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RESEARCH ARTICLE

"SIX SIGMA METRICS": INDICATOR OF QUALITY ASSURANCE FOR CLINICAL BIOCHEMSITRY

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Abstract

Introduction: In present scenario Quality is the important aspect of laboratory practices. Mostly internal and external quality control are utilized to maintain quality in laboratory. Quality assurance of laboratory services is the need of present time in health care which require Quality Planning, Quality Control (QC), Quality Assessment (QA) and Quality Improvement .

Aims & Objectives:

1. To quantify the defects and errors in analytical phase of laboratory testing by sigma metrics and to represent the calculated sigma value.
2. Application of six sigma test in laboratory with the IQC and EQAS to maintain quality laboratory services.

Methodology: Study was conducted at Clinical Biochemistry Laboratory, GMC Akola. We run IQC samples on daily basis and EQAS samples are running on monthly basis. Retrospectively we utilized data of IQC and EQAS from January to October 2023 for 16 Biochemical Analytes. Sigma metrics for each parameter was calculated.

Result: The sigma metrics for IQC indicated that 1 out of 16 analytes qualified six sigma quality performance. Of these 15 analytes performance with sigma metrics was beteween three and six. We found different sigma value like more than6 for only HDL cholesterol and more than 3 for Amylase, Total Bilirunbin, Creatinine, Cholesterol, Glucose, Phosphorus, total Protein , SGPT , TG, UA, Urea, SGOT, which is among the acceptable range of performance.

Conclusion: In our study sigma value was highest for HDL cholesterol and other 15 analytes show sigma value between 3 to 6 which is acceptable range. Sigma analysis is a continuous procedure and by taking the help of method decision chart we can improve on decision on making in clinical chemistry laboratory regarding optimising QC procedure.

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Introduction:-

Around 70 % of test are carried in Clinical Biochemistry Laboratory, so it plays an important role in diagnosis and treatment pattern of any diseases. It is necessary to follow a proper quality management system to provide accurate and reliable reports in a specified time limit.[1]The testing process in clinical Biochemistry lab consist of three phases namely Pre-analytical phase, Analytical phase and post –analytical phase. All the phases are prone to error.

Laboratory error can be defined as any defect or deviation of result from true value. For a laboratory testing process, caliberation is a good example of a cost incurred to prevent problems.[2] Internal Quality Control (IQC) and External Quality Assurance Services (EQAS) are presently the procedure that are being used for quality control in the Analytical phase.

The IQC shows the amount of variation that occurs in our clinical biochemistry laboratory, the results are in the form of imprecision while EQAS helps in evaluating accuracy or trueness of our result. All phases have a some tendency of error generation. In 1981, Dr. James O Westgard proposed several graphical process control rules with levy-Jenningcharts for evaluation Quality Control (QC) performances.

Six Sigma metrics are being adopted at the universal measure of quality to be applied to their process and the processes of their suppliers.[2] It provides a more quantitative frame work for evaluating process performance and more objective evidence for process improvement.[2] It is mainly used to measure the defects and denoted by a Greek letter (sigma) and used to measure standard deviaton .

Defects or laboratory error can be counted or converted to defects per million (DPM). This DPM can be converted into a sigma metrics. Six sigma is the ideal goal or world class quality equivalent to 3.4 defects per million. [3,5]

David Nevelainen in 2001, did first study and nailed the laboratory quality in six sigma scale.[6] Six sigma have been used as a tool in laboratory to check method quality, QC optimization,change the number of rules and control run and to change the frequency of QC . To asses the quality of an instrument by six sigma was done by Xuehui Mao et al. Yong Xia et al, used six sigma for risk assessments connecting test results to patient care.[7,8]

Six sigma is used as a tool not only to count defects but also to assess analytical methods,optimise QC plans and compare analytical quality of instruments. Laboratories face many quality challenges and it is needed to improve their process and work cultures. Six sigma would be added as a quality toolto improve the quality of laboratory i.eself improvement.

Aims & Objectives:-

1. To quantify the defects and errors in analytical phase of laboratory testing by sigma metrics and to represent the calculated sigma value.
2. Application of six sigma test in laboratory with the IQC and EQAS to maintain quality laboratory services.

Materials &Methods:-

The retrospective study was conducted in the Central Biochemistry laboratory in Govt. Medical College, Akola, Maharashtra, India. Internal and external quality assurance scheme data was collected for a period of 10 months from January -October 2023 for 16 biochemical analyteswhich were included in the study.

Inclusion Criteria:

1. Analytesrun routinely on daily basis.
2. Analytes for which internal quality control (Erba Norm) was run daily as routine procedure.
3. Analytes included for EQUAS schedule (CMC vellore) which we send the data to reference lab and got peer group mean from EQUAS.

Analytes Included:

Albumin, Alkaline Phosphatase (ALP), Amylase, Total Bilirubin (T.BIL), Calcium, Creatinine, Total Cholesterol, Glucose, HDL Cholesterol, Phosphorous, Total Protein, Alanine Transferase (ALT), Triglyceride, Uric Acid, Urea, Aspartate Transferase (AST).

Exclusion Criteria:
1. The Analytesthat were not run on daily basis.
2. The Analyteswhich were not in EQUAs were excluded from the study.

We performed all the tests on Fully Automated BiochemsitryAnalyser XL-640- A machine by Transasia, Germany Mannhein

Statistical Analysis:
Data for all analytes (IQC & EQAS) and mean calculated, as all data subjected to calculation for various parameters like Bias %, CV%, Sigma value, TEa , QGI and assessed statistically

According to laboratory policy of internal quality control program, only Erba Norm of control material (ERBA) was being used daily for IQC data. Our laboratory is participating monthly in the external QC survey of CMC Vellore . The results obtained from IQC and external QC scheme were used to estimate the sigma metrics. Laboratory and peer group mean result of analytes were retrieved from monthly external QC program records .

Formulae used for statistical analysis:
Bias is the systematic difference between the results obtained by the laboratory's test method and the result obtained from the peer group mean. Bias was obtained from external quality assurance records with the following formula.[9]

Bias =(Lab mean-Peer group mean) X 100/peer group mean

CV is the coefficient of variation of the analytical test method. It was determined from the calculate laboratory mean and calculated standard deviation was obtained from 10 months of IQC Data.[3]

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

Six sigma Calculation
Sigma metrics for each parameter was calculated using the following formula.[3]

Sigma = (TEa-Bias)/CV

TEa
TEa were followed as per the clinical Laboratory improvement Amendamnets (CLIA) guidelines.[1] Total error (TE) of parameters was also calculated by the following formula.[11]

TE=Bias+1.65CV

Quality Goal Index Ratio
QGI represents the relative extent to which both bias and precision meet their respective quality goals. It was calculated using the following formula.

QGI= Bias/1.5 CV

QGI represents the reason behind lower sigma value i.e imprecision, inaccuracy or both.
For analytes which fall short of six sigma quality, a QGI score of <0.8 indicates Imprecision, QGI>1.2 indicates inaccuracy and QGI 0.8-1.2 indicates both imprecision and inaccuracy.[3]

Results: Table 1 summarises the average CV% of Erba Norm of 16 Analytes.

Table 1:- The CV % OF 16 Parameters Of Level 1 Internal Quality Control For A Period Of 10 Months (Jan-October 2023) And Their Average .

Sl.no	ANALYTE	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	AVRG	STD DEV	CV
1	ALBUMIN	3.36	3.17	3.11	3.44	3.49	2.73	2.69	2.58	2.65	2.87	3.009	0.35	11.56
2	ALP	103	130	147	127	182	131	132	11	94	117	117.4	44.44	37.85
3	AMYLASE	52	48	59	53	64	59	53	64	54	56	56.2	5.25	9.33
4	T. BILIRUBIN	1.34	1.51	1.38	1.49	1.48	1.23	1.42	1.43	1.59	1.43	1.43	0.10	6.95
5	CALCIUM	6.6	8	9.3	-13.2	8.1	8.9	4.2	10.9	5.1	9	5.69	6.93	121.87
6	CREATININE	1.29	1.42	1.19	1.29	1.31	1.17	1.51	1.16	1.41	1.34	1.309	0.12	8.83
7	T. CHOLES	138	152	157	150	148	146	141	146	132	141	145.1	7.29	5.03
8	GLUCOSE	87.9	87.7	92.3	78.5	94.9	91.4	74.7	100.8	107	108	92.32	10.97	11.88
9	HDL C	45.5	41.3	49.5	45.5	41.3	51.5	49.5	51.5	45.5	41.3	46.24	4.10	8.87
10	PHOSPHORUS	4.51	4.5	5.27	5.76	4.81	4.15	3.75	3.27	5.29	4.31	4.562	0.75	16.50
11	T. PROTEIN	6.03	5.72	5.92	6.48	6.8	6.31	5.79	6	5.75	5.83	6.063	0.36	5.89
12	SGPT	29.5	38	37.2	31.6	43	41.1	40.2	48.2	37.1	42	38.79	5.46	14.07
13	TRIGLYCERIDE	100.9	100.2	101.4	103.2	47.4	92.7	104.7	100.1	111.9	99	96.15	17.79	18.51
14	URIC ACID	6.5	6.1	4.8	5.1	6.3	5.2	4.8	5.4	5.6	5.8	5.56	0.61	10.90
15	UREA	33.9	34.3	35.8	38.6	35.6	33.6	27.8	32.1	39.9	35.6	34.72	3.36	9.67
16	SGOT	50.2	38.2	39	43	47.4	40.5	36.6	45.4	41.5	37.2	41.9	4.56	10.88

Table 2:- Summarises the performances of the 16 analytes of average bias%,sigma metrics and quality goal index.

Sl.no	ANALYTE	AVERAGE	CV%	BIAS %	TEA	SIGMA	QGI
1	ALBUMIN	3.009	11.55	-3.6	39.57	3.7	-0.21
2	ALP	117.4	37.85	9.65	145.81	3.6	0.17
3	AMYLASE	56.2	9.33	-10.5	34.54	4.8	-0.75
4	T. BILIRUBIN	1.43	6.94	11.6	47.72	5.2	1.11
5	CALCIUM	5.69	121.87	-2.9	403.78	3.3	-0.02
6	CREATININE	1.309	8.83	20.5	71.77	5.8	1.55
7	T. CHOLES	145.1	5.02	7.3	32.70	5.1	0.97
8	GLUCOSE	92.32	11.88	-1.7	40.81	3.6	-0.10
9	HDL C	46.95	9.622	34.53	101.04	7.5	2.39
10	PHOSPHORUS	4.562	16.49	-1.9	56.04	3.5	-0.08
11	T. PROTEIN	6.063	5.89	-1.7	21.02	3.9	-0.19
12	SGPT	38.79	14.06	-1.9	48.02	3.5	-0.09
13	TRIGLYCERIDE	96.15	18.50	-15	62.66	4.2	-0.54

14	URIC ACID	5.56	10.89	-11.8	37.48	4.5	-0.72
15	UREA	34.72	9.67	-4.6	33.46	3.9	-0.32
16	SGOT	41.9	10.87	-2.25	37.50	3.7	-0.14

Table 2 Summarizes the average CV% of Erba Norm, Average Bias%, Sigma Metrics anQuality Goal index of the 20 parameters.

Six sigma for the ERBA Norm– the sigma metrics for ERBA Norm indicated that 1 analyte (HDL- CHOL) out of the 16 analytes qualified six sigma quality performance. Of these other 15 analytes (Albumin, ALP, Amylase, Total Bilirubin, Calcium, Creatinine, cholesterol, glucose, phosphorous, protein, SGPT, Triglyceride, Urica acid, Urea, SGOT) performances with sigma metrics was between 3 and 6.

Discussion:-

Yong Xia et all showed sigma metrics was used for traditional risk assessment, i. e connecting test result to patient care. Cao and Quin used sigma metrics to evaluate the quality of reagents. (8,11).it is a powerful tool used for various purposes like assessing the method quality, change the number of rules applied ,optimizing QC procedure, change the frequency of run and number of controls run. Quality of instrument is also assess by using sigma metrics.

In our study we analysed 16 analytes on sigma metrics and method decision chart was ploted for these analytes. We found that in our laboratory,performance for HDL-Cholesterol is more than n6 sigma. It was the highest sigma value and the lowest for calcium. HDL-C is closest to the origin or bulls's eye i.e highest sigma and very few defects are generated while calcium indicating low sigma value and generates more defects beyond acceptable limit. World class quality us attained for HDL-C , Albumin, ALP, Amylase, Total Bilirubin, Calcium, Creatinine, cholesterol, glucose, phosphorous, protein, SGPT, Triglyceride, Urica acid, Urea, SGOT therefore quality control rules followed for these analytes can be relaxed i.e only 13s or even wider control limit can be used for these analytes. If we translate this sigma metrics to the frequency of quality control run, then a minimum of 1000 patients sample can be run between each quality control run. Probability of false rejections will be greatly reduced which will ultimately lead to reduced reagent consumption, save time and labour. Total allowable error is also high for these analytes.

The six sigma is almost same to Total quality management which include "plan DO, check, Act" cycle. The key scientific model of six sigma metrics is 'Define,Measure,Analyse, improve and control ."it is one step ahead in modern quality management. It helps in preventing the recuurence of defects. i.eif any error is detected ,it has to to be solved and prevented from affecting the process again. With these steps errors are affectively decreased until a desired degree of quality is obtained. [12]

In this study, only HDL-C showed a sigma of > 7.5 for Erbanorm and more than 3 for Amylase, Total Bilirubin, Creatinine, Cholesterol, Glucose, Phosphorus, total Protein , SGPT , TG, UA, Urea, SGOT, which is among the acceptable range of performance.

QGI ration for parameter with sigma >5 showing, QGI HDL-C(2.61) and Creatinine(1.55) inaccuracy. And QGIof Total cholesterol (0.97) and Total bilirubin (1.11) show inaccuracy and imprecision. And rest all paramters showing imprecision.

Sigma scale range from one to six though the sigma values can exceed six fro certain parametres for which total allowable error is more than 20%. Minimal acceptable sigma level for manufacturing industries is 3 which may be different for clinical chemistry laboratory. Like Vermaet al observed that sigma metrics scale have certain limitations while applied to clinical chemistry laboratory. [13]

It can be applied with certain precautions and not to overestimate the error leading to false rejection, wastage of labour, control materials, calibrators and reagents. if sigma metrics is cutaiously used in laboratory it can prove to be a very powerful tool in detection of errors and reducing cost, labour ,effort by optimising QC according to sigma analysis. [14]Table 3 shows sigma metrics tools for QC design and frequency.[15]

Table 3:- Sigma metrics tool for QC design and frequency.

Sigma metrics	Control rule	Qc frequency
Six sigma	1 3s,n=2	1 per 1000 patients samples
Five sigma	13s/2 2s/r4s ,n=2	1 per 450 patient samples.
Foursigma	13s/2,2s/r 4s/4 1s,n=4	1 per 200 sample samples.
Three sigma	All " westgard rules" n=6	1 per 45 patients sample
Two sigma and below	Max "westgard rules" n=6	1 per 10 patients sample.

As sigma metrics increases-

1. Fewer QC rules needed
2. Fewer Controls needed
3. Fewer reccalirations
4. Fewer trouble shooting experiences
5. Fewer technical support calls and service visits.

Conclusions:-

In our study sigma value was highest for HDL-C and lowest for Calcium. Sigma analysis is a continuous procedure and it improvises on decision making in the clinical chemistry lab regarding frequency of internal quality control run, shows poor assay performance ,optimising QC procedures and thus can contribute optimally to patient health care quality without incurring loss on reagents, control materials, caliberators, labour and effort.

Limitations Of Study

In this study we have used single IQC control as Erba Norm.
Have not applied method decision curves for improving decision making in clinical biochemistry laboratory.

Importance of study:

It will have an entire benefit to patient population due to stringent quality maintenance in the laboratories. Six sigma calculations will be an added toolin quality assurance schemes that will help in warning the change of reagents or methods when the fail to reach the desired levels. It willopitmise resource managements by decreased used of QC run. As both imprecision and bias are taken into consideration, six sigma involves a more holistic approach to quality management in medical testing laboratories. In lab evidence based evidence , further reinforcement of quality through this tool gives an insight on choice of test methodology, reagents as well as maximum utility of the laboratory investigation not only for the lab personnel but also treating physicians.

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Conflict of interest :

None declared.

Ethical approval:

Approved .

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