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Six sigma in clinical biochemistry: It matters, measure it

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Abstract

Introduction: Accurate test results are the core of healthcare system since physician's decisions mostly depends on the laboratory results. The evaluation of laboratory performance is critical to maintain accurate laboratory results. Nowadays six sigma is the newest version of total quality management. It is quantitative goal for process performance. We aimed to gauge our clinical biochemistry laboratory performance on sigma metrics.

Materials and Method: Internal Quality control (QC) and proficiency testing data for 12 clinical chemistry analytes for two COBAS 400 *Plus* clinical biochemistry auto-analyzers were analyzed retrospectively over a period of 12 months from July 2012 to June 2013. For all 12 analytes the coefficient of variation was calculated for both the levels of IQC, percentage bias was calculated from EQAS. Process sigma was calculated using CV%, Percentage bias and TE_a values of various parameters were taken from Clinical Laboratories Improvement Act (CLIA) guidelines.

Results: Satisfactory sigma values (> 6) were derived for Alkaline Phosphatase, Aspartate aminotransferase, Alanine aminotransferase (L2), Triglycerides, Uric acid, Glucose (L2) signifying less stringent QC rules in an order to achieve high error detection and low false rejection. For parameters - Albumin, Alanine aminotransferase (L1), Total Cholesterol, Total Bilirubin, Glucose (L1), Total Protein the sigma values were found between 3 & 6, signifying more QC rules to be implemented. Urea and Creatinine analytes performed poorly on the sigma scale with sigma < 3, signifying needs improvement in these methods. No significant difference was found in both COBAS equipments in context to sigma value.

Conclusion: Application of six sigma principles would significantly helps in improving IQC process as well provides the scientific basis for recommendation of amount of QC that is actually needed.

Keywords: Clinical Chemistry, Six sigma, Total allowable error, Bias, Coefficient of variance

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Introduction

Clinical laboratories are indispensable part of healthcare services, as most of the time physicians have to makes their crucial decisions in an accordance with clinical laboratory results for screening, diagnosis and monitoring diseases.[1] For that reason the laboratory must be able to produce not only an accurate but precise test result too. In an order to produce accurate as well as precise test results, all clinical laboratories need to follow strict Quality planning. Quality planning defines quality standards on the basis of quality laboratory processes, quality control (QC), quality assessment (QA) and quality improvement. Quality control validation is used to determine the statistical QC procedures appropriate for distinguishing variations critical for clinical interpretation of the test.[2]

The term "quality control" (QC) has been introduced in the clinical laboratory setting many years ago. Quality controls (QCs) in the Clinical biochemistry laboratory setup are of two types, internal QC and external QC. The internal quality control is run daily and results are interpreted by the standard Westgard rules. While the external quality control is run only once a month and results are interpreted by Z score and Standard deviation index (SDI). Commonly, a Z score of less than 1.0, from zero is excellent and up to 2.0 it is acceptable. If we talk about SDI zero indicates perfect comparison, an SDI < 2.0 is acceptable and > 2.0 is unacceptable. But exact number of errors done by the laboratory cannot be assessed by running internal and external QCs.[3,4]

In clinical laboratory, recently new quality assessment (QA) systems Six Sigma became more popular because it offers a different approach to problems. The Six Sigma plan measures the degree to which any process deviates from its goal. Actually sigma (σ) is the mathematical symbol for standard deviation (SD).[5] Motorola Company has developed six sigma methodology as part of quality measurement and improvement program in early 1980s since then it has been applied widely in business and industry to reduce the cost of products, eliminate defects and decrease variability in processing. It consists of five steps: define, measure, analyze, improve and control (DMAIC).[6-8] Six sigma can be applied to all sectors of industry, business and healthcare laboratory too. The sigma value shows how often errors or defect are likely to occur and it is measured as defects per million (DPM). The number of errors or defects done by the laboratory can be quantified by employing six sigma in the laboratory. The relationship between sigma metrics and defects are as follow: 1 sigma (σ) represents

6,90,000 errors/million reports, 2 sigma represents 3,08,000 errors/million reports, 3 sigma represents 66,800 errors/ million reports, 4 sigma represents 6,210 errors/million reports, 5 sigma corresponds to 230 errors/million reports and 6 sigma represents 3.4 errors/million reports.[9] Higher the sigma value, it is less likely that the process will produce errors. Six Sigma focuses on controlling a process to 6 SDs, which equates to 3.4 DPM opportunities. Achievement of Six Sigma quality is considered to be a standard of excellence. Performance at the 3-sigma level is considered the minimum acceptable quality for a production process.[10] If a method has a sigma value below 3, the method is considered to be unreliable and should not be used for routine test purposes.[5]

The present study was undertaken to evaluate the performance of clinical chemistry analytes of two COBAS integra 400 plus auto-analysers by calculating the sigma metrics for individual parameters and to determine the errors associated with each parameter.

Aims and Objectives

To understand the value of Six Sigma performance and apply it to quantify our laboratory performance on Sigma metrics.

Materials and Method

We had analyzed internal quality control data in the clinical biochemistry laboratory which is a part of central diagnostic laboratory. Our clinical biochemistry laboratory having NABL accreditation since more than 7 years provides service to 650 bedded tertiary care hospital, which is NABH accredited. Internal quality control (IQC) data of 12 analytes were analyzed retrospectively over a period of 12 months from July 2012 to June 2013 for two COBAS integra 400 *plus* fully automated chemistry analyzers for both normal (L1) and pathological (L2) levels. Two levels of internal QC materials were assayed daily for all 12 analytes, results were plotted on Leavy-jennings chart and followed westgard rules to monitor quality of test results before commencing reporting of patient samples. Both equipments were calibrated as per manufacturers' guidelines and as and when required. Our laboratory is also participated in monthly Bio-Rad EQAS (External Quality Assessment Scheme) program.

The analytes assessed were plasma Glucose, Urea, Creatinine, Uric acid, Total Bilirubin, Total Protein, Albumin, Alanine Aminotransferase, Aspartate Aminotransferase, Alkaline phosphatase, Total Cholesterol and Triglycerides. Total allowable error (TEa): It is the total allowable difference from accepted reference value seen in the deviation of single measurement from the target value. TE_a values of various parameters were taken from Clinical Laboratories Improvement Act (CLIA) guidelines.[11]

Bias: Bias is the systematic difference between the expected results obtained by the laboratory's test method and the results that would be obtained from an accepted reference method. Bias was derived from proficiency testing (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

Coefficient of Variance (CV%) is the analytical coefficient of variation of the test method. Coefficient of variance (CV) was calculated from Randox internal QC material data for all the parameters.

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

Sigma metrics were calculated from CV, percentage bias and total allowable error for all the parameters by the following formula:

Process Sigma Σ (σ) = (TE_a - bias) / CV% [TE_a = total allowable error, CV% = Coefficient of variance]

Observation and Result

Internal Quality control (QC) and proficiency testing data for 12 clinical chemistry analytes for two COBAS 400 *Plus* clinical biochemistry auto-analyzers were analyzed retrospectively over a period of 12 months from July 2012 to June 2013. For all 12 analytes the coefficient of variation was calculated for both the levels of IQC, percentage bias was calculated from EQAS. Process sigma was calculated using CV%, Percentage bias and TE_a values of various parameters were taken from Clinical Laboratories Improvement Act (CLIA) guidelines. Following results were obtained.

Table 1: TEa, CV (%), bias (%) for different parameters for both levels of quality control for instrument 1

Parameter	TEa	BIAS %	CV % (L1)	CV % (L2)
Albumin	10	0.88	1.88	2.06
Alkaline Phosphatase	30	3.82	2.86	2.66
Alanine Aminotransferase	20	3.79	3.56	1.74
Aspartate Aminotransferase	20	2.39	2.27	1.64
Bilirubin Total	20	3.41	3.7	3.31
Cholesterol Total	10	2.05	1.78	1.35
Creatinine	15	5.04	4.31	3.56
Glucose	10	1.09	1.7	1.43
Total Protein	10	1.47	1.85	1.68

Triglycerides	25	2.38	1.57	1.26
Uric Acid	17	2.86	1.51	1.32
Urea	9	3.28	2.8	2.21

Table 2: TEa, CV(%) , bias (%) and sigma value for different parameters for both levels of quality control for instrument 2

Parameter	TEa	BIAS %	CV % (L1)	CV % (L2)
Albumin	10	1.78	2.04	1.89
Alkaline Phosphatase	30	3.43	3.08	2.74
Alanine Aminotransferase	20	4.25	3.33	1.61
Aspartate Aminotransferase	20	1.71	2.33	1.58
Bilirubin Total	20	3.74	4	3.77
Cholesterol Total	10	1.52	1.94	1.65
Creatinine	15	6.11	3.6	3.53
Glucose	10	1.79	1.93	1.59
Total Protein	10	1.43	2.05	1.85
Triglycerides	25	2.3	1.87	1.84
Uric Acid	17	1.4	1.65	1.49
Urea	9	2.99	3.2	2.65

Average percentage bias was calculated from data of external quality assurance program provided by Bio-Rad (EQAS) for the months of July 2012 to June 2013 for the different parameters. This is tabulated in Table 1 & 2.

Table 3: Six sigma metrics (σ) of all parameters by CLIA (clinical laboratories improvement amendments act) guidelines for TEa

Six Sigma Metrics (σ)				
Parameter	Cobas Integra 400 plus 1		Cobas Integra 400 plus 2	
	L1	L2	L1	L2
Albumin	4.85	4.43	4.03	4.35
Alkaline Phosphatase	9.15	9.84	8.63	9.7
Alanine Aminotransferase	4.55	9.32	4.73	9.78
Aspartate Aminotransferase	7.76	10.7	7.85	11.6
Bilirubin Total	4.48	5.01	4.07	4.31
Cholesterol Total	4.47	5.89	4.37	5.14
Creatinine	2.31	2.8	2.47	2.52
Glucose	5.24	6.23	4.25	5.16
Total Protein	4.61	5.08	4.18	4.63
Triglycerides	14.4	18	12.1	12.3
Uric Acid	9.36	10.7	9.45	10.5
Urea	2.04	2.59	1.88	2.27

The sigma value > 6 was observed for ALP, AST, triglyceride, uric acid; 3-6 for albumin, bilirubin total, cholesterol, glucose and total protein; < 3 for creatinine and urea for both the levels of QC for both instruments. ALT depicted a sigma value of > 6 for pathological level of QC whereas sigma value of 4.94 and 4.32 were observed for normal level of QC for both instruments Table 3.

Discussion

Physician and surgeons depends on laboratory doctor for make their crucial decision. As a laboratory person it is our duty to provide quality test result to physician or surgeons, as single errors or defect in test result may alter plan of treatment, for that we need to maintain quality of test result. We can define quality as a spectrum of activities and processes that shape the characteristics of a product or service. For the same we are using six sigma in clinical biochemistry laboratory, six sigma focuses on gathering data, analyzing the collected data and thereafter improving the quality. The sigma metrics is based on the statistical concept: laboratory errors can be reduced by maintaining 6 standard deviations between the parameter average and its upper and lower limits.

Table 4: Describes the comparison of our sigma values with various other studies

		Bhavna Sing et al.[9]	Sunil Nanda et al.[10]	Nitinkumar et al.[11]	Present study
Total analytes		15	13	10	12
Study period		6 months	6 months	4 months	12 months
Instrument used		Olympus biochemistry analyser	Cobas integra auto-analyser	ILAB-650 auto-analyser	Cobas integra 400 plus auto-analyser
Total instrument		1	1	1	2
Internal Quality Control material		Randox	Bio-Rad	Bio -Rad	Randox
QC level		2	2	2	2
EQAS		Randox	CMC	Bio-rad	Bio-Rad
TEa Guidelines		CLIA	CLIA	CLIA	CLIA
Six sigma	> 6	Creatinine, HDL, ALP, Bilirubin	Bilirubin, UA, ALT, AST, ALP		ALP, AST, ALT (L2), TG, UA, Glucose (L2)
	3-6	Glucose, Urea, ALT, AST, CK, Amylase	Creatinine, TG, Urea	Glucose, ALP, total protein, TG, HDL, UA Amylase	Albumin, ALT (L1), Total Cholesterol, Total bilirubin, Glucose (L1), Total protein
	<3	Cholesterol, TG, Protein, Na, K	Protein, Albumin, Cholesterol, Cl^-	ALT, AST, Cholesterol	Urea, creatinine

The discrepancy in sigma metrics by various study compared can be attributed to difference in method of analytes, different IQC material, difference in bias calculated due to different proficiency testing bodies (Table 4).

Sigma values are useful for guiding QC strategy design. When goal of any method is set at six sigma, it is mandatory to follow stringent internal QC rules. However in such cases to minimize false rejections we can relax control limits up to 3 SD [J]. If the method has sigma $\leq$ 3, we need to employ a newer or better method, as quality of the test result can't be assured even after multiple QC repetition.[10] Any parameters demonstrate a wide difference in sigma values in the levels of QC need to evaluate with caution and if required the methodology should be re-evaluated. Particularly for that methodology there is also a requirement of strict follow-up of westgard multi rules as well as increase QC runs in term of numbers to prevent discrepancy. Finally the ultimate goal of six sigma methodology in clinical laboratory is to promote our medical laboratory service quality, achieve good cost-effective outcome and provide the best patient care. It will also helpful by effectively decreasing the probability of false rejection (Pfr) and increasing the probability of error detection (Ped).

Conclusion

Application of six sigma principles would significantly helps in improving IQC process as well provides the scientific basis for recommendation of amount of QC that is actually needed. Six Sigma methodology is the ideal choice to solve analytical and managerial problems in laboratory medicine as well to decrease errors to a negligible level. We assessed 12 analytes of clinical chemistry of two levels of two instruments by sigma scale. Sigma value of more than six was found for ALP, AST, TG and uric acid which does not require stringent quality control .Sigma value of 3-6 was found for albumin, cholesterol, total bilirubin and total protein. Whereas sigma was found below 3 for creatinine and urea, which requires adoption of a newer and better method or more stringent QC runs and rules application. We did not find significant differences in performance of QC on the 2 analyzers.

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