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Original Research Article

Quantification of Uncertainty of Common Laboratory Parameters in a Clinical Laboratory in a Tertiary Care Institute

Chatterjee S.[1], Sinha S.[2], Ghosh A.[3], Ghosh S.[4]

[1]Associate Professor, Department of Biochemistry, College of Medicine and Sagore Dutta Hospital, West Bengal, India

[2]Demonstrator, Department of Biochemistry, College of Medicine and Sagore Dutta Hospital, West Bengal, India

[3]Consultant Biochemist, Suraksha Diagnostics Ltd, Kolkata, West Bengal, India

[4]Junior Resident, Department of Periodontology, Kusum Devi Sunderlal Dugar Jain Dental College and Hospital, Kolkata, West Bengal, India

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Corresponding author: Dr. Sanchayan Sinha

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Abstract

Introduction: The uncertainty tool has an important role for evaluation of analytical performance in any clinical laboratory. For having the quality of the analytical performance & planning the strategy of quality control, sigma metrics and QGI ratio are used as an uncertainty measurement tools. The study was done to estimate the analytical performance of clinical biochemistry laboratory of College of Medicine & Sagore Dutta Hospital by calculating Sigma metrics and QGI ratio.

Methodology: the study was done in the Department of Biochemistry, College of Medicine and Sagore Dutta Hospital. The past 6 months' (September 2025 to February 2026) of internal Quality Control reports of daily QC run as a part of routine analytical and maintenance performance of autoanalyzer ERBA XL 640 of routine parameters were analysed. The common Laboratory Parameters were used Blood glucose, Urea, Creatinine, Cholesterol, Triglyceride, HDL, LDL, ALP, SGPT, SGOT, Total Protein, Albumin, Total Bilirubin and Direct Bilirubin.

Result: The sigma levels of Level 1 the values of urea, creatinine, ALP and total protein are having their sigma levels in between 3 and 4. Sigma level L2 the value of total bilirubin is also is below 3 (2.99б) indicating unacceptable performance. Which can be considered as marginal performance and needs to improve the performance to maintain the quality. According to the Quality goal indicator values of these marginal and unacceptable performances indicate the possibilities of random errors.

Conclusion: the marginal and unacceptable performences are mostly due to random errors which indicates the need of strict adherence to the SOPs and regular practices.

Keywords: Sigma Matrix, Quality Goal Indicator, Quality Control.

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Introduction

According to ISO 15189[1] Section 5.5.1.4, "the laboratory shall determine measurement uncertainty for each measurement procedure in the examination phases used to report measured quantity values on patients' samples". In the field of laboratory Medicine or clinical chemistry uncertainty has been a common problem. It is almost impossible to get exact same result in different measurements because of biological variations. Measurement uncertainty is defined as a nonnegative parameter belongs to the vocabulary of metrology. The uncertainty tool has an important role for evaluation of analytical performance in any clinical laboratory [2] proper diagnosis, correct and timely treatment and the timely monitoring and follow up are essential part of any hospital service. the monitoring of risk assessment are very important factors on the laboratory's point of view and is essentially related to patient wellbeing. A laboratory can produce any results but we need to ensure the precision and accuracy of the measurement. [3-4] For having the quality of the analytical performance & planning the strategy of quality control, sigma metrics and QGI ratio are used as an uncertainty measurement tools. 6 sigma matrices are considered as quality tool which says more than or equal to 4 sigma can be considered as acceptable and reportable level of laboratory

performances and 6 sigma is the world class performance [5]. The Westgard multi rule are also considered to be the measurement of internal Quality control.[6] Though the total quality management (TQM) has become popular by late 1990s and its application becomes well documented as far[7] but the revolution of six sigma methodology was implemented widely in business and industry since the mid-1980s to reduce the cost of product, eliminate defects and decrease variability in Processing.[8] In a word sigma is a metric that quantifies the performance of a process at a rate of defects-per-million.[9]

The higher the sigma value, the lower chance of false test results by the laboratory. It can easily quantify the exact number of errors by combining bias, precision and Total allowable error (TEa).[8,10] When the performance falls below 3 sigma, the process is considered as unstable and unacceptable. It should not be used for routine test purposes. [5,11] While a good performance is indicated by a sigma level >3.4. Sigma level of 6 or greater indicates world class performance.[8]A QGI score of <0.8 indicates imprecision, QGI > 1.2 indicates in accuracy and QGI score 0.8-12 indicates both imprecision and inaccuracy.[12]

On the basis of sigma metrics and QGI, laboratory will have appreciable plan and scientific basis for quality control strategy not only identifying the defects along with root cause analysis of the defects, establishing the tolerance limits for standard, proper evaluation of process improvement and Quality management. [13-14]

Clinicians compare most measurement results with reference values and with immediate past results obtained from the same patient. If the match found it enough for their satisfaction but there may be obviously some lacuna at these are not sufficient for eliminating the errors. When verifying the performance characteristics of a routine measurement procedure, repeatability experiments are usually performed i.e. replicate measurements of the same sample with conditions kept as constant as possible. If the measuring system is sufficiently sensitive, a range of different results will usually be obtained. Which is the true result for the sample? We obviously can't say, but clearly the results must contain some error, and the magnitude of error is not the same for the differing results. There is therefore uncertainty as to what the true value is. A dispersion of results is similarly obtained if a patient sample is repeatedly measured under replicate conditions.

Even though automation, standardization and technological advances have significantly improved the analytical reliability of laboratory tests [15] analytical errors still do occur. Analytical errors are classified into two categories namely, systemic errors and random errors.

Objective: the study was done to estimate the analytical performance of clinical biochemistry laboratory of College of Medicine & Sagore Dutta Hospital by calculating Sigma metrics and QGI ratio. Also, to achieve the ability of satisfactory results with world class performance for analytes preceding the accreditation by the National Board for Testing and Calibration of Laboratories (NABL)

Methodology

The study was done in the Department of Biochemistry, College of Medicine and Sagore Dutta Hospital, 578 B.T. Road, Kamarhati, Kolkata West Bengal, India, Pin Code 700058. It is a 1500 bedded Government Medical College and Hospital, in Kolkata having a functional automated Clinical Chemistry Laboratory and automated Hormonal Laboratory in the Department of Biochemistry.

This analytical retrospective Study was done after obtaining the approval of institutional ethics Committee. We studied the past 6 months' (September 2025 to February 2026) of internal Quality Control reports of daily QC run as a part of routine analytical and maintenance performance of autoanalyzer ERBA XL 640 of routine parameters.

All passed IQC for both the level. (Normal & Path), Laboratory mean & Peer group mean and Total Allowable Error (TEa) from ERBA XL 640 autoanalyzer were considered in the study. Calibration data points, Calibration history, Patient's Data and IQC ± 3s (followed by Westgard Rule) were excluded from the study

QC data for 6 months both L1 & L2 were considered as sample size. Minimum for robust analysis in tertiary care hospital: ≥ 60. For 6 months study for each analyte and each control level: Daily IQC once per day X 144working= 144 result for each level [15] So, for L1: 144 samples and L2: 144 samples were considered as final sample size.

We used both levels passed IQC graphs system generated in the biochemistry auto analyzer nullifying all the possibilities of pre-analytical, analytical and post analytical errors.

The data collected, were entered in MS Excel spreadsheet. The data sheet was checked for consistency, Quality and maintenance of data. The quantitative data was expressed in Bias%, CV%, Sigma and QGI ratio. Proper statistical analysis was done as per data available.

Autoanalyzer used: ERBA XL 640 and **QC Materials used:** L1 (ERBA NORM) and L2 (ERBA PATH) system packs

Formula used for calculation of Sigma matrices and QGI: [15,16]

Sigma = (TEa – Bias%) / CV% (TEa: Total Allowable error)

CV% = (SD/Mean) X 100

Bias% = (Lab Mean – Target Mean) X 100

Target Mean

TEa = (1.65 X CV %) + Bias%

QGI = Bias% / (1.5 X CV)

Table 1: shows the target mean and interval of the analytes of Level 1 control (L1/ ERBA NORM) (LOT no. S062501, manufactured by Transasia Bio Medicals Ltd)

Parameters	Methodology used	Units	Value (target mean)	Interval
Glucose	Glucose Oxidase Peroxidase	Mg/dL	95.30	80.99-109.61
Urea	Urease-GLDH	Mg/dL	34.04	28.94- 39.14
Creatinine	Jaffe's Kinetics	Mg/dL	1.18	0.94-1.42
Cholesterol	CHOD-PAP	Mg/dL	138.52	117.73-159.31
Triglyceride	GPO	Mg/dL	121.67	103.43-139.91
HDL	Direct	Mg/dL	37.58	30.05-45.11
LDL	Direct	Mg/dL	79.77	63.81-95.73
ALP	AMP	U/L	108.58	86.82-130.26
Bilirubin Total	Diazo	Mg/dL	1.33	1-1.66
Bilirubin Direct	Diazo	Mg/dL	0.72	0.54-0.9
Total protein	Biuret	g/dl	6.05	4.85-7.25
Albumin	BCG	g/dl	3.70	3.13-4.27
SGPT	IFCC	U/L	42.04	33.64-50.44
SGOT	IFCC	U/L	39.06	31.26-46.86

Table 2: shows the target mean and interval of the analytes of Level 2 control (L1/ ERBA PATH) (LOT no. S062502, manufactured by Transasia Bio Medicals Ltd)

Parameters	Method	Units	Target Mean	Interval
Glucose	GOD POD	Mg/dL	281.91	239.61-324.21
Urea	Urease-GLDH	Mg/dL	103.11	87.63-118.59
Creatinine	Jaffe's Kinetic	Mg/dL	3.72	2.94-4.5
Cholesterol	CHOD-PAP	Mg/dL	250.97	213.32-288.62
Triglyceride	GPO	Mg/dL	217.09	184.54-249.64
HDL	Direct	Mg/dL	62.44	49.96-74.92
LDL	Direct	Mg/dL	145.13	116.09-174.17
ALP	AMP	U/L	403.66	322.93-484.39
Total Bilirubin	Diazo	Mg/dL	4.67	3.56-5.96
Direct Bilirubin	Diazo	Mg/dL	1.87	1.39-2.35
Total Protein	Biuret	g/dl	9.32	7.46-11.18
Albumin	BCG	g/dl	5.33	4.52-6.14
SGPT	IFCC	U/L	148.61	118.88-178.34
SGOT	IFCC	U/L	142.74	114.18-171.3

Results

Total 72 control values L1 and 72 control values of L2 (taken from 6 months observation period) as the part of daily run of Internal Quality Control. All the data set were tabulated in EXCEL sheet. The mean, standard deviation, CV%, Bias%, Total Allowable error (TEA), Sigma values and Quality Goal Indicator (QGI) were calculated

The Bar diagram of Mean and SD were plotted in Bar Diagrams and all the above mentioned data calculated using standardized formula and plotted in table.

Table 3: shows the Mean, SD, CV%, Bias%, TEA, Sigma Matrix and QGI of L1 (ERBA NORM)

Parameters	Mean	SD	CV%	Bias%	TEA	Sigma	QGI
Glucose (mg/dL)	104.864	4.18	1.99	0.14	8.4	4.1	0.91
Urea (mg/dL)	33.27	1.78	2.05	0.44	7.17	3.28	0.28
Creatinine (mg/dL)	1.06	0.065	2.13	0.41	8.91	3.65	0.46
Cholesterol (mg/dL)	140.2	3.003	1.35	0.22	5.62	4.01	0.95
Triglyceride (mg/dL)	129.08	5.82	2.15	0.91	4.18	1.53	0.14
HDL (mg/dL)	38.28	2.24	1.8	0.12	9.65	5.29	1.15

LDL (mg/dL)	80.88	3.77	1.4	0.51	9.14	6.16	0.99
ALP (IU/L)	117.68	5.16	2.3	0.13	8.57	3.65	0.41
Total Bilirubin (mg/dL)	1.58	0.11	2.27	0.17	6.36	2.84	0.31
Direct Bilirubin (mg/dL)	0.9	0.06	1.11	1.11	6.21	4.6	0.86
Total Protein (g/dl)	6.14	0.189	1.4	0.52	4.94	3.5	0.45
Albumin (g/dl)	3.52	0.136	0.91	0.18	4.53	4.78	0.92
SGPT (U/L)	45.48	1.66	0.95	0.32	4.15	4.03	0.86
SGOT (U/L)	40.8	2.01	1.9	0.13	8.18	4.23	0.85

Table 4: shows the Mean, SD, CV%, Bias%, TEA, Sigma Matrix and QGI of L1 (ERBA NORM)

Parameters	Mean	SD	CV%	Bias%	TEA	Sigma	QGI
Glucose (mg/dL)	272.25	3.98	1.97	0.16	8.7	4.2	0.88
Urea (mg/dL)	104.91	1.59	1.98	0.38	6.91	3.15	0.45
Creatinine (mg/dL)	3.56	0.08	2.15	0.48	8.58	3.86	0.53
Cholesterol (mg/dL)	247.1	2.954	1.12	0.25	5.87	4.08	0.99
Triglyceride (mg/dL)	206.4	5.14	1.96	0.78	4.56	3.34	0.27
HDL (mg/dL)	64.1	1.89	1.3	0.09	9.98	5.63	1.10
LDL (mg/dL)	124.1	3.16	1.2	0.47	9.16	6.15	0.98
ALP (IU/L)	379.1	4.31	1.8	0.11	8.49	3.81	0.67
Total Bilirubin (mg/dL)	4.5	0.10	2.14	0.13	6.97	2.99	0.38
Direct Bilirubin (mg/dL)	1.7	0.09	1.14	1.19	6.46	4.7	0.96
Total Protein (g/dl)	9.1	0.196	1.3	0.42	5.16	3.8	0.71
Albumin (g/dl)	4.8	0.126	0.86	0.14	5.23	4.91	0.97
SGPT (U/L)	161.2	1.61	0.97	0.38	4.67	4.01	0.82
SGOT (U/L)	141.3	1.89	1.4	0.11	8.96	4.71	0.89

Discussion

Quality has immense importance not only for the Laboratory Medicine perspective, but also for the overall hospital services. Laboratory results guide 60 to 70% of clinical decisions. The practice of Quality control ensures the accuracy and precision of the test result and thus the reliability and reproducibility. It has direct link with the patient safety and overall patient satisfaction. Practice of Quality control not only detect the errors but it also prevents the errors. [2,3]

Universal proposal of the total Quality management is focused to the patient care service, ensures commitment to the hospital administration, and finds the need of training and development program of all the staffs.

85% of all errors in any clinical laboratory are due to process problems and the rest 15% require the improvement of individual employees. [3,6]

The present project was done to estimate the analytical performance of clinical biochemistry laboratory of College of Medicine & Sagore Dutta Hospital by calculating Sigma metrics and QGI ratio.

The common Laboratory Parameters were used Blood glucose, Urea, Creatinine, Cholesterol, Triglyceride, HDL, LDL, ALP, SGPT, SGOT, Total Protein, Albumin, Total Bilirubin and Direct Bilirubin. 2 levels of commercially available Control are run every day in the Clinical Biochemistry Laboratory L1 (ERBA norm) and L2 (ERBA PATH). The value of the parameters of ERBA NORM are having the mean Value of Biological Reference Interval of our Indian population, while, the value of the ERBA PATH are having the mean value higher than the Biological Reference range (pathological level).

The target mean and the interval of all the parameters are given in table number 1 (for L1/ERBA NORM) and table number 2 (for L2/ ERBA PATH)

The mean, SD, CV%, Bias%, Total allowable error (TEA), sigma value and the values of the Quality Goal Indicator (QGI) of all parameters are given in table number 3 (for L1/ERBA NORM) and table number 4 (for L2/ ERBA PATH) Sigma level ≥4 is considered as good performance and <3 is unacceptable. [2,4,8]

In table 3, the sigma levels of L1 have been shown. Among the all-parameters Glucose, Cholesterol, HDL, LDL, direct bilirubin, albumin, SGOT and SGPT have sigma levels >4Ϭ, which can be considered as good performance. Sima level of LDL has crossed 6 Ϭ level and it indicates the world class performance. Sigma level of LDL has >5Ϭ. It is also considered as excellent performance.

The sigma levels of urea, creatinine, ALP and total protein are having their sigma levels in between 3 and 4. Which can be considered as marginal performance and needs to improve the performance to maintain the quality

But the sigma levels of Triglyceride (1.53σ) and total bilirubin (2.84σ) having their sigma level <3 and these are the indications of unacceptable performance and the defects need to be identified and corrected not only for maintaining the quality and safety but also to maintain the overall reputation of the laboratory.

In table 4, the sigma levels of L2 have been shown. Here also the glucose, cholesterol, HDL, LDL, SGOT, SGPT, albumin and direct bilirubin have achieved their sigma level >4σ indicating satisfactory performance and urea, creatinine Alp, total protein and triglyceride have their sigma levels in between 3 and 4. But the sigma level of total bilirubin is L2 also is below 3 (2.99σ) indicating unacceptable performance.

The Quality goal indicator of the parameters have shown in table no.3 and 4 for L1 and L2 respectably. The QGI for the parameters which are less than 4σ are important to identify whether the defect is due to random errors or systematic errors.

For table 3 (L1), the QGI of the parameters have been shown. Urea has QGI 0.28, creatinine 0.46, triglyceride 0.14, ALP 0.41 and total bilirubin 0.31. All of these values we have got, shows the possibility of random errors as per available literatures (QGI <0.8 is considered as imprecision). [16, 17]

For table 4 (L2) the QGI shown, urea has its QGI level 0.45, creatinine 0.53, triglyceride 0.27, ALP 0.67, total bilirubin 0.38 and total protein has QGI 0.71. for the L2 also all values of QGI indicate the possibility of random errors due to imprecision.

The possibility of random errors in a clinical can be due to the instrument errors (small unpredictable variations in instrument performance like fluctuations in photometer light intensity, electronic noise) or pipetting errors due to minor inconsistencies in sample or reagent volume delivery like air bubble in pipette, inconsistent technique leading to variations between replicate measurement. [17,18]

Reagent variability like lot-to-lot variations or within lot variations, instability in the reagent during use also can cause the random errors. Environmental factors like temperature, humidity, vibration changes can also be the cause of random errors.

There are also the possibilities of operator dependent random errors like human inconsistencies during manual steps like timing difference, mixing variability or specimen related random errors like minor heterogeneity in the sample

Random errors affect the precision, not the accuracy. The random errors cannot be completely eliminated but can be minimized by improving precision and consistency across all steps of testing. [18] Examples of remedies to avoid or reduce random errors are proper instrument maintenance like regular calibration, ensuring stable power supply, routine internal quality checks, and accurate pipetting technique, maintaining consistent pipetting angles, avoiding air bubbles in the tips and preferring automated pipetting. [15,16]

Reagent quality control has important role to avoid random errors. Use of fresh and properly stored reagents, avoiding expired or contaminated reagents, maintenance of consistent reagent lot and maintaining temperature during storage or transport of reagent lots can reduce random errors [18]

Strict adherence to standardized operating procedures (SPOs), uniform timing, mixing and incubation steps are very useful to avoid random errors

Proper training and supervision of the staffs minimizes intra operative variability and encourages the consistent technique among all staffs.

Proper sample handling and maintaining internal quality control guidelines and use of automated analyzers and replicate measurements in the modern-day analytics very much suitable for avoiding the random errors.

Conclusion

Some parameters of both L1 and L2 control levels measured by daily control runs in the given time frame showed unacceptable performances some some parameters showed marginal performance. The causes of these types of performances were due to random errors and can be corrected by daily maintenance of the instrument, robust quality control practices, regular training of the all level of staffs and strict adherence to the SOPs.

Limitation: All the analysis we have performed here are based on daily internal quality controls. But for better understanding any bias or slowly developing any inaccuracy we could also considered the results of External Quality Assurance (EQAS) reports of past 6 months. Due to time constraints, we only consider the internal quality control reports

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