Sigma Metrics as a Measure to Evaluate Internal Quality Control Performance in a Clinical Chemistry Laboratory

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ABSTRACT

Objective: To determine the sigma metrics of biochemical parameters in a clinical chemistry laboratory and to evaluate their individual performance on the sigma scale using the quality goal index (QGI) ratio.

Study Design: Retrospective cross-sectional study.

Place and Duration of the Study: Department of Pathology, Shalamar Medical and Dental College, Lahore, Pakistan, from October 2023 to September 2024.

Methodology: After ethical approval from the Institutional Review Board, data for 20 biochemical parameters enrolled in the proficiency testing programme were collected. Data were obtained for the internal quality control coefficient of variation percent (%CV) and the external quality assurance scheme (EQAS)-%bias for included parameters. Sigma values were calculated by using the formula (TAE–Bias) / CV. After the calculation of sigma values, the QGI ratio was utilised to analyse the cause of low sigma values for particular analytes.

Results: Out of 20 biochemical parameters, both levels of uric acid, bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), triglycerides (TGs), high–density lipoprotein (HDL), potassium, creatine phosphokinase (CPK), and level 2 glucose, urea, albumin, calcium, magnesium, and phosphate showed world-class performance with sigma values ≥6. Level 1 calcium, magnesium, sodium, as well as level 2 total protein and total cholesterol showed excellent performance with sigma values 5. Unacceptable performance was shown by level 1 of urea, creatinine, albumin, total protein, and total cholesterol with sigma values <3. The QGI ratio calculated for the evaluation of the problems with sigma score ≤3 showed that low sigma value of level 1 glucose, urea, creatinine, and total proteins were due to inaccuracy; that of level 1 total cholesterol was due to both imprecision and inaccuracy, while that oxsf level 1 phosphorous was due to imprecision.

Conclusion: World-class performance on the basis of sigma values were observed for uric acid, total bilirubin, ALT, AST, ALP, TGs, HDL, CPK, and potassium, while certain parameters of level 1, such as urea, creatinine, total protein, albumin, and total cholesterol, showed unacceptable performance. Sigma metric analysis provides a standard for improving assay performance and optimising quality control (QC) operations in the clinical chemistry laboratory.

Key Words: *Quality control, Internal quality control, Assay performance, Sigma metric, Six sigma, Sigma score, Internal quality control performance*.

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INTRODUCTION

Six Sigma is one of the most popular tools for improving processes in quality management systems. Six Sigma techniques are typically used when the results of a process are measurable. In biochemical laboratories, the Six Sigma metric is an effective instrument for improving error rates and giving priority to significant enhancements in laboratory quality control (QC).[1,2]

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Six Sigma is a quantitative method that aims to improve the quality of workflows and procedures. It shows the error rate of 3.4 defects per million opportunities (DPMO). In this content, the standard deviation (SD) represents a measure of data dispersion. Various laboratories have successfully used the Six Sigma method to evaluate the performance in the recent years.[3] Excellent or real world-class quality is defined as a sigma value of 6, while adequate laboratory performance as a value of >3.[3,4]

Routine execution and evaluation of internal QC (IQC) and external quality control (EQC) are the main components of QC management at the analytical phase in a diagnostic laboratory.[5,6] Participation in QC programmes, ideally run by the outside suppliers of the analytical control materials, is necessary for this reason. For internal and external quality studies, individual parameter performance is evaluated in terms of Westgard rules and Z score, respectively.[7,8] In addition to integrating IQC and EQC, Six

Sigma also helps find system weaknesses, thereby enhancing laboratory performance.[9,10] Sigma metrics are a high-quality instrument for evaluating the performance of a clinical chemistry laboratory during the analytical phase. Sigma metric analysis provides a standard for developing an IQC technique, identifying poorly performing assays, and assessing the effectiveness of existing laboratory procedures. The Six Sigma method helps evaluate the quality of laboratory testing procedures and the frequency of QC needed to achieve the required performance characteristics. The evaluation of IQC according to Westgard rule for individual biochemical parameters is important; however, the analytical performance can be improved further by evaluating sigma values.[11]

Sigma metric analysis gives laboratories a standard for building IQC protocols, addressing assay performance issues, and assessing the efficacy of existing laboratory practices.

This study aimed to identify the sigma metrics for each biochemical parameter, so that performance could be assessed on a sigma scale. Poorly performing analytes were further evaluated using the quality goal index (QGI) ratio to find the cause of poor performance, such as imprecision, inaccuracy, or both.

METHODOLOGY

A retrospective, cross-sectional study was conducted at the Department of Pathology, Shalamar Medical and Dental College, Lahore, Pakistan, from October 2023 to September 2024. Data were collected after taking ethical clearance from the concerned Institutional Review Board (IRB No. 0789; REF: SMDC-IRB/AL/2024-117; Dated: 22-11-2024). Twenty biochemical parameters were enrolled in the proficiency testing (PT) programme in the routine clinical chemistry laboratory. A convenient sampling technique was used. Biochemical parameters enrolled in the PT programme, having data for IQC and the external quality assessment scheme (EQAS) – %bias, were included. Biochemical parameters not enrolled in the PT programme from July 2023 to June 2024 were excluded. IQC data points rejected by the laboratory due to faulty runs, such as pipetting errors or equipment breakdown during analysis, were excluded from the calculation of mean IQC and coefficient of variation percent (%CV).

Data were obtained for IQC %CV and EQAS %bias across 20 clinical chemistry parameters, including glucose, urea, uric acid, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, alkaline phosphatase (ALP), albumin, total protein, cholesterol, triglycerides (TGs), high density lipoprotein (HDL), creatinine phosphokinase (CPK), calcium, magnesium, phosphate, sodium, potassium, and chloride. Among these, glucose, urea, uric acid, creatinine, ALT, AST, total bilirubin, ALP, albumin, total protein, cholesterol, TGs, HDL, calcium, magnesium, phosphate, and CPK were analysed on the automated chemistry analyser Cobas c311, and sodium, potassium, and chloride on the Medica Easylyte electrolyte analyser. Sigma values were calculated using the formula: total allowable Error – Bias/coefficient of variation (TAE – Bias)/CV. The Clinical Laboratory Improvement Amendments (CLIA) 88 criteria for PT specify the requirements for analytical quality by using total allowable error (TAE) as the benchmark for acceptable performance of each parameter.[11] Bias indicates the systematic error, while CV indicates the random error. The systematic discrepancy between the expected outcomes of a laboratory test method and the outcomes of a recognised reference method is known as bias. It was calculated by using the formula (bias = lab result-peer group mean/peer group SD).

Data were entered and analysed using SPSS version 25. After the calculation of sigma values, the QGI ratio was used to assess the cause of low sigma values for particular analytes. The calculation of the QGI score was performed by using the following formula: bias/1.5 × %CV. The criteria for the interpretation of the QGI ratio was as follows: <0.8 showed imprecision, 0.8-1.2 showed imprecision and inaccuracy, while >1.2 showed inaccuracy. The sigma score was evaluated as follows: sigma score ≥6: World-class performance; sigma score <5: Excellent performance; sigma score <4: Good performance; sigma score <3: Poor performance; sigma score <3: Unacceptable performance.

RESULTS

The IQC %CV (level 1) for all 20 biochemical parameters is presented in Table I, and the IQC %CV (level 2) in Table II. Table III shows laboratory results, peer group mean, peer group SD, standard deviation index (SDI), and expresses bias in terms of SD, for all parameters. Table IV presents the average %bias, TAE, sigma score, and QGI ratio, along with its evaluation according to sigma values. For parameters with sigma values ≤3, the QGI ratio was used to identify the type of problem, whether due to inaccuracy, imprecision, or both. Of the total 20 biochemical parameters, both levels of uric acid, total bilirubin, ALT, AST, ALP, TGs, HDL, potassium, CPK, and level 2 glucose, urea, albumin, calcium, magnesium, and phosphate showed world-class performance with sigma values ≥6 (Table IV). Level 1 calcium, magnesium, sodium and level 2 total protein and cholesterol showed excellent performance with sigma values of 5. Unacceptable performance was shown by level 1 urea, creatinine, albumin, total protein, and total cholesterol with sigma values <3 as shown in Table IV. The QGI ratio calculated for the evaluation of the problems with sigma score ≤3 showed that low sigma values of level 1 glucose, urea, creatinine, and total protein was due to inaccuracy; that of level 1 total cholesterol was due to both imprecision and inaccuracy, while that of level 1 phosphorus was due to imprecision (Table IV). Figure 1 shows the frequency of biochemical parameters with respect to the sigma score of level 1, while Figure 2 shows the frequency of biochemical parameters with respect to the sigma score of level 2.

Table I: The IQC %CV level 1 for all biochemical parameters (n = 20).

Parameters	IQC %CV level 1 (month-wise)											
	October 2023	November 2023	December 2023	January 2024	February 2024	March 2024	April 2024	May 2024	June 2024	July 2024	August 2024	September 2024
Glucose	2.90	2.16	2.295	2.08	2.22	2.43	2.50	2.46	2.20	2.25	2.58	2.30
Urea	5.39	4.26	4.67	3.78	5.47	4.70	5.90	5.05	5.59	5.26	5.87	5.25
Creatinine	8.33	11.84	6.59	7.06	8.89	10.37	10.51	12.92	10.01	8.89	8.97	7.76
Uric acid	1.69	1.67	2.28	2.17	1.87	2.14	2.04	2.07	1.86	1.92	2.25	2.06
Total bilirubin	4.10	3.41	1.71	3.20	4.01	1.89	4.10	4.04	1.95	4.01	1.72	1.72
ALT	3.56	2.52	3.13	3.00	2.49	2.27	3.28	2.85	2.39	2.30	2.04	2.50
AST	3.54	4.10	3.88	2.53	3.35	2.47	3.22	3.49	2.63	2.36	3.45	3.37
ALP	2.96	2.46	2.49	2.88	2.75	2.42	2.39	2.87	2.49	2.48	2.56	3.01
Total protein	2.94	3.14	3.03	2.59	3.07	3.11	3.10	3.09	3.27	2.96	3.21	3.08
Albumin	5.53	4.60	4.76	4.00	5.21	5.06	5.19	5.06	4.49	3.98	4.75	5.67
Total Cholesterol	4.26	4.69	4.10	4.40	4.66	4.45	4.92	4.13	4.42	4.34	4.77	4.42
Triglycerides	1.85	1.88	1.92	2.46	2.08	2.30	1.72	2.46	2.18	2.30	1.73	2.29
HDL	4.06	2.36	3.14	3.24	2.79	2.73	4.02	3.75	3.14	2.22	2.71	3.66
Calcium	2.71	2.59	1.03	2.47	2.99	1.61	2.27	2.70	1.55	1.62	1.55	2.19
Magnesium	3.70	3.71	3.88	5.38	3.53	3.80	3.58	3.89	3.94	3.56	3.81	3.87
Phosphate	3.01	2.92	2.91	3.22	4.14	3.10	3.08	2.83	3.10	3.19	3.27	2.89
Sodium	1.20	0.76	0.68	1.02	0.67	1.21	0.74	0.71	0.83	1.18	1.19	0.99
Potassium	1.10	1.17	1.13	1.19	1.18	1.02	1.13	1.56	1.14	1.14	1.23	1.11
Chloride	0.84	0.87	0.79	0.73	0.80	0.87	0.80	0.78	0.80	0.79	0.88	0.84
CPK	1.45	1.48	1.66	1.60	1.52	1.68	1.55	1.59	1.66	1.55	1.52	1.64

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; HDL: High density lipoprotein; CPK: Creatinine phosphokinase.

Table II: The IQC %CV level 2 for all biochemical parameters (n = 20).

Parameters	IQC %CV level 2 (month-wise)											
	October 2023	November 2023	December 2023	January 2024	February 2024	March 2024	April 2024	May 2024	June 2024	July 2024	August 2024	September 2024
Glucose	0.67	0.79	0.67	1.35	0.81	0.87	0.66	0.76	0.71	0.79	0.78	0.79
Urea	1.12	1.09	1.37	1.08	1.08	1.37	0.75	1.31	1.43	1.16	1.03	1.35
Creatinine	3.29	3.54	3.98	3.13	3.67	3.63	3.64	2.90	3.88	3.88	4.12	2.98
Uric acid	0.83	0.93	0.96	1.08	0.95	1.06	0.92	0.89	0.88	0.91	0.90	0.88
Total bilirubin	1.19	1.47	1.31	1.67	1.23	2.01	1.21	1.26	1.34	1.38	1.20	1.06
ALT	3.58	2.69	2.88	2.60	2.71	3.04	2.82	2.70	3.56	3.14	3.52	3.09
AST	1.21	0.76	1.24	1.38	1.10	0.82	1.50	1.51	0.75	0.78	1.52	0.76
ALP	1.71	2.35	1.85	2.35	2.09	1.89	2.46	1.95	1.73	2.17	1.73	1.75
Total protein	1.18	1.25	1.39	1.41	1.16	1.18	1.30	1.21	1.15	1.32	1.28	1.37
Albumin	1.22	1.66	1.22	1.51	1.05	1.09	1.05	1.06	0.96	1.04	1.09	1.09
Total Cholesterol	1.79	1.69	1.62	3.55	2.97	1.64	2.08	1.50	1.74	1.70	1.55	1.46
Triglycerides	1.68	1.81	1.54	1.49	1.56	1.73	1.62	1.64	1.65	1.56	1.52	1.64
HDL	2.65	2.50	0.89	3.17	0.89	2.53	0.89	2.87	1.80	2.68	3.24	1.96
Calcium	1.11	1.03	0.96	1.46	1.09	0.92	0.92	0.86	1.03	0.80	0.83	0.90
Magnesium	1.84	1.87	2.14	1.70	2.01	2.01	1.43	1.98	2.00	2.00	1.85	1.70
Phosphate	1.15	1.25	1.20	1.33	1.40	1.35	1.16	1.31	1.02	1.38	1.15	1.25
Sodium	1.15	1.15	1.05	1.01	1.04	1.25	1.15	1.17	1.18	1.05	1.12	1.19
Potassium	0.98	0.88	1.06	1.52	1.19	1.17	1.30	1.28	0.81	1.21	1.06	1.09
Chloride	0.90	0.89	0.91	0.70	0.83	0.81	0.80	0.78	0.90	0.89	0.92	0.93
CPK	0.56	0.57	0.56	0.62	0.58	0.51	0.58	0.61	0.62	0.54	0.57	0.53

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; HDL: High-density lipoprotein; CPK: Creatinine phosphokinase.

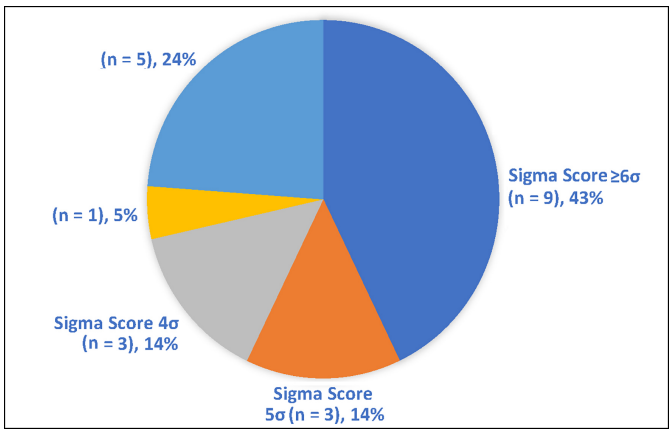

Figure 1: Frequencies of biochemical parameters (level 1) with respect to sigma scores (n = 20).

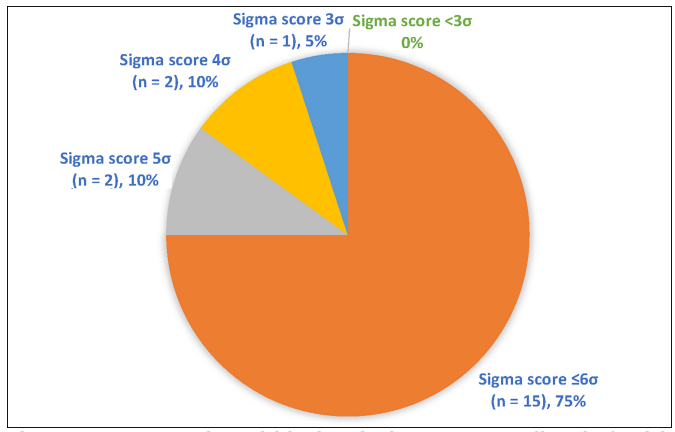

Figure 2: Frequencies of biochemical parameters (level 2) with respect to sigma scores (n = 20).

DISCUSSION

The recommendations of national accreditation bodies are commonly used by laboratories to determine the frequency of QC procedures for the number of runs and levels for IQC scheduled each day.[11]

However, according to standard laboratory practice, each laboratory must establish its unique methodology and individualised QC procedures based on the Sigma score derived from Sigma metrics analysis. By using the sigma value for IQC planning, the likelihood of laboratory errors can be reduced.[11]

Table III: Laboratory result, peer group mean, peer group SD, SDI (bias), and average bias (%) for all biochemical parameters (n = 20).

Parameters	Lab results	Peer group mean	Peer group SD	SDI (bias)	Average bias (%)
Total bilirubin	3.3	3.19	0.15	+0.7	0.48
	4.9	4.67	0.15	+1.5	
	1.1	1.05	0.10	+0.5	
	0.1	0.15	0.06	-0.8	
	2.4	2.33	0.13	+0.5	
Glucose	116.0	113.10	2.23	+1.3	1.06
	70.0	69.00	1.05	+0.9	
	213.0	209.80	4.57	+0.7	
	257.0	254.50	3.63	+0.7	
	49.0	47.40	0.97	+1.7	
Urea	19.2	19.23	0.66	0.0	-0.44
	9.8	10.04	0.26	-0.9	
	36.0	34.81	0.87	+1.4	
	43.0	44.04	1.12	-0.9	
	18.2	19.13	0.50	-1.8	
Creatinine	4.30	4.159	0.152	+0.9	1.04
	5.80	5.390	0.215	+1.9	
	3.30	3.212	0.114	+0.8	
	2.00	1.944	0.088	+0.6	
	0.80	0.703	0.100	+1.0	
Uric acid	6.6	6.30	0.13	+2.3	1.86
	5.1	4.81	0.11	+2.5	
	10.7	10.26	0.25	+1.7	
	12.1	11.69	0.29	+1.4	
	1.9	1.82	0.06	+1.4	
ALT	91	94.2	2.3	-1.4	-0.64
	40	42.4	1.4	-1.8	
	175	176.1	4.0	-0.3	
	229	229.1	5.8	0.0	
	117	116.2	2.9	+0.3	
AST	111	115.3	5.3	-0.8	-1.7
	41	41.0	1.7	0.0	
	243	244.4	7.8	-0.2	
	325	320.9	10.7	+0.4	
	122	129.9	7.1	-1.1	
ALP	143	144.5	3.5	-0.4	-0.36
	63	64.2	1.8	-0.7	
	293	296.5	8.7	-0.4	
	398	401.1	10.1	-0.3	
	156	155.8	5.6	0.0	
Albumin	2.9	2.88	0.08	+0.3	0.6
	2.6	2.57	0.09	+0.4	
	2.7	2.58	0.08	+1.4	
	3.0	2.92	0.08	+1.0	
	5.2	5.22	0.12	-0.1	
Total protein	4.4	4.11	0.09	+3.0	2.6
	3.7	3.51	0.08	+2.3	
	3.9	3.74	0.09	+1.7	
	4.6	4.35	0.10	+2.6	
	8.8	8.25	0.16	+3.4	
Sodium	142	142.3	2.1	-0.1	
	147	146.5	2.2	+0.2	0.3
	130	129.4	1.8	+0.3	
	127	125.2	1.6	+1.1	
	162	162.1	4.5	0.0	
Potassium	4.9	4.98	0.07	-1.2	-0.86
	5.8	5.98	0.08	-2.2	
	3.3	3.28	0.06	+0.4	
	2.3	2.26	0.06	+0.8	
	4.9	5.07	0.08	-2.1	
Chloride	104	102.2	1.5	+1.2	1.32
	108	106.9	1.5	+0.7	
	93	91.5	1.6	+0.9	
	88	86.7	1.6	+0.8	
	117	112.2	1.6	+3.0	
Cholesterol	148.0	148.044	4.242	0.0	
	118.0	116.427	3.567	+0.4	0.34
	172.0	168.809	4.690	+0.7	
	206.0	203.075	5.423	+0.5	
	261.0	260.211	5.783	+0.1	
Triglycerides	149.0	145.058	4.887	+0.8	1.08
	143.0	137.249	5.608	+1.0	
	110.0	104.359	3.559	+1.6	
	118.0	112.639	3.283	+1.6	
	316.0	311.445	10.239	+0.4	
HDL	54.00	56.469	2.041	-1.2	-1.32
	40.00	41.712	1.612	-1.1	
	70.00	74.159	2.539	-1.6	
	85.00	89.484	3.295	-1.4	
	73.00	76.676	2.884	-1.3	
CPK	219	217.6	6.1	+0.2	0.36
	187	180.9	5.9	+1.0	
	150	147.7	6.3	+0.4	
	186	184.9	7.7	+0.1	
	609	608.0	15.0	+0.1	

Continued...

Parameters	Lab results	Peer group mean	Peer group SD	SDI (bias)	Average bias (%)
Calcium	9.70	9.462	0.153	+1.6	1.64
	8.80	8.543	0.147	+1.7	
	12.60	12.145	0.194	+2.4	
	13.30	13.059	0.186	+1.3	
	6.20	6.064	0.113	+1.2	
Magnesium	4.40	3.849	0.079	+7.0	3.06
	5.20	4.819	0.087	+4.4	
	2.40	2.376	0.065	+0.4	
	1.40	1.322	0.049	+1.6	
	3.20	3.063	0.072	+1.9	
Phosphate	5.00	4.936	0.094	+0.7	0.3
	6.10	6.019	0.112	+0.7	
	3.30	3.317	0.070	-0.2	
	2.20	2.207	0.055	-0.1	
	4.30	4.271	0.079	+0.4	

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; HDL: High density lipoprotein; CPK: Creatinine phosphokinase.

Table IV: Sigma score and QGI ratio of all biochemical parameters (n = 20).

Parameters	IQC level	%CV	Average bias	TAE ± %	Sigma values	QGI ratios	Problems
Glucose	Level 1	2.36	1.06	10	3.79	1.7	Inaccuracy
	Level 2	0.80			11.18	-	None
Urea	Level 1	5.09	-0.44	9	1.68	1.5	Inaccuracy
	Level 2	1.17			7.32	-	None
Creatinine	Level 1	9.35	1.04	15	1.49	6.4	Inaccuracy
	Level 2	3.55			3.93	2.5	Inaccuracy
Uric acid	Level 1	2.0	1.86	17	7.47	-	None
	Level 2	0.93			16.28	-	None
Total bilirubin	Level 1	1.304	0.48	20	14.97	-	None
	Level 2	1.36			14.35	-	None
ALT	Level 1	2.69	-0.64	20	7.2	-	None
	Level 2	3.02			6.41	-	None
AST	Level 1	2.93	-0.34	20	6.71	-	None
	Level 2	1.11			17.71	-	None
ALP	Level 1	2.64	-0.36	30	11.23	-	None
	Level 2	2.00			14.82	-	None
Albumin	Level 1	4.85	0.42	10	1.98	1.358	Inaccuracy
	Level 2	1.17			8.19	-	None
Total protein	Level 1	3.04	2.60	10	2.43	5.26	Inaccuracy
	Level 2	1.26			5.87	-	None
Total cholesterol	Level 1	4.46	0.34	10	2.17	1.01	Imprecision and inaccuracy
	Level 2	1.94			4.98	-	None
Triglycerides	Level 1	2.09	1.08	25	11.44	-	None
	Level 2	1.62			14.77	-	None
HDL	Level 1	3.15	-1.32	30	9.1	-	None
	Level 2	2.17			13.22	-	None
Calcium	Level 1	2.11	1.64	11.9	4.86	-	None
	Level 2	0.99			10.36	-	None
Magnesium	Level 1	3.88	3.06	25	5.65	-	None
	Level 2	1.87			11.73	-	None
Phosphate	Level 1	3.13	0.30	10	3.1	0.626	Imprecision
	Level 2	1.20			8.08	-	None
Sodium	Level 1	0.93	0.3	5.6	5.7	-	None
	Level 2	1.12			4.73	-	None
Potassium	Level 1	1.17	-0.86	17.4	14.14	-	None
	Level 2	1.12			14.77	-	None
Chloride	Level 1	0.81	1.32	5	4.54	-	None
	Level 2	0.85			4.33	-	None
CPK	Level 1	1.57	0.36	30	18.88	-	None
	Level 2	1.09			27.19	-	None

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; HDL: High-density lipoprotein; CPK: Creatinine phosphokinase.

This study calculated the sigma value for 20 biochemical parameters enrolled in the EQA programme. Most biochemical parameters showed world-class performance in both QC levels, while some achieved world-class performance only in level 2 and excellent in level 1. These findings were inconsistent with those repeated by Kumar and Mohan.[12] The QGI ratios showed that low sigma values of level 1 glucose, urea, total protein, albumin, and creatinine (both level 1 and 2) are due to inaccuracy, that of level 1 phosphate was due to imprecision, and that of level 1 total cholesterol was due to both inaccuracy and imprecision.

A study conducted by Kumar and Mohan on Sigma metrics for IQC in a chemical laboratory showed that ALP, magnesium, TGs, and HDL were the four analytes that demonstrated ideal performance with a sigma level 6 for level 1 IQC, while five analytes (urea, total bilirubin, albumin, cholesterol, and potassium) demonstrated average performance (1.2), indicating inaccuracy.[12] In a study conducted in the Clinical Chemistry section of the Dow Diagnostic Reference and Research Laboratory (DDRRL), Karachi, Pakistan, the Sigma level was found to be acceptable (=3) for glucose (L2), cholesterol, TGs, HDL, creatinine, and direct bilirubin (both levels). The sigma metric for the other analytes was <3. At level 2, the chloride showed the lowest sigma value (1.1). At level 3, creatinine showed the highest sigma value (10.1). At both control levels, HDL had the highest sigma values (8.8 and 8.0 at Level 2 and Level 3, respectively). It was determined that analytes having a sigma value <3 require close monitoring and modification of their QC procedures.[13]

Six Sigma is a management methodology that aims to enhance the quality of process outputs by minimising process variations and locating and removing the causes of defects (errors). It provides a quantitative description that connects the process specifications with client requirements.[14] This tool is used in clinical laboratories for both analytical performance evaluation and method selection.[15,16]

Higher sigma values for urea, creatinine, sodium, and potassium were seen in the urine control matrix compared to the serum control, suggesting that these parameters performed better in the former matrix than in the letter. Creatinine, sodium, and potassium showed higher sigma values using TAE from CLIA compared to TAE from Bureau Veritas (BV) in the same matrix (serum control). Between the two sources, sodium had the largest difference in sigma value.[17]

A study conducted by Karattuthazhathu *et al*. to evaluate the performance of different parameters in the clinical laboratory on the sigma scale showed that 37% of parameters had sigma metrics <3 (poor performance), 29% had sigma metrics between 3-6 (excellent performance), and 34% had sigma metrics >6 (world-class performance).[18] Moreover, the authors concluded that sigma metric analysis offers a standard framework for laboratories to create an IQC methodology, address subpar assay performance, and evaluate the effectiveness of existing procedures. Strict QC procedures and sigma analysis form the foundation of this approach.[18]

Rasheed *et al*., evaluating the performance of 19 biochemical parameters enrolled in the PT programme, reported that most of the parameters showed satisfactory performance on the sigma scale. Control frequency for parameters with a score of >6 can be decreased to save laboratory resources, while parameters with a sigma score of 3 require close monitoring. The Six Sigma tool enables laboratories to determine the best procedure, rule, and frequency of controls to improve patients' health and medical results and to ensure the best possible patient outcome.[19]

Another study conducted by Aggrawal *et al*. on sigma metrics evaluation for improving performance in a clinical chemistry laboratory showed that, for level 2, six of the 20 analytes met the requirements for Six Sigma quality performance. Seven analytes had sigma metrics below three, indicating performance below the minimum acceptable standard, while seven had sigma metrics between three and six. On the basis of this study, it was concluded that amylase had the highest sigma value and potassium had the lowest. To improve the performance of potassium, certain alternative methods can be used, such as reagent change.[20]

Sigma metrics is a good quality tool for evaluating the performance of a clinical chemistry laboratory. There are certain limitations of sigma value. For some parameters, %CV and %bias are considered more reliable than sigma values when they fall within the acceptable performance criteria defined by CLIA. Nevertheless, Sigma values should be calculated for all parameters used in the laboratory, and this quality improvement tool should be used across all phases of the laboratory testing cycle.

CONCLUSION

Both levels of uric acid, total bilirubin, ALT, AST, ALP, TGs, HDL, CPK, and potassium showed world-class performance on the basis of sigma value, while some parameters of level 1, such as urea, creatinine, total protein, albumin, and total cholesterol showed unacceptable performance. Sigma metric analysis gives a standard framework for laboratories to improve the efficiency of assay performance, decision-making in IQC procedures, and the optimisation of QC operations. This ensures the best possible contribution to patient care quality without resulting in losses of reagents, control materials, calibrators, labour, and effort.

ETHICAL APPROVAL:
Ethical approval was obtained from the Institutional Review Board of Shalamar Medical and Dental College, Lahore, Pakistan (IRB No. 0789; REF: SMDC-IRB/AL/2024-117; Dated: 22-11-2024).

PATIENTS' CONSENT:
Informed consent was obtained from all participants included in this study.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
RT: Concept, design, data collection, and analysis.
SSHZ: Concept, design, and the final approval of the manuscript.
AI, HA: Data analysis, manuscript writing, and proofreading.
AN: Data collection, interpretation, and manuscript writing.
TAK: Data analysis and proofreading.
All authors approved the final version of the manuscript to be published.

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