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Original Research Article

Evaluation of Laboratory Performance of Biochemical Parameters using Sigma Metrics

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Abstract

Introduction : Since the time of Hippocrates the Latin phrase "*primum non nocere*" i.e. "*first, do no harm*" has been taught to medical students. In laboratory practice, this is applicable to minimizing error rates,as clinical decision making is based largely in accordance with the laboratory results. Modern quality management tools such as Six Sigma can be the solution towards achieving error free laboratory reports. Six sigma refers to world class quality with a defect rate of 3.4 defects or errors per million opportunities.. The present study was undertaken to analyse the performance of biochemical parameters routinely tested in our laboratory in terms of six sigma scale and to develop a strategy for continuous quality improvement process.

Materials and Methods: This was retrospective study to analyse and evaluate the performance of 25 biochemical tests in our laboratory from January to December 2017. All the biochemical analytes were run on Dade Dimension RxL Max. Internal and External controls were procured from Biorad Laboratories, USA. Two levels of IQC Normal (Level 1) and Abnormal (Level 2) were run for each parameter twice a day. The TEa for calculating sigma metrics were taken from CLIA Guidelines.

Results :-. In Level 1, 4 analytes: Chloride, SGPT (ALT), Calcium and Urea sigma value was below 3, 7 analytes: Lipase, Albumin, Direct Bilirubin, Total Bilirubin, Cholesterol, Creatinine and Glucose sigma value was between 3–6, 14 analytes: Potassium, Sodium, Alkaline Phosphatase, Amylase, SGOT (AST), HDL Cholesterol, LDL Cholesterol, GGT, Iron, Phosphorus, Total Protein, TIBC, Triglycerides, Uric Acid sigma value was above 6.

In Level 2, 2 analytes: Chloride, Calcium sigma value was below 3, 7 analytes: Lipase, Albumin, Total Bilirubin, Direct Bilirubin, Cholesterol, Glucose, Total Protein and TIBC, sigma value was between 3 – 6, 16 analytes: Potassium, Sodium, Alkaline Phosphatase, SGPT (ALT (SGPT)), Amylase, SGOT (AST (SGOT)), Total Bilirubin, Direct Bilirubin, HDL Cholesterol, LDL Cholesterol, Creatinine, GGT, Iron, Phosphorus, Triglycerides, Uric Acid sigma value was above 6.

Conclusion: A Rational QC design is needed to be optimize the QC procedures, reduce the cost of running daily QC and to solve analytical problems and decrease the number of errors to a minimal level. Using six sigma in clinical laboratories has been shown to refine patient care by eliminating the need to retrace steps, correcting errors in laboratory reports and re-performing tests which are wasteful processes both in terms of economics as well as patient dissatisfaction and discomfort

Keywords: Six Sigma; Total Quality Management; QC.

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Introduction

Since the time of Hippocrates the Latin phrase "*primum non nocere*" i.e. "*first, do no harm*" has been taught to medical students. In laboratory practice, this is applicable to minimizing error rates, as clinical decision making is based largely in accordance with the laboratory results [1]. From this point of view, performance of a laboratory can be evaluated depending upon the accuracy of the laboratory results [2]. It has been reported by the Institute of Medicine, that every year in USA approximately 98,000 people succumb to medical errors [3]. It is said that to "err is human" but finding solutions to these errors is also a part of human nature. Modern quality management tools such as Six Sigma can be the solution towards achieving error free laboratory reports. The total testing procedure in a laboratory is divided into pre-analytical, analytical and post-analytical phases and it is estimated that about 30-75% errors occurs in the pre-analytical phase, 4-30% in the analytical phase and 9-55% in the post-analytical phase of the total testing process [4]. The main objective of the internal quality control in a laboratory is to ensure that accurate and precise results are produced. In a medical laboratory quality is controlled by a statistical process to monitor and evaluate the testing process. In recent years Six Sigma has been implemented in medical laboratories to improve clinical quality and outcomes. ISO 15189 has recommended monitoring of quality management system in the laboratory to improve the laboratory services [5]. The implementation of Six Sigma principles and tools can be applied to assess laboratory performance and measure error rates and to assess to which degree any process deviates from its objective. Six sigma refers to world class quality with a defect rate of 3.4 defects or errors per million opportunities [6]. Higher the six sigma, lower the possibility of error in the system and better is the performance of the system [7,8]. In the clinical laboratory, it has now been widely used to assess laboratory performance in the terms of accuracy of results, customer satisfaction and to establish benchmarks in total quality management [9,10]. The present study was undertaken to analyse the performance of biochemical parameters routinely tested in our laboratory in terms of six sigma scale and to develop a strategy for continuous quality improvement process.

Materials and Methods

This was retrospective study to analyse and evaluate the performance of 25 biochemical tests in our laboratory from January to December 2017. The biochemical parameters are given in Table 1.

Table 1: Showing parameters included in the study

Sl. No.	Parameters
1	Lipase
2	Chloride
3	Potassium
4	Sodium
5	Albumin
6	Alkaline Phosphatase
7	ALT (SGPT)
8	Amylase
9	AST (SGOT)
10	Direct Bilirubin
11	Total Bilirubin
12	Calcium
13	HDL Cholesterol
14	LDL Cholesterol
15	Cholesterol
16	Creatinine
17	GGT
18	Glucose
19	Iron
20	Phosphorus
21	Total Protein
22	TIBC
23	Triglycerides
24	Urea
25	Uric Acid

Table 2: Showing the CV% of parameters from January – June 2017

S. No.	Parameter	Jan.		Feb.		Mar.		Apr.		May		Jun.		Jul.		Aug.		Sept.		Oct.		Nov.		Dec.		Average	
		L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2
1	Lipase	4.6	6.2	4.7	8.5	3.1	5.1	3.3	1.8	6.2	7.9	14.7	13.7	7.79	4.6	7.1	8.4	10.0	11.9	4.2	4.9	4.7	5.7	3.7	3.8	6.33	6.73
2	Chloride	2.88	2.09	2.37	4.87	1.6	1.57	1.44	0.95	1.71	1.02	1.41	1.07	1.01	1.48	1.26	1.00	2.9	1.75	0.77	0.48	0.49	0.59	0.67	0.47	1.43	1.56
3	Potassium	1.67	3.14	3.06	0.75	2.42	1.23	3.36	2.05	1.07	1.11	1.38	0.8	1.68	1.77	1.98	1.17	5.63	0.64	1.69	0.87	1.43	0.62	1.69	0.98	1.59	1.93
4	Sodium	1.77	1.92	1.63	1.59	1.64	1.18	1.33	1.35	0.83	0.65	0.98	0.77	0.98	2.00	1.21	1.48	1.08	0.68	0.8	0.79	0.5	0.58	0.77	0.77	1.24	1.07
5	Albumin	2.5	3.8	2.1	1.9	3.0	1.9	1.8	2.3	1.7	1.7	1.7	2.2	1.9	2.3	2.0	2.1	3.1	2.9	2.1	2.4	2.1	1.6	2.1	2.4	2.20	2.26
6	Alkaline Phosphatase	3.8	4.2	3.7	1.8	3.8	2.8	4.9	3.5	4.1	3.2	4.4	3.1	5.3	2.8	4.0	2.2	4.2	2.3	3.8	2.8	4.1	2.6	4.2	3.2	3.39	3.69
7	ALT (SGPT)	8.8	4.5	7.5	2.4	7.9	2.6	8.8	3.3	7.1	2.5	6.8	2.5	6.2	3.3	5.0	1.4	4.6	2.0	5.0	3.7	4.4	2.5	4.6	4.2	5.34	3.97
8	Amylase	1.3	3.1	1.5	1.2	1.6	1.2	1.5	2.0	1.2	1.6	1.6	1.8	2.2	1.5	1.0	0.8	2.3	2.0	1.9	1.8	2.1	1.6	2.2	1.9	1.53	1.89
9	AST (SGOT)	3.7	4.0	3.7	1.9	3.1	1.6	7.4	3.7	3.1	2.3	3.0	2.3	4.1	2.6	2.5	2.1	2.4	2.2	3.5	2.6	3.6	2.6	4.1	3.2	3.28	3.00
10	Bilirubin - Direct	8.2	4.1	5.2	1.9	4.4	1.5	8.6	2.6	5.2	1.7	7.3	1.3	6.9	2.6	9.5	2.7	9.7	3.6	5.0	2.2	4.8	2.0	4.9	2.2	4.52	4.49
11	Bilirubin - Total	4.2	4.3	2.9	1.8	2.7	1.8	6.8	3.2	5.1	2.2	3.1	2.2	2.7	1.6	3.1	1.7	3.5	2.2	3.9	2.2	3.4	1.9	2.7	1.7	3.01	2.90
12	Calcium	2.6	3.7	2.3	1.9	2.4	1.9	2.3	2.4	3.7	2.8	3.0	3.0	2.4	2.5	2.9	1.9	1.6	2.1	2.3	2.8	3.2	3.1	2.0	2.1	2.57	2.51
13	HDL Cholesterol	4.2	9.5	1.9	3.5	3.5	1.7	2.8	5.0	2.2	2.9	2.0	3.2	1.9	2.8	3.5	7.8	2.4	7.5	2.9	3.3	2.0	2.2	2.1	2.5	3.56	3.39
14	LDL Cholesterol	2.7	4.1	2.2	1.8	2.2	1.6	3.0	3.6	3.0	3.1	2.6	3.6	4.3	4.3	1.7	2.6	1.4	2.6	2.5	3.0	2.7	2.5	2.6	3.3	2.84	2.66
15	Cholesterol	2.0	4.4	1.8	3.4	2.2	3.9	2.5	2.7	2.0	3.0	2.1	2.5	2.6	3.0	2.3	1.9	1.4	2.1	2.4	2.2	2.4	2.8	2.7	3.3	2.33	2.81
16	Creatinine	4.5	5.0	3.1	2.6	3.1	2.1	3.0	2.7	3.0	2.3	2.4	2.4	3.7	2.6	2.0	1.6	2.8	2.4	3.2	2.1	2.6	2.1	2.9	2.2	2.68	2.86
17	GGT	6.9	4.2	2.3	2.0	2.1	1.6	2.6	2.8	3.2	2.2	2.4	2.3	3.4	2.2	2.0	1.8	3.2	2.4	3.2	2.2	2.4	3.2	2.5	2.1	2.79	2.65
18	Glucose	1.3	3.5	1.7	1.5	1.8	1.6	2.2	2.2	1.7	1.7	1.8	2.1	2.0	2.3	2.0	1.7	2.5	2.1	2.4	2.5	2.4	2.0	2.1	1.5	1.89	2.17
19	Iron	3.0	4.4	1.3	1.3	1.1	2.2	2.1	3.3	2.0	3.3	1.6	2.6	1.8	2.0	0.7	1.7	1.2	2.0	1.5	1.9	2.3	1.8	1.5	2.1	1.89	2.18
20	Phosphorus	1.7	3.5	1.6	1.6	1.6	1.1	2.6	2.5	2.1	1.5	3.2	2.3	3.8	2.5	2.0	2.1	1.9	1.6	2.3	1.6	2.9	2.4	2.2	1.6	2.05	2.30
21	Total Protein	2.9	4.0	2.2	3.5	1.6	2.0	2.1	2.4	1.6	2.0	1.5	1.9	1.3	1.6	1.7	1.7	1.3	1.7	2.6	2.5	1.3	1.6	1.5	1.8	1.90	2.13
22	TIBC	3.2	6.1	3.1	3.9	2.6	5.2	2.7	4.4	2.3	3.6	2.8	3.3	3.1	3.6	2.3	4.3	2.7	5.3	3.9	4.4	2.1	3.6	4.4	4.3	3.52	3.75
23	Triglyceride	2.2	3.3	1.2	2.1	1.5	2.3	2.1	3.2	1.9	4.6	2.5	3.3	2.2	3.5	1.7	2.2	1.6	2.6	1.9	2.1	2.0	1.9	2.4	3.5	2.27	2.55
24	Urea	7.0	5.4	3.4	2.6	3.4	2.3	4.1	3.1	3.7	2.9	3.0	2.4	4.8	5.4	2.2	1.9	2.8	2.7	3.7	3.1	2.9	2.3	4.2	3.2	3.60	3.28
25	Uric Acid	2.4	2.8	1.7	1.5	1.4	1.4	2.6	2.3	2.0	1.4	2.1	2.0	1.9	1.2	1.6	0.8	1.4	1.3	3.0	1.7	2.5	1.3	2.8	1.7	1.68	2.05

Sigma value of each parameter was determined from January to December 2017 and was calculated with the formula:

$$\text{Sigma Metrics} = \frac{\text{TEa \%} \quad \text{Bias \%}}{\text{CV \%}}$$

Where TEa% is total allowable error percentage and CV% is coefficient of variation (Table 2)

The precision or closeness of agreement between independent results was calculated as CV % from Internal Quality Control data with the formula:

$$\text{CV\%} = \frac{\text{SD}}{\text{Mean}} \text{X100}$$

Monthly CV % of all biochemical analytes is shown in Table 2 The Bias% was calculated from EQAS data with the formula:

$$\text{Bias} = \frac{[\text{Our Lab–Peer Group Mean}]}{[\text{Peer Group Mean}]} \text{X100}$$

The Bias % is shown in Table 3

All the biochemical analytes were run on Dade Dimension RxL Max. Internal and External controls were procured from Biorad Laboratories, USA. Two levels of IQC Normal (Level 1) and Abnormal (Level 2) were run for each parameter twice a day. The TEa for calculating sigma metrics were taken from CLIA Guidelines (Table 4).

A total of 25 biochemical analytes were included in the study. Westgrad rules 1_{2s}, 1_{3s}, R-4s and 10X were used for monitoring IQC results. For EQAS, the 'Z' score or Standard Deviation Index (SDI) between +/- 2.0 was considered to be acceptable. If there was any bias noted, corrective actions were taken to eliminate the bias. The total error was calculated from the formula:

TE = 1.96 x CV% + Bias%

which takes into account both the precision and accuracy of the analyte being measured. If the total error (TE) is less than the total allowable error (TEa), the process is considered to be performing satisfactorily.

The six sigma scale ranges from zero to six with some of the analytes exceeding the

Table 3: Showing Bias% of parameters

Sl. No.	Parameter	BIAS%
1	Lipase	1.38
2	Chloride	1.44
3	Potassium	-2.18
4	Sodium	-0.67
5	Albumin	1.51
6	Alkaline Phosphatase	2.42
7	ALT (SGPT)	-2.31
8	Amylase	-1.72
9	AST (SGOT)	-0.55
10	Bilirubin - Direct	0.73
11	Bilirubin - Total	-0.99
12	Calcium	-1.61
13	HDL Cholesterol	1.55
14	LDL Cholesterol	-0.33
15	Cholesterol	-0.73
16	Creatinine	0.34
17	GGT	0.28
18	Glucose	0.27
19	Iron	0.66
20	Phosphorus	0.54
21	Total Protein	-0.62
22	TIBC	1.22
23	Triglycerides	-1.61
24	Urea	-0.92
25	Uric Acid	-1.17

Table 4: Shows TEa (CLIA) with TE of laboratory

Sl. No.	Parameter	TEa CLIA	Total Error (TE)	
			Level 1	Level 2
1	Lipase	+/-30	13.78	14.56
2	Chloride	+/-5	4.24	4.49
3	Potassium	+/-30	0.93	1.60
4	Sodium	+/-20	1.75	1.42
5	Albumin	+/-10	5.82	5.94
6	Alkaline Phosphatase	+/-30	9.05	9.64
7	ALT (SGPT)	+/-20	8.15	5.47
8	Amylase	+/-30	1.27	1.97
9	AST (SGOT)	+/-20	5.87	5.33
10	Bilirubin - Direct	+/-20	9.58	9.53
11	Bilirubin - Total	+/-20	4.90	4.69
12	Calcium	2.4	3.43	3.31
13	HDL Cholesterol	+/-30	8.53	8.18
14	LDL Cholesterol	+/-30	5.23	4.88
15	Cholesterol	+/-10	3.83	4.78
16	Creatinine	+/-15	5.58	5.95
17	GGT	+/-30	5.74	5.47
18	Glucose	+/-10	3.96	4.51
19	Iron	+/-20	4.35	4.92
20	Phosphorus	+/-12	4.56	5.05
21	Total Protein	+/-10	3.10	3.55
22	TIBC	+/-20	8.11	8.57
23	Triglycerides	+/-25	2.83	3.39
24	Urea	+/-9	6.14	5.50
25	Uric Acid	+/-17	2.12	2.85

six sigma level. In industries, other than healthcare, 3 sigma is considered to be performing properly. When it is below 3, the performance needs to be evaluated with proper corrective and preventive actions (Table 5).

Table 5: Shows Sigma metrics of Biochemical analytes

SI. No.	Parameter	Sigma	
		Level 1	Level 2
1	Lipase	5.72	5.49
2	Chloride	2.32	2.71
3	Potassium	17.53	31.43
4	Sodium	20.37	33.65
5	Albumin	4.00	3.84
6	Alkaline Phosphatase	6.65	10.17
7	ALT (SGPT)	3.63	8.58
8	Amylase	12.19	12.48
9	AST (SGOT)	6.06	8.50
10	Bilirubin - Direct	3.18	9.04
11	Bilirubin – Total	5.92	9.76
12	Calcium	1.73	1.74
13	HDL Cholesterol	11.53	8.23
14	LDL Cholesterol	12.52	11.04
15	Cholesterol	5.11	4.15
16	Creatinine	5.05	6.20
17	GGT	10.9	13.17
18	Glucose	5.03	5.04
19	Iron	13.39	9.06
20	Phosphorus	7.50	8.87
21	Total Protein	6.42	5.25
22	TIBC	6.69	4.52
23	Triglycerides	14.53	9.85
24	Urea	2.82	3.44
25	Uric Acid	9.28	12.64

Result

A total of 25 Biochemical analytes were included in the study during the period from January to December 2017. The sigma metric was calculated for each analyte and sigma scale of 3 was considered to be minimal acceptable for satisfactory performance of the analyte. The sigma metrics calculated for analytes were divided into 3 categories:

i. 0 – 3 sigma

ii. 3 – 6 sigma

iii. Above 6 sigma

In Level 1, 4 analytes: Chloride, SGPT (ALT), Calcium and Urea sigma value was below 3, 7 analytes: Lipase, Albumin, Direct Bilirubin, Total Bilirubin, Cholesterol, Creatinine and Glucose sigma value was between 3–6, 14 analytes: Potassium, Sodium, Alkaline Phosphatase, Amylase, SGOT (AST), HDL Cholesterol, LDL Cholesterol, GGT, Iron, Phosphorus, Total Protein, TIBC, Triglycerides, Uric Acid sigma value was above 6.

In Level 2, 2 analytes: Chloride, Calcium sigma value was below 3, 7 analytes: Lipase, Albumin, Total Bilirubin, Direct Bilirubin, Cholesterol, Glucose, Total Protein and TIBC, sigma value was between 3–6, 16 analytes: Potassium, Sodium, Alkaline Phosphatase, SGPT (ALT (SGPT)), Amylase, SGOT (AST (SGOT)), Total Bilirubin, Direct Bilirubin, HDL Cholesterol, LDL Cholesterol, Creatinine, GGT, Iron, Phosphorus, Triglycerides, Uric Acid sigma value was above 6.

Lowest sigma was observed for Calcium and highest for Sodium and Potassium reaching upto 33.65 sigma scale.

Discussion

Six sigma methodology has been used in business and industries since 1980s for assessment of quality and its management. It was first introduced by Motorola to reduce the costs, to reduce the defects and to minimize differences in processing [12,13]. There are two popular methods for evaluating performance of a process. One is by inspecting the outcomes of any measurement and the other is to evaluate the variation in a process and thereby predicting its performance.

The first approach is done by calculating errors or defects per million and converting it into a sigma scale. In healthcare industry specially, in a laboratory, errors have to be minimized. An error rate of 0.033% is considered to be excellent in any healthcare organization. 1 – 5%. Error rates are considered acceptable corresponding to a sigma scale of 3.85 sigma and above 6 sigma is considered to be of world class quality [14].

When performance falls below 3 sigma, the process is considered to be unstable and unacceptable and proper corrective and preventive action have to be taken.

Six sigma scale provides a universal bench mark for world class quality in any process. In a biochemical laboratory, it compares tests carried out between different instruments, different labs and different methods all over the world.

Nevalainen et al in their study observed that many of the data in all the three phases of the laboratory work did not fit into acceptable six sigma scale [15]. Nanda et al. in their study observed that out of 13 analytes evaluated, 5 analytes showed excellent performance above 6 sigma and 4 showed poor performance [16]. Singh et al. in their study observed poor performance of 3 analytes out of 15 analytes measured in their laboratory [17].

Manchana Lakshman et al in their study found that 11 out of 23 analytes had excellent performance above 6 sigma, 10 analytes between 3-6 sigma and 2 analytes below 3 sigma [18].

The significance of Rational QC design was emphasized by Schoemaker et al by stressing on the need to use Westgrad operational specifications chart (OP Specs Chart) in clinical biochemical laboratories [19].

In our study we observed that in Level 1, 4 analytes out of 25 (16 %) to be below 3 sigma scale, 14 analytes out of 25 (56 %) had excellent performance. 28% analytes showed performance between 3 – 6 sigma scale and in Level 2, 2 analytes out of 25 (8%) to be below 3 sigma scale, 16 analytes out of 25 (64 %) had excellent performance. 28% analytes showed performance between 3 – 6 sigma scale.

Conclusion

Out of 25 biochemical analytes evaluated on a Six Sigma scale in our laboratory 14 analytes in Level 1 and 16 analytes in Level 2 exceeded six sigma scale of world class quality while 4 analytes in Level 1and 2 analytes in Level 2showed below acceptable performance. A Rational QC design is needed to be optimize the QC procedures, reduce the cost of running daily QC and to solve analytical problems and decrease the number of errors to a minimal level. Using six sigma in clinical laboratories has been shown to refine patient care by eliminating the need to retrace steps, correcting errors in laboratory reports and re-performing tests which are wasteful processes both in terms of economics as well as patient dissatisfaction and discomfort. Improving the quality of healthcare is of paramount importance both in terms of customer satisfaction for the services provided as well as clinical outcome of the patient.

Healthcare industry is in its infancy stage with regards to six sigma application. As more and more laboratories will incorporate six sigma for improvement it will bring a radical change in the medical laboratory performance.

Conflict of Interest

None

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