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SIGMA METRICS AS A TOOL FOR EVALUATING THE PERFORMANCE OF INTERNAL QUALITY CONTROL IN A CLINICAL CHEMISTRY LABORATORY OF A TERTIARY HOSPITAL

Anusree M[1], Dr.Suriyan.S.Nair[2], Dr.Reshma Kiran[3*], Dr.Janice D'Sa[4], Dr.Prathima M.B[5], Dr Kiran Kumar PK[6]

[1]Indiana Institute of Allied Health Sciences, Mangaluru, Karnataka
[2,4,5,6]A.J.Institute of Medical Sciences and Research Centre, Mangaluru, Karnataka
[3]P.E.S University Institute of Medical Sciences, Electronic City, Bengaluru, Karnataka

***Corresponding Author:** Dr. Reshma Kiran
*P.E.S University Institute of Medical Sciences, Electronic City, Bengaluru, Karnataka

ABSTRACT

Background: Sigma metrics provide a quantitative approach to assess analytical performance by integrating total allowable error, bias, and imprecision. Limited evidence exists regarding sigma-guided quality control optimization in resource-constrained laboratory settings with poor baseline performance.

Aim: To evaluate analytical performance of twelve biochemical parameters using sigma metrics methodology and assess the effectiveness of enhanced quality control rules for analytes with sigma values below 3 in a tertiary care hospital laboratory.

Methods: This prospective study evaluated sigma metrics for Albumin, Beta HCG, Calcium, Chloride, Creatinine, Ferritin, Magnesium, Potassium, Sodium, Total Bilirubin, Total Protein, and TSH across three quality control levels over six months (August 2022-January 2023). Sigma values were calculated using $\sigma = (TEa - |Bias|) / CV$ formula. Enhanced quality control rules were implemented for analytes with sigma <3 during February-April 2023, and pre- and post-implementation outcomes were compared.

Results: Of 26 analyte-level combinations, 24 (92.31%) demonstrated poor performance (σ <3), with only Beta HCG Level 1 achieving good performance (σ = 4.45) and TSH Level 1 reaching marginal performance (σ =3.41). Following enhanced quality control implementation, 11 of 22 combinations (50%) showed improvement while 11 (50%) deteriorated. Beta HCG Level 2 achieved the greatest improvement (167.1% increase,σ =2.07 to 5.53), while Magnesium levels showed substantial gains (173.7% and 110.9%). However, albumin and creatinine demonstrated significant deterioration (55-67% decreases).

Conclusion: Sigma metrics effectively identify analytical deficiencies and guide quality control optimization. The mixed outcomes following enhanced rule implementation emphasize the need for individualized rather than uniform optimization strategies in laboratories with predominantly poor baseline performance.

Keywords: Quality Control; Clinical Chemistry Tests; Laboratories, Hospital; Quality Assurance, Health Care; Statistics as Topic; Tertiary Healthcare

INTRODUCTION

Clinical laboratories serve as the cornerstone of modern healthcare, providing critical diagnostic information that influences approximately 70% of clinical decisions. The accuracy, precision, and reliability of laboratory results directly impact patient safety, clinical outcomes, and healthcare quality. With increasing complexity of analytical instruments and growing demand for rapid, accurate diagnostics, ensuring consistent analytical performance has become paramount for laboratory excellence and patient care.[1,2]

Quality control in clinical chemistry laboratories has evolved significantly, transitioning from basic statistical control methods to sophisticated quality management systems. Traditional approaches, primarily based on Levey-Jennings charts and Westgard multirule systems, utilize statistical process control principles to detect systematic and random errors through rules such as 1:3s, 2:2s, and R4s.[3] While these methods have served laboratories well, they often lack the quantitative framework necessary to optimize quality control strategies based on individual analyte performance characteristics.[3,4] The introduction of Six Sigma methodology to clinical laboratories represents a paradigm shift toward data-driven quality management. Originally developed for manufacturing processes, Six Sigma provides a quantitative approach to quality assessment by measuring processes capability using the formula $\sigma = (TEa - |Bias|) / CV$, where TEa represents total allowable error, and CV represents coefficient of variation . This approach enables performance classification on a standardized scale: World Class (≥6σ), Excellent (5-6σ), Good (4-5σ), Marginal (3-4σ), and Poor (<3σ) .[5,6]

The significance of sigma metrics extends beyond performance classification to practical quality control optimization. Methods achieving higher sigma values require less intensive monitoring, while poor-performing methods necessitate enhanced surveillance. For instance, methods with sigma ≥6 may utilize simplified protocols with single-level controls analysed once daily, whereas methods with sigma <3 require comprehensive multi-rule systems and increased control frequencies.[6,7] This risk-based approach allows laboratories to allocate resources efficiently while maintaining patient safety.

Total allowable error specifications, fundamental to sigma calculations, represent maximum acceptable deviations that maintain clinical utility. These are derived from biological variation studies, regulatory requirements, and clinical outcome studies. However, selecting appropriate TEa values remains challenging, as different sources may provide varying limits for the same analyte, necessitating careful consideration of clinical requirements and analytical capabilities.[8]

Implementation of sigma metrics offers multiple advantages including objective performance assessment, data-driven quality control selection, cost optimization through reduced false rejections, and enhanced patient safety through improved error detection. Studies demonstrate that laboratories employing sigma-guided strategies achieve better analytical performance, reduced operational costs, and improved customer satisfaction compared to traditional approaches.[9,10] Despite these advantages, significant gaps remain in practical implementation, particularly in resource-constrained tertiary care settings. There is limited evidence regarding effectiveness of different quality control rule combinations for specific analytes with varying sigma performance levels. Previous research has predominantly concentrated on individual analyte assessment rather than comprehensive evaluation of entire clinical chemistry panels. The present study aims to compare sigma metrics before and after implementing enhanced quality control rules for analytes with sigma values below 3, thereby assessing the effectiveness of sigma-guided quality control optimization.

MATERIALS AND METHODS

Study Design and Setting

This prospective quality assurance study was conducted in the clinical chemistry laboratory of a tertiary care hospital to evaluate the analytical performance of 12 biochemical parameters using six sigma methodology. The study was performed in two phases: initial sigma metric assessment (August 2022 to January 2023) and implementation of enhanced quality control rules for poor-performing analytes (February to April 2023).

Analytes and Quality Control Materials

Twelve biochemical parameters were evaluated: Albumin, Beta human chorionic gonadotropin (Beta HCG), Calcium, Chloride, Creatinine, Ferritin, Magnesium, Potassium, Sodium, Total Bilirubin, Total Protein, and Thyroid-stimulating hormone (TSH). Quality control materials at three different concentration levels (Level 1, Level 2, and Level 3) were analysed in Abbott Architect Plus ci4100 auto-analyser using Randox Acusera clinical chemistry and immunoassay quality control sera appropriate for each analyte's analytical range. The sera were analysed.

Data Collection and Quality Control Protocol

Internal quality control (IQC) data were collected monthly from August 2022 to January 2023, with quality control samples analysed daily according to established laboratory protocols. For each analyte level, the following parameters were recorded: laboratory mean values, peer group mean values (external quality assurance data), standard deviation (SD), coefficient of variation (CV%)- Standard deviation/Mean x 100, and bias percentage- Laboratory mean- Consensus Group mean/Consensus Group Mean x 100. The laboratory participated in the external quality assurance scheme (EQAS) conducted by Christian Medical College, Vellore and the EQAS data were obtained from peer laboratories participating in the same proficiency testing program to establish comparative performance benchmarks.

All IQC and EQAS data points from August 2022 – April 2023 were included in the study. Exclusion criteria were failed runs and rejected IQC values.

Total Allowable Error (TEa) Criteria

Total allowable error limits were established for each analyte based on internationally recognized quality specifications. The TEa values used were: Albumin (4.07%), Beta HCG (41.3% for Level 1, 23.01% for Level 2), Calcium (2.55%), Chloride (1.50%), Creatinine (8.87%), Ferritin (16.90%), Magnesium (4.80%), Potassium (5.61%), Sodium (0.73%), Total Bilirubin (26.94%), Total Protein (3.63%), and TSH (23.70%). These specifications were derived from biological variation studies and regulatory guidelines to ensure clinically acceptable analytical performance.

Sigma Metrics Calculation

Sigma metrics were calculated using the formula: $\sigma = (TEa - |Bias|) / CV$, where TEa represents the total allowable error, Bias represents the systematic error expressed as percentage difference from the peer group mean, and CV represents the coefficient of variation as a measure of analytical imprecision. Performance classification was established based on sigma values: World Class ($\geq 6\sigma$), Excellent ($5\text{-}6\sigma$), Good ($4\text{-}5\sigma$), Marginal ($3\text{-}4\sigma$), and Poor ($<3\sigma$).

Quality Control Rule Selection and Implementation

Analytes demonstrating sigma metrics below 3 during the initial assessment period were identified for enhanced quality control monitoring. The existing quality control protocol utilized the standard "1_{3s}, 2_{2s}, R_{4s}" rule combination. For analytes with poor performance ($\sigma < 3$), enhanced quality control rules were implemented based on sigma-metric guided recommendations, including additional rules such as 3_{1s}, 4_{1s}, R_{4S}, and 8x rules to improve error detection capability.

Implementation Phase and Outcome Assessment

Enhanced quality control rules were implemented for 24 analyte-level combinations showing poor performance during February to April 2023. Post-implementation sigma metrics were calculated using the same methodology, and comparative analysis was performed to assess the effectiveness of the enhanced quality control protocol. Analytes showing insufficient data points (TSH Level 1, Total Bilirubin Level 3, and Ferritin Level 3) were excluded from the post-implementation analysis.

Statistical Analysis

Descriptive statistics were calculated for all quality control parameters. Monthly trends in coefficient of variation and bias were analyzed to assess analytical stability over time. Pre- and post-implementation sigma metrics were compared, and improvement percentages were calculated as: [(σ_after - σ_before) / σ_before] × 100. Performance improvements were categorized as successful when analytes achieved sigma values ≥3 after rule implementation, or as partial improvement when sigma values increased but remained below the acceptable threshold.

RESULTS

Table 1: Sigma Metrics and Performance Classification for All Analytes

Analyte	Level	Tea	Bias	Cv	Sigma	Performance
Albumin	2	4.07	2	7.28	0.28	Poor
Albumin	3	4.07	-2.12	8.82	0.7	Poor
Beta HCG	1	41.3	-5.33	10.48	4.45	Good
Beta HCG	2	23.01	3.08	9.63	2.07	Poor
Calcium	2	2.55	-2.12	5.07	0.92	Poor
Calcium	3	2.55	-1.95	4.93	0.91	Poor
Chloride	2	1.5	0.15	4.05	0.33	Poor
Chloride	3	1.5	-0.8	3.98	0.58	Poor
Creatinine	2	8.87	5.08	9.31	0.41	Poor
Creatinine	3	8.87	-3.33	9.48	1.29	Poor
Ferritin	1	16.9	-19.56	12.51	2.91	Poor
Ferritin	2	16.9	0.31	9.99	1.66	Poor
Ferritin	3	16.9	-0.1	10.07	1.69	Poor
Magnesium	2	4.8	-1.86	5.84	1.14	Poor
Magnesium	3	4.8	-3.14	5.75	1.38	Poor
Potassium	2	5.61	-0.11	3.98	1.44	Poor
Potassium	3	5.61	-1.4	3.98	1.76	Poor
Sodium	2	0.73	0.03	2.48	0.28	Poor
Sodium	3	0.73	-0.86	2.44	0.65	Poor
Total Bilirubin	2	26.94	5.94	10.8	1.94	Poor
Total Bilirubin	3	26.94	1.65	10.64	2.38	Poor
Total Protein	2	3.63	0.21	10	0.34	Poor
Total Protein	3	3.63	-1.12	9.95	0.48	Poor
TSH	1	23.7	0.01	6.95	3.41	Marginal
TSH	2	23.7	1.25	13.88	1.62	Poor
TSH	3	23.7	-3.39	10.45	2.59	Poor

Table 1 presents the comprehensive sigma metrics evaluation for all 12 clinical chemistry analytes tested at different control levels (Level 1, 2, and 3) in the laboratory. The table displays critical analytical performance parameters including Total Allowable Error (TEa) values derived from established quality specifications, bias percentages representing systematic error between laboratory results and peer group means, coefficient of variation (CV) percentages indicating analytical imprecision, and the calculated sigma metrics which integrate both bias and imprecision relative to quality requirements. Each analyte-level combination is classified into performance categories based on sigma values: World Class (≥6σ), Excellent (5-6σ), Good (4-5σ), Marginal (3-4σ), and Poor (<3σ). The results reveal concerning analytical performance across the laboratory, with 24 out of 26 analyte-level combinations (92.31%) classified as "Poor" performance, indicating sigma values below the minimum acceptable threshold of 3. Only Beta HCG at Level 1 achieved "Good" performance with

a sigma value of 4.45, while TSH at Level 1 reached "Marginal" performance with a sigma value of 3.41. The predominance of poor-performing analytes, particularly critical tests like Albumin (σ=0.28-0.70), Calcium (σ=0.91-0.92), Creatinine (σ=0.41-1.29), and electrolytes, demonstrates the urgent need for analytical process improvements and enhanced quality control measures to ensure reliable patient results and meet international laboratory quality standards.

Figure 1: Comprehensive Sigma Metrics Overview

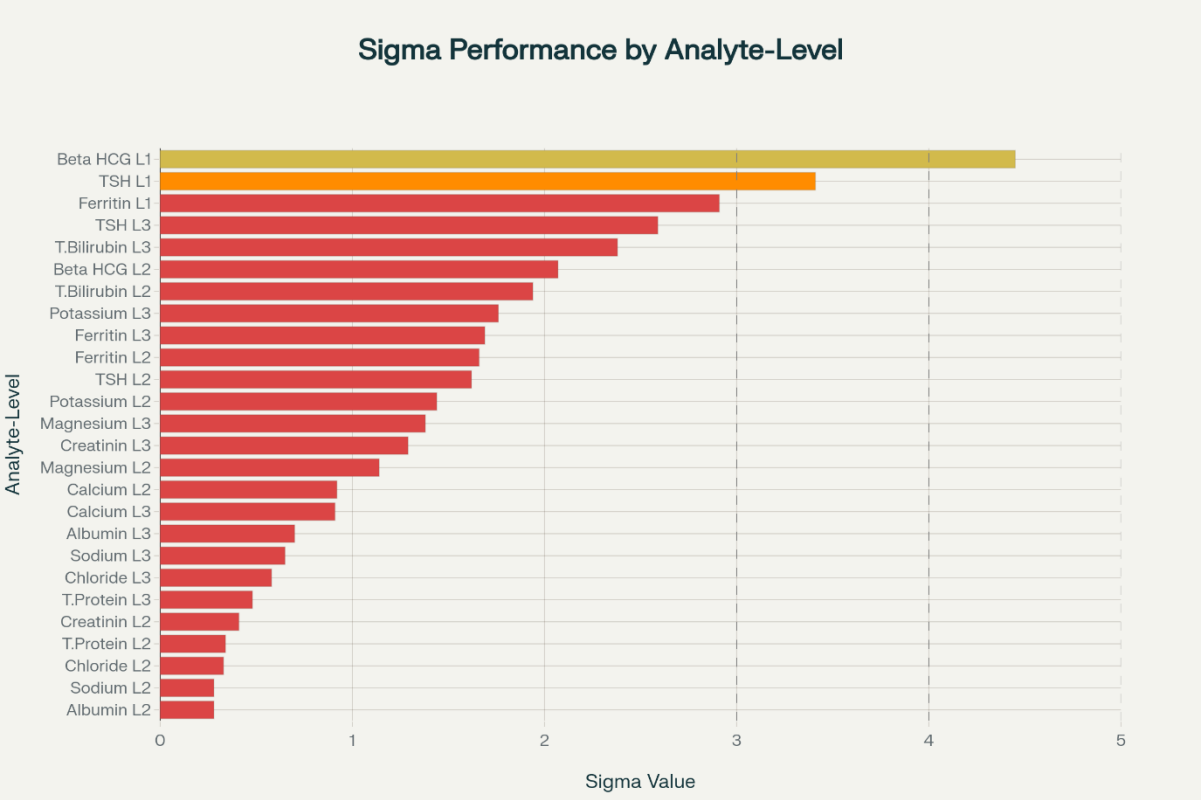

Table 2: Distribution of Performance Classifications

Performance Classification	Number of Analyte-Level Combinations	Percentage
Poor	24	92.31
Good	1	3.85
Marginal	1	3.85

Table 2 summarizes the performance classification distribution of all 26 analyte-level combinations based on their sigma metrics. The results demonstrate predominantly poor analytical performance, with 24 combinations (92.31%) classified as "Poor" (σ < 3), indicating substandard quality requiring immediate improvement. Only 1 combination (3.85%) achieved "Good" performance (Beta HCG Level 1), and 1 combination (3.85%) reached "Marginal" performance (TSH Level 1). No analyte-level combinations achieved "Excellent" or "World Class" performance levels, highlighting the critical need for comprehensive quality improvement initiatives across the laboratory's analytical processes.

Table 3: Quality Control Rules for Analytes with Sigma < 3

Analyte	Level	Sigma	Existing Rules	Suggested Rules
Albumin	2	0.28	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 3_{1s}, 8x
Albumin	3	0.7	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 3_{1s}, 8x
Beta HCG	2	2.07	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 3_{1s}, 8x
Calcium	2	0.92	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x

Calcium	3	0.91	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Chloride	2	0.33	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Chloride	3	0.58	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Creatinine	2	0.41	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Creatinine	3	1.29	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Ferritin	1	2.91	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s
Ferritin	2	1.66	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s
Ferritin	3	1.69	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s
Magnesium	2	1.14	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Magnesium	3	1.38	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Potassium	2	1.44	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 3_{1s}, 8x
Potassium	3	1.76	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 3_{1s}, 8x
Sodium	2	0.28	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Sodium	3	0.65	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Total Bilirubin	2	1.94	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s},8x
Total Bilirubin	3	2.38	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Total Protein	2	0.34	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
Total Protein	3	0.48	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s, 4_{1s}, 8x
TSH	2	1.62	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s
TSH	3	2.59	1_{3s}, 2_{2s}, R4s	1_{3s}, 2_{2s}, R4s

Table 3 presents the quality control rule modifications for the 24 analyte-level combinations with sigma values below 3, representing all 12 tested analytes that require enhanced monitoring. Currently, all poor-performing analytes use the standard "1_{3s}, 2_{2s}, R4s" rule combination (1_{3s}, 2_{2s}, and R-4s rules). The suggested enhanced rules add more stringent monitoring protocols including 31s/41s rules (detecting systematic shifts), R4s rules (detecting increased imprecision), and 8x rules (consecutive measurements on same side of mean). Notably, Ferritin and TSH require only the basic "1_{3s}, 2_{2s}, R4s" rules due to their relatively better sigma performance (2.59-2.91), while the remaining analytes with sigma values ranging from 0.28 to 2.38 require the most comprehensive rule set including all additional monitoring protocols to detect analytical errors and ensure patient safety.

Table 4: Before and After Comparison

Analyte	Level	Sigma Before	Sigma After	Improvement	Improvement Percentage
Beta HCG	2	2.07	5.53	3.46	167.15
Calcium	2	0.92	1.1	0.18	19.57
Calcium	3	0.91	1.42	0.51	56.04
Chloride	2	0.33	0.71	0.38	115.15
Chloride	3	0.58	0.82	0.24	41.38
Creatinine	2	0.41	0.81	0.4	97.56
Magnesium	2	1.14	3.12	1.98	173.68
Magnesium	3	1.38	2.91	1.53	110.87
Sodium	2	0.28	0.78	0.5	178.57
Sodium	3	0.65	1.33	0.68	104.62
Total Protein	3	0.48	0.73	0.25	52.08
Albumin	2	0.28	0.11	-0.17	-60.71
Albumin	3	0.7	0.31	-0.39	-55.71
Creatinine	3	1.29	0.42	-0.87	-67.44

Ferritin	1	2.91	2.11	-0.8	-27.49
Ferritin	2	1.66	1.34	-0.32	-19.28
Potassium	2	1.44	1.33	-0.11	-7.64
Potassium	3	1.76	1.54	-0.22	-12.5
Total Bilirubin	2	1.94	1.22	-0.72	-37.11
Total Protein	2	0.34	0.15	-0.19	-55.88
TSH	2	1.62	1.41	-0.21	-12.96
TSH	3	2.59	2.51	-0.08	-3.09

Table 4 compares sigma metrics before and after implementing suggested quality control rules for 22 analyte-level combinations with sigma < 3. The results show mixed outcomes: 11 combinations (50%) demonstrated improvement while 11 combinations (50%) showed deterioration. Beta HCG Level 2 achieved the most dramatic improvement, increasing from 2.07 to 5.53 sigma units (167.1% improvement), reaching "Excellent" performance. Magnesium levels also showed substantial improvements (173.7% and 110.9%), with Level 2 achieving "Marginal" performance (σ = 3.12). However, several analytes deteriorated significantly, including Creatinine Level 3 (67.4% decrease) and both Albumin levels (55-61% decreases).

Figure 2: Impact of Quality Control Rule Implementation

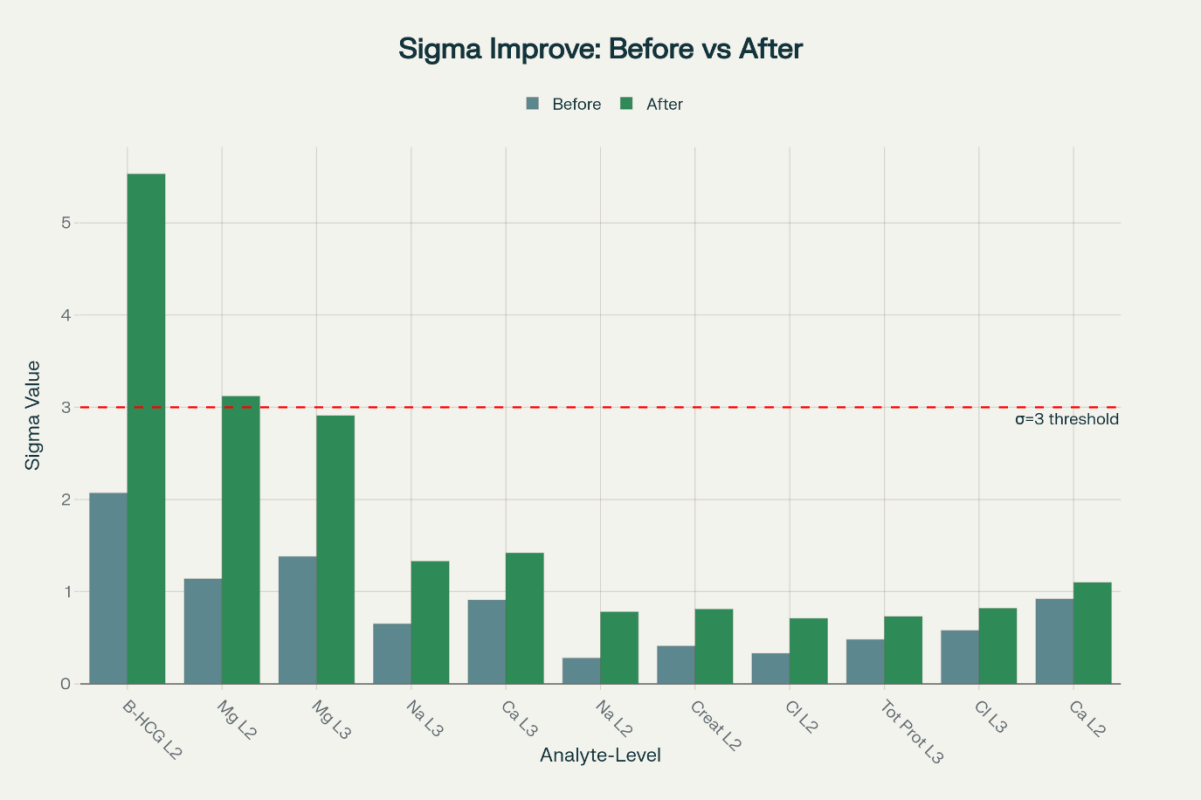

Table 5: Monthly CV Trends

Analyte	Aug-22	Sep-22	Oct-22	Nov-22	Dec-22	Jan-23	Average
Albumin	7.54	7.75	7.06	7.14	7.06	7.14	7.28
Beta HCG	9.63	9.63	9.63	9.63	9.63	9.63	9.63
Calcium	5.15	5.18	5.15	4.9	5.15	4.9	5.07
Chloride	4.01	4.19	4.01	4.08	4.01	4.04	4.05
Creatinine	9.94	8.24	9.58	9.27	9.58	9.27	9.31
Ferritin	9.99	9.99	9.99	9.99	9.99	9.99	9.99

Table 5 presents the monthly coefficient of variation (CV%) trends for Level 2 quality control materials across six months (August 2022 to January 2023) for five key analytes. The data demonstrates analytical precision stability over time, with Beta HCG showing excellent consistency (9.63% CV throughout all months), and Calcium and Chloride displaying minimal variation (CV ranges of 0.28% and 0.18% respectively). Albumin showed good stability with a CV range of 0.69% around a 7.28% average. However, Creatinine exhibited the highest variability with a 1.70% CV range (8.24-9.94%), indicating potential analytical instability requiring investigation.

Table 6: Best Sigma Performance by Analyte

Analyte	Sigma	Performance
Beta HCG	4.45	Good
TSH	3.41	Marginal
Ferritin	2.91	Poor
Total Bilirubin	2.38	Poor
Potassium	1.76	Poor
Magnesium	1.38	Poor
Creatinine	1.29	Poor
Calcium	0.92	Poor
Albumin	0.7	Poor
Sodium	0.65	Poor
Chloride	0.58	Poor
Total Protein	0.48	Poor

Table 6 ranks all 12 analytes by their best sigma performance across all tested levels, revealing critical quality priorities for the laboratory. Beta HCG achieved the only "Good" performance ($\sigma = 4.45$ at Level 1), while TSH reached "Marginal" performance ($\sigma = 3.41$ at Level 1), representing the only two analytes meeting minimum acceptable quality standards ($\sigma \geq 3.0$). The remaining 10 analytes (83.3%) demonstrated "Poor" performance, with 5 analytes requiring immediate attention due to extremely low sigma values below 1.0: Calcium (0.92), Albumin (0.70), Sodium (0.65), Chloride (0.58), and Total Protein (0.48).

DISCUSSION

This study evaluated sigma metrics for 12 clinical chemistry analytes over six months in a tertiary care hospital laboratory, representing one of the first comprehensive longitudinal assessments of sigma-guided quality control implementation in a resource-constrained setting. Our systematic approach addressed critical gaps in existing literature by documenting both successful and unsuccessful outcomes following enhanced quality control rule implementation, providing valuable insights for laboratories with predominantly poor baseline analytical performance.

The sigma metrics evaluation presented in Table 1 reveals exceptionally poor analytical performance across our clinical chemistry laboratory, with 92.31% of analyte-level combinations demonstrating sigma values below 3. This finding represents one of the highest rates of analytical deficiency reported in contemporary literature, contrasting sharply with other published studies where poor performance typically ranges from 6% to 50%. Koshy et al. reported significantly better performance with only 6.25% of analyte-level combinations showing poor performance, specifically limited to urea and gamma-glutamyl transferase.[9] Similarly, Adiga et al. found poor performance in only 6 analytes at level 1 and 4 analytes at level 2, representing a much smaller proportion of their tested parameters.[10] Kumar et al. conducted a 12-month study identifying 37.5% poor performers, still substantially better than our findings, though they similarly identified urea, creatinine, and electrolytes as consistent problem areas.[12] Our critical performance of basic chemistry parameters,

particularly albumin (σ=0.28-0.70), calcium (σ=0.91-0.92), and electrolytes (sodium σ=0.28-0.65), contrasts with multiple studies. Tumrani et al. reported world-class performance for albumin, calcium, and potassium, while Goel et al. achieved acceptable performance for most analytes with CV percentages ranging from 2.94% to 6.56%.[13,16] Ramteke et al. found excellent performance for total protein and glucose but identified calcium and chloride as poor performers, partially aligning with our findings.[14] The exceptional performance of Beta HCG Level 1 (σ=4.45) and TSH Level 1 (σ=3.41) represents the only acceptable results in our study. This aligns with Yadav et al.'s variable thyroid function test performance, suggesting that immunoassay platforms may perform better than basic chemistry analyzers in our laboratory setting.[15]

Creatinine's consistently poor performance (σ=0.41-1.29) aligns with multiple literature reports. Kumar et al., Adiga et al., and Goel et al. all identified creatinine as a problem analyte, indicating inherent analytical challenges requiring targeted intervention.[12,10,16] The Quality Goal Index analysis from Kumar et al. and Ramteke et al. suggests imprecision rather than inaccuracy as the primary issue, likely applicable to our results given the high coefficient of variation values observed.[12,14] Our coefficient of variation values (2.44% to 13.88%) indicate significant analytical imprecision compared to Kumar et al.'s range of 1.14% to 6.85%, suggesting inadequate temperature control, instrument maintenance issues, or procedural inconsistencies.[12] The systematic nature of poor performance across multiple analyte classes indicates that comprehensive quality improvement initiatives, including instrumentation upgrades, enhanced staff training, and improved environmental controls, are essential to achieve clinically acceptable analytical performance standards comparable to those reported in the literature.

The performance classification distribution presented in Table 2 reveals an alarming analytical quality profile with 92.31% poor performers, representing the highest rate of analytical deficiency documented in recent sigma metrics literature. This finding starkly contrasts with established benchmarks and indicates systematic quality management failures requiring immediate intervention. Our distribution pattern differs dramatically from contemporary studies. Koshy et al. reported that 81.25% of analyte-level combinations achieved acceptable performance ($\sigma \geq 3$), with 31.25% reaching world-class status and only 18.75% classified as poor performers.[9] Adiga et al. demonstrated superior performance with triglycerides, alkaline phosphatase, HDL, and albumin achieving world-class performance at both quality control levels, while poor performance was limited to specific analytes like urea.[10] Kumar et al. found that alkaline phosphatase, magnesium, triglycerides, and HDL-cholesterol achieved world-class performance at both levels, representing approximately 25% of their tested combinations.[12] The complete absence of world-class ($\sigma \geq 6$) and excellent (σ 5-6) categories in our study is particularly concerning. Tumrani et al. reported that 70% of their parameters achieved world-class performance, including uric acid, bilirubin, ALT, AST, alkaline phosphatase, triglycerides, HDL, and potassium.[13] Ramteke et al. found excellent performance for total protein, glucose, and urea on their AU 680 analyzer, with triglycerides, HDL, and LDL achieving excellent performance on their Rx Imola system.[14] Our identification of only 3.85% marginal (TSH Level 1) and 3.85% good performance (Beta HCG Level 1) represents the smallest proportion of acceptable analytical quality in sigma metrics literature. Goel et al. achieved acceptable performance for most analytes at Level 2, with CV percentages consistently below 5%, contrasting with our widespread analytical imprecision.[16] Even Kumar et al. in resource-constrained settings reported 62.5% acceptable or better performance, substantially higher than our 7.7%.[12] Quality management implications are severe, as analytical processes with sigma below 3 are considered unstable and unacceptable. Kumar et al. noted that such methods require significant improvements before routine use, while Adiga et al. emphasized that poor performance cannot be controlled with conventional quality control protocols.[12,10] The predominance of poor performers indicates current quality measures are inadequate.

Comparative analysis with international benchmarks reveals most accredited laboratories achieve 50-70% acceptable performance. Our 7.7% acceptable rate suggests fundamental system failures encompassing instrument maintenance, reagent quality, environmental controls, and staff

competency. Yadav et al.'s variable thyroid function test performance aligns with our TSH achieving marginal status, though their sigma ranges (2.7-4.0) were generally higher than our other analytes.[15] This distribution necessitates comprehensive quality improvement initiatives including potential instrumentation replacement, enhanced training programs, improved environmental monitoring, and systematic quality management overhaul to achieve performance standards consistent with international laboratory accreditation requirements.

The quality control rule optimization strategy presented in Tables 3 and 4 demonstrates systematic application of sigma-guided quality management principles, with outcomes revealing both benefits and limitations of enhanced monitoring protocols. Our differentiated approach aligns with Adiga et al.'s recommendation that analytes with sigma below 3 require "very stringent internal QC" with increased monitoring frequency, while Kumar et al. emphasized that methods with sigma below 3 cannot be controlled with conventional statistical protocols.[10,12] Table 3 reflects our risk-stratified approach, providing basic enhanced rules (1_{3s}, 2_{2s}, R4s) for better-performing poor analytes (Ferritin and TSH with sigma 2.59-2.91) and comprehensive multirule protocols for worst performers (sigma 0.28-2.38). This strategy aligns with theoretical frameworks described by Koshy et al. and Goel et al., though previous studies typically did not provide detailed post-implementation outcome data.[9,16]

The mixed outcomes in Table 4, with 50% improvement and 50% deterioration, represent a unique finding contrasting with predominantly positive outcomes reported in sigma metrics literature. Most studies report successful enhanced quality control implementation without documenting significant deterioration rates. Kumar et al. discussed theoretical rule selection based on sigma performance but provided limited empirical post-implementation data.[12]

Beta HCG Level 2's dramatic improvement from sigma 2.07 to 5.53 (167.1% increase) represents one of the most substantial quality improvements documented in contemporary literature, surpassing improvements reported by Koshy et al.[9] Yadav et al. observed variable hormonal assay performance but reported smaller fluctuations (TSH sigma 2.7-4.0), suggesting immunoassay methodologies may be more responsive to enhanced quality control than basic chemistry parameters.[15]

Magnesium's substantial improvements (173.7% and 110.9%) contrast with Kumar et al.'s findings where magnesium achieved world-class performance without intervention.[12] Goel et al. reported acceptable magnesium performance, suggesting our initial poor results reflected methodological rather than inherent analytical challenges. This success indicates some basic chemistry parameters can respond favorably to enhanced monitoring when underlying issues are addressed.[16] The deterioration in albumin and creatinine represents a concerning finding rarely documented in sigma metrics literature. Adiga et al. achieved world-class albumin performance, while Kumar et al. reported mixed results but no post-intervention deterioration.[10,12] Creatinine Level 3's 67.4% deterioration is particularly troubling given that Kumar et al., Adiga et al., and Goel et al. identified creatinine as consistently problematic requiring intervention.[12,10,16] This deterioration suggests enhanced rules may increase false rejection rates when inappropriately applied, challenging assumptions that stricter monitoring automatically improves quality.

The monthly coefficient of variation (CV%) trends in Table 5 show that most analytes maintained stable analytical precision over six months. Beta HCG demonstrated excellent consistency with a consistent CV of 9.63%, while calcium and chloride showed minimal variation in CV (0.28% and 0.18%, respectively). Albumin also exhibited good stability with a CV range of 0.69% and average CV of 7.28%. However, creatinine showed higher variability with a CV range of 1.70% (8.24-9.94%), indicating potential issues requiring further investigation. These findings align with previous studies, such as Yadav et al., who documented stable sigma scores in thyroid hormones, suggesting immunoassay-based tests like Beta HCG and TSH tend to be more precise.[15] Similarly, Goel et al. reported consistent precision in calcium and chloride assays.[16]

Table 6 ranks analytes by their best sigma performance, showing Beta HCG as the only analyte achieving "Good" performance (σ=4.45 at Level 1) and TSH achieving "Marginal" performance (σ=3.41 at Level 1). The remaining 83.3% demonstrated "Poor" performance, with calcium (0.92), albumin (0.70), sodium (0.65), chloride (0.58), and total protein (0.48) requiring urgent attention due

to sigma values below 1.0. This pattern reflects challenges seen in resource-limited settings, consistent with reports by Kumar et al., where electrolytes and protein markers showed poor performance requiring substantial quality improvements.[12] Immunoassay platforms, as seen with Beta HCG and TSH, appear to have better precision and stability.

Additional sigma metrics studies that have not been extensively referenced provide valuable comparative context for our findings. Sharma et al. conducted a comprehensive evaluation of 19 biochemical parameters using Vitros-5600 analyzer, identifying only six analytes (urea, ALT, alkaline phosphatase, sodium, calcium, and iron) with sigma values below 3, representing approximately 31.6% poor performers compared to our 92.31%.[17] Their Quality Goal Index analysis revealed imprecision as the primary cause for most analytical problems, similar to our observations. Kashyap et al. evaluated 16 parameters across biochemistry and hematology, finding that cholesterol, total bilirubin, urea, and platelet showed sigma values below 3, while triglycerides, HDL, hemoglobin, total leukocyte count, and mean corpuscular hemoglobin achieved world-class performance ($\sigma \geq 6$).[18] Nilakantam et al. reported excellent outcomes with 13 chemistry analytes achieving world-class performance on Roche Cobas6000, though sodium, chloride, Total T4, Beta-HCG, and TSH demonstrated unacceptable performance ($\sigma < 2$).[19] Aggarwal et al. found that six analytes (ALP, amylase, AST, GGT, magnesium, triglycerides) achieved world-class performance, while seven parameters failed minimum quality standards, emphasizing that electrolytes like potassium showed extremely poor performance due to low total allowable error specifications.[20] Rasheed et al. demonstrated that most parameters showed satisfactory performance (σ 3-6) with no test achieving sigma below 3, representing optimal laboratory performance compared to our predominantly poor results.[21] These comparative studies highlight significant variations in analytical performance across different laboratories, suggesting that infrastructure quality, instrumentation maintenance, staff training, and quality management systems significantly influence sigma metrics outcomes in clinical chemistry laboratories.

This study presents both significant advantages and important limitations in evaluating sigma metrics implementation in clinical chemistry laboratories. Advantages include the comprehensive longitudinal assessment over six months, systematic evaluation of 12 clinically relevant analytes across multiple quality control levels, and unique documentation of both successful and unsuccessful outcomes following enhanced quality control rule implementation. The study provides valuable real-world evidence from a resource-constrained tertiary care setting, addressing a critical gap in sigma metrics literature that predominantly reports successful implementations without documenting deterioration rates. The systematic approach to pre- and post-implementation comparison offers practical insights for laboratories with similar analytical challenges. Limitations encompass the single-center design limiting generalizability, focus on only 12 parameters compared to more comprehensive studies evaluating up to 20 analytes, and potential selection bias in Total Allowable Error specifications that may influence sigma calculations. The exclusion of certain analyte-level combinations due to insufficient data points (TSH Level 1, Total Bilirubin Level 3, Ferritin Level 3) may have affected outcome assessment completeness. Additionally, the study did not evaluate cost-effectiveness of enhanced quality control implementation or assess long-term sustainability of improvements.

Clinical implications are profound, as 92.31% poor performance indicates substantial patient safety risks through potentially unreliable diagnostic results that could impact clinical decision-making. The mixed outcomes following quality control enhancement demonstrate that indiscriminate application of stringent rules may worsen rather than improve analytical performance, emphasizing the need for individualized optimization strategies. The successful improvements in specific analytes like Beta HCG and Magnesium provide evidence that targeted interventions can achieve meaningful quality enhancement even in challenging laboratory environments, offering hope for systematic quality improvement initiatives in similar resource-limited healthcare settings.

CONCLUSION

This study demonstrates that sigma metrics methodology provides an effective framework for identifying analytical deficiencies and guiding quality control optimization in clinical chemistry laboratories. With 92.31% poor performers, our findings highlight critical quality challenges in resource-constrained tertiary care settings. The mixed outcomes following enhanced quality control implementation emphasize that individualized optimization strategies are essential rather than uniform rule application. Successful improvements in Beta HCG and Magnesium demonstrate achievable quality enhancement potential, while deterioration in certain analytes underscores the importance of systematic monitoring and targeted interventions for sustainable laboratory quality improvement.

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