the application of superlative analytical methods in order to improve laboratory performance. Thus, clinical biochemists should set the realistic quality goals for the clinical labs. Along with that clinical biochemists should also look after the natural random errors and performance potential of biochemistry analyzers. It is also critical to execute suitable Quality Control planning to facilitate the most admirable laboratory performance. On application of QGI for parameters <3 sigma, the problem is identified to be inaccuracy for SGPT and SGOT. Therefore, sigma metric analysis provides point of reference to design a protocol for IQC for the laboratory, address poor assess performance, and assess the existing laboratory process efficiency.

Conflicts of interest

Authors declare no conflicts of interest.

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