Original Article

DOI: 10.7860/JCDR/2026/85766.23568

Comparing the Results of Nine Laboratory Analytes Using Internal Quality Control and Patient-based Real-time Quality Control: A Retrospective Observational Study

Biochemistry Section

SUBHASISH NAYAK[1], VANISHREE BUBANALE[2]

ABSTRACT

Introduction: Internal Quality Control (IQC) strategies, which form the basis of most Quality Control (QC) procedures, rely on routinely analysing commercially available QC materials with known analyte concentrations. These materials, however, may not accurately reflect patient samples, causing potential issues with sensitivity (failure to detect errors) or specificity (incorrectly rejecting valid results).

Aim: To evaluate the efficiency of Patient-Based Real-Time Quality Control (PBRTQC) and IQC for nine clinical chemistry analytes.

Materials and Methods: The present retrospective observational study was conducted at Dr. Prabhakar Kore Hospital, Belagavi, Karnataka, India, from January 2025 to December 2025. Nine clinical chemistry analytes, whose results were within predefined truncation limits, were chosen, which include albumin, aspartate transaminase, alanine transaminase, alkaline phosphatase, creatinine, chloride, potassium, sodium and total protein. The efficiency was evaluated using moving average analysis with simulated systematic errors. Using Statistical Package for Social Sciences (SPSS) 29.0, non-normally distributed variables were compared using the Mann-Whitney U test ($p < 0.05$), with continuous data reported as frequencies.

Results: The PBRTQC system demonstrated a superior 89% error detection rate for positive biases compared to 0% for IQC, identifying clinically significant biases within 4-5 patient samples N-S-D (Number of Samples to Detect). Despite this high sensitivity, the system maintained exceptional specificity with a false alarm rate of <1.5%. These findings indicate that PBRTQC, utilising the native patient matrix, provides a highly efficient and reliable real-time alternative to traditional batch-based QC.

Conclusion: The present study concludes that PBRTQC significantly outperforms traditional IQC by detecting systematic errors more effectively than IQC. The results highlight that PBRTQC offers superior sensitivity to matrix-related biases that commercial QC materials often miss, particularly in detecting shifts that IQC failed to flag. Ultimately, it is recommended to use a hybrid QC model that leverages PBRTQC for continuous, real-time monitoring alongside IQC to ensure comprehensive detection of both systematic and random errors.

Keywords: Analytical performance, Moving average, Quality assurance, Systematic error detection

INTRODUCTION

Accurate and reliable laboratory test results are essential for appropriate clinical decision-making and patient safety [1]. Clinical chemistry laboratories must consequently maintain strong QC systems to assure analytical dependability throughout the testing process. The International Organisation for Standardisation (ISO) 15189:2022 emphasises continuous quality assurance, risk-based thinking, and the prevention of erroneous result reporting as core requirements for medical laboratories [2]. QC practices play a central role in fulfilling these requirements by enabling early detection of analytical errors.

Conventional IQC using commercially available control materials has long been the standard approach for monitoring analytical performance [1]. IQC is typically performed at predefined intervals and is effective in identifying many systematic and random errors. However, this intermittent nature of IQC limits its ability to detect errors that occur between control measurements [3]. Additionally, the analytical behaviour of QC materials may not accurately reflect that of patient samples due to issues related to specimen commutability. Non-commutable materials can fail to detect clinically relevant biases, thereby compromising the reliability and harmonisation of laboratory results across measurement systems [4,5].

The concept of utilising patient results for quality monitoring was first introduced through the Average of Normals (AoN) approach by Hoffmann RG and Waid ME in 1965, and guidelines for its practical implementation were later established by Cembrowski GS et al., [6,7]. This approach formed the foundation of what is now referred to as PBRTQC. PBRTQC uses aggregated patient data to continuously monitor analytical performance, offering the advantage of real-time error detection without reliance on external control materials. Because PBRTQC is based on native patient samples, it inherently overcomes commutability-related limitations and aligns more closely with the true clinical population [8].

A significant limitation of existing literature is the scarcity of studies directly comparing PBRTQC with IQC under controlled error conditions defined by regulatory standards. While retrospective analyses are common, few have rigorously evaluated QC system performance by mathematically simulating systematic errors based on the Clinical Laboratory Improvement Amendments (CLIA) Total Allowable Error (TEa) criteria [9-11]. CLIA TEa limits define acceptable analytical performance thresholds and are widely used for method validation and performance assessment. However, the application of these limits to rigorous mathematical simulations where specific systematic errors are introduced to historical data to stress-test QC protocols remains insufficiently explored [8,9,11].

Advancements in laboratory automation, information systems, and data analytics have renewed interest in PBRTQC as a complementary QC strategy. A comprehensive review by Badrick

T et al., highlighted the theoretical strengths of PBRTQC, including continuous monitoring, enhanced sensitivity to small systematic shifts, and improved alignment with patient risk. The authors also emphasised that PBRTQC should be tailored to individual analytes and population characteristics and validated against conventional QC systems [8]. Despite these advantages, PBRTQC adoption remains limited in routine practice, largely due to concerns regarding implementation complexity, false alarm rates, and lack of standardised performance evaluation [12].

Another important consideration in QC evaluation is the balance between error detection capability and false alarm rates. Excessive false rejections can lead to unnecessary repeat testing, increased workload, and alarm fatigue, whereas delayed error detection increases the risk of reporting clinically misleading results [13]. While PBRTQC has been proposed as a tool capable of earlier error detection compared to IQC, limited evidence exists quantifying its false alarm behaviour and comparative efficiency across multiple routine clinical chemistry analytes [8].

Furthermore, recent literature has increasingly addressed the clinical impact of QC system performance by shifting the focus from analytical metrics to patient risk quantification. Parvin CA established that the frequency of QC testing directly influences the "Expected Number of unreliable finals" (E(Nuf)), thereby quantifying the clinical risk of reporting erroneous results during periods of undetected error [3]. Building on this patient-centric approach, Loh T et al., recommended verifying PBRTQC performance using the 'Number of Patient samples until Error Detection' (Nped) metric to explicitly limit the window of clinical risk [9]. Practical evidence of this impact was demonstrated by Ma C et al., who utilised daily antibody positivity rates to detect systematic reagent errors that had bypassed traditional IQC, proving that PBRTQC effectively prevents the release of clinically misleading data that would otherwise remain undetected [14].

The ultimate objective of QC is to prevent clinically significant patient harm rather than merely detect statistical deviations [2,3]. Demonstrating how earlier error detection influences patient result reporting and potential clinical interpretation is therefore essential to justify the integration of PBRTQC into routine laboratory practice.

The present study introduces a novel approach by mathematically simulating systematic errors specifically calibrated to the CLIA TEa goals. The rationale for this design was to move beyond theoretical modelling and rigorously stress-test PBRTQC under clinically relevant conditions, thereby quantifying its superior ability to minimise the 'blind spots' inherent in traditional IQC. The study aimed to compare the results of nine laboratory analytes using IQC and PBRTQC.

MATERIALS AND METHODS

The present retrospective, observational study was conducted in the Department of Biochemistry, Jawaharlal Nehru Medical College, in collaboration with the Hi-Tech Laboratory of Dr. Prabhakar Kore Hospital, Belagavi, Karnataka, India, from January 2025 to December 2025. The study protocol was reviewed and approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College, Belagavi, Karnataka, India on 26 April 2024 (IEC approval number: MDC/JNMCIEC/267), and the study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and institutional ethical guidelines.

As a time-bound study, data collection was restricted to the six-month period from January 2025 to June 2025, followed by data analysis from July 2025 to December 2025. The 181 measurements per analyte represent all eligible patient samples collected during the six-month data collection period that met the inclusion criteria.

Inclusion and Exclusion criteria: The study included routine patient samples analysed for the nine selected clinical chemistry analytes: Albumin, Alanine aminotransferase (ALT) Aspartate aminotransferase (AST), Alkaline Phosphatase (ALP), creatinine, chloride, potassium, sodium, and total protein-during the study period, provided the results fell within predefined truncation limits (based on local reference intervals to exclude pathological outliers). Furthermore, only samples meeting laboratory acceptance criteria for pre-analytical quality, characterised by appropriate sample volume and the absence of gross haemolysis, lipaemia, or icterus, were included. Conversely, repeat measurements from the same patient encounter were excluded to prevent duplication bias. The analysis also excluded any results flagged for pre-analytical or post-analytical errors by the Laboratory Information System, as well as samples processed during periods of analyser maintenance, calibration, reagent lot change validation, or instrument downtime.

Study Procedure

The PBRTQC system was implemented using a Simple Moving Average (SMA) algorithm, a well-known patient-based quality control approach that continually monitors analytical performance using routine patient data rather than control materials alone [15]. The SMA estimates the unweighted mean of a set number of consecutive patient outcomes, smoothing out short-term physiological volatility and increasing sensitivity to systematic analytical alterations. To guarantee that the moving average accurately reflected analytical variation rather than pathological extremes, truncation restrictions were applied as the sole inclusion criterion. These limits were defined using the locally generated reference interval endpoints for each analyte [Table/Fig-1], ensuring they were unique to the study population. Patient values falling outside these predefined boundaries were categorised as outliers and excluded from the moving average computation.

Parameters	Lower limit	Upper limit	CLIA (TEa goal)
Albumin	3.5 g/dL	5.5 g/dL	+ or - 8%
AST	8 IU/L	33 IU/L	+ or - 15%
ALT	0 IU/L	45 IU/L	+ or - 15%
ALP	44 IU/L	147 IU/L	+ or - 20%
Creatinine	0.7 mg/dL	1.3 mg/dL	+ or - 10%
Chloride	96 mEq/L	106 mEq/L	+ or - 5%
Potassium	3.5 mEq/L	5.2 mEq/L	+ or - 0.5 mEq/L
Sodium	135 mEq/L	145 mEq/L	+ or - 4 mEq/L
Total protein	6.0 g/dL	8.0 g/dL	+ or - 8%

[Table/Fig-1]: Acceptable truncation limits of the nine analytes with their respective Clinical Laboratory Improvement Amendments (CLIA) Total allowable Error (TEa) goals.
AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase

The PBRTQC was implemented using optimised truncation limits to filter physiological skew and minimise false rejections, in line with recommendations of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) [8]. Reference intervals were applied as truncation boundaries to exclude pathological outliers while retaining analytical sensitivity.

The SMA value, Z(t), for the current patient result was calculated using the following formula:

$$Z(t)= \frac{\chi(t) + \chi(t-1) + \chi(t-2) + \ldots \chi(t-n+1)}{n}$$

Where, $\chi(t)$ represents the individual patient result and "n" is the batch (block) size. A fixed batch size of (n=5) was used for all analytes to balance responsiveness and false alarm rates [16]. Control limits {Lower Control Limit (LCL); Upper Control Limit (UCL)} were retrospectively determined from stable analytical periods using post-truncation "normal" patient data [10].

Error detection was evaluated via mathematical simulation by introducing systematic biases equivalent to CLIA TEa targets [11,17]. Detection performance was expressed as the Number of Samples to Detect (N-S-D). System specificity was assessed by tracking the

false alarm rate during analytically stable periods. A false alarm rate of less than 1% was regarded as acceptable, ensuring adequate filtration of physiological fluctuation without superfluous alarms. PBRTQC performance was compared to concurrent IQC data, which was analysed once per eight-hour shift for each selected analyte, to assess error detection consistency. Detection rates were examined to see if IQC materials exhibited the same analytical biases observed by PBRTQC. Discordant occurrences were given special attention, such as cases where IQC results remained within control limits despite a large shift in patient moving averages [7].

STATISTICAL ANALYSIS

Statistical analyses were performed with IBM SPSS software version 29.0 and Microsoft Excel. Descriptive statistics were performed for all variables using median and range. Normality was assessed using the Kolmogorov-Smirnov test. Continuous variables were presented as medians and interquartile ranges. Box plots were used for the graphical representation of the comparison between the two QC methods for each parameter. As all the parameters showed non-normal distribution, the comparison between real time QC and IQC was done using the Mann-Whitney U test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Albumin showed a PBRTQC median of 4.51 g/dL with a tight IQR of 0.06, whereas IQC showed a median of 4.36 g/dL with a wider IQR of 0.19. Similarly, for enzymes like ALP, the PBRTQC IQR (3.44 IU/L) was considerably lower than that of IQC (9.04 IU/L), reflecting the known variability of commercial enzyme controls.

Statistically, the Mann-Whitney U test indicated significant differences ($p<0.05$) in the distribution of medians for eight out of nine analytes, including Albumin, ALP, AST, ALT, Chloride, Potassium, Sodium, and Total Protein. However, Creatinine showed no statistically significant difference (U=14413, p=0.101), with nearly identical medians (PBRTQC: 0.998 mg/dL vs. IQC: 0.997 mg/dL) [Table/Fig-2,3a-i].

The established upper and lower control limits for all nine analytes were presented, with the calculated boundaries reflecting the varying stringency required for different parameters, demonstrating notably narrower acceptable performance ranges for tightly controlled electrolytes compared to the wider acceptable variance for enzymes [Table/Fig-4].

The PBRTQC system demonstrated differential sensitivity depending on the direction of the error. The system exhibited high efficiency in detecting positive systematic shifts, identifying the error in 89% (8/9) of the analytes tested, with the sole exception being the +15% positive bias for ALT. For creatinine, the system flagged +10% bias within just four patient samples (N-S-D=4). The system was less sensitive to negative shifts. While it successfully detected negative biases for ALT (-15%) and Potassium (-0.5 mEq/L) within 5 samples (N-S-D=5), it did not flag negative errors for the remaining seven analytes, suggesting a directional sensitivity in the moving average algorithm for these specific truncation limits [Table/Fig-5].

In contrast, the concurrent IQC protocol missed the error in all positive bias scenarios. The only errors detected by IQC were the negative biases for ALT and Potassium, which PBRTQC also detected.

For eight out of nine analytes (Albumin, ALP, ALT, AST, Chloride, Potassium, Sodium, Total Protein), the PBRTQC system maintained a 0% false alarm rate, meaning no false flags were generated during the stable period. Creatinine was the only analyte to show a minor deviation, with a false alarm rate of <1.5%, which is well within acceptable limits for clinical operations. The efficiency of the two systems was assessed by comparing sensitivity (N-S-D) and specificity (false alarm rate). PBRTQC successfully detected 89% (8/9) of positive systematic biases with a false alarm rate of <1.5%. In contrast, IQC detected 0% of positive bias conditions, though it maintained a 0% false alarm rate [Table/Fig-6].

DISCUSSION

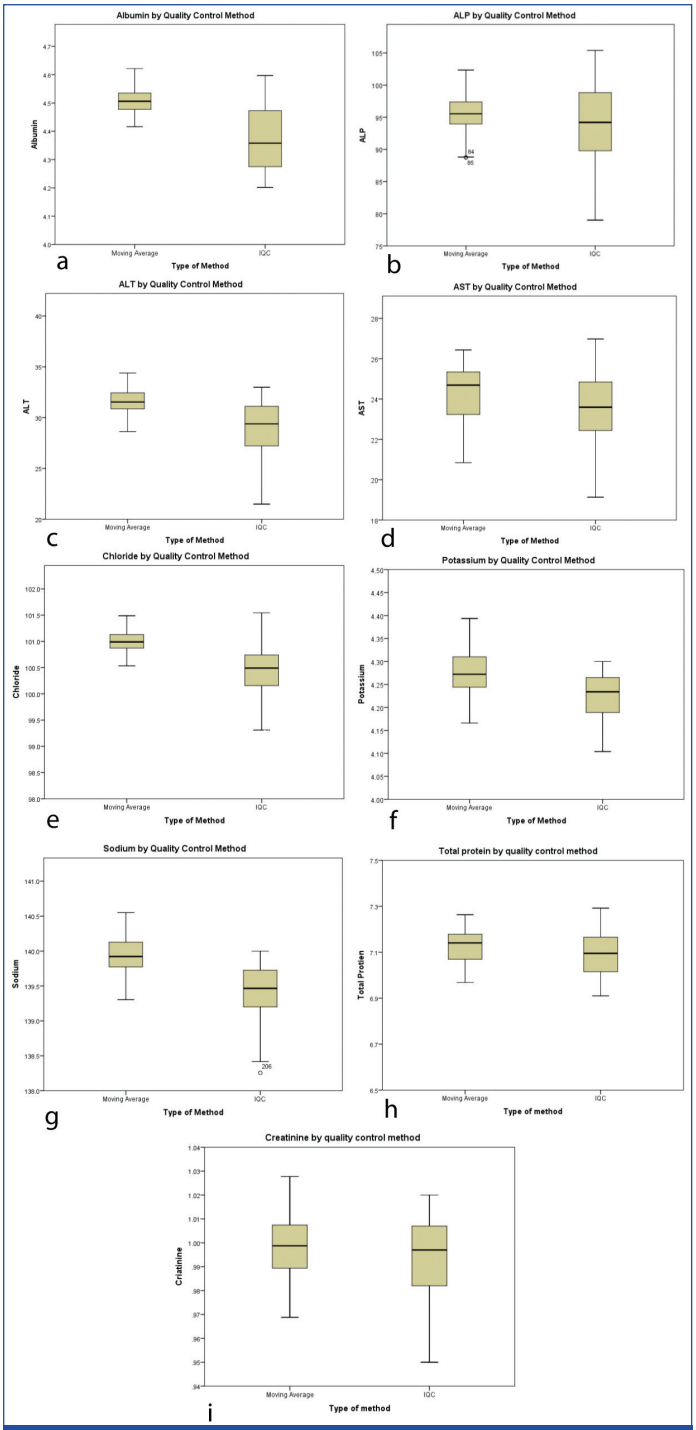
In this study, the overlapping medians and ranges observed in [Table/Fig-2] reflect the stable operating period, serving as a validation that PBRTQC accurately mirrors the analytical performance of standard IQC under normal conditions. In contrast, the detection efficiency (89% for PBRTQC vs. 20% for IQC) refers specifically to the systematic error simulation phase, where systematic biases equal to CLIA TEa targets were mathematically introduced to the data stream. The divergence in performance during this specific phase highlights the superior sensitivity of PBRTQC's continuous moving average in flagging rapid deviations that the intermittent, batch-based IQC protocol often misses. These findings are consistent with the ideas outlined by Badrick T et al., who stressed that PBRTQC methods can detect analytical shifts in real time without relying on external control materials hence lowering the chance of reporting incorrect results between standard IQC runs [18].

The N-S-D was used to assess the efficiency of the PBRTQC system in this investigation, with the majority of analytes- including electrolytes and enzymes-flagged within 4 to 5 samples. For example, Creatinine had the maximum efficiency, with a N-S-D of 4. This quick detection is compatible with van Rossum's recommended settings, in which continuous PBRTQC generates a new value for each newly available test result, acting as a near-real-time QC tool [10]. Similar rapid error detection has been reported by Duan X et al., who demonstrated that moving average algorithms significantly reduce the error detection lag compared to batch testing [12].

The PBRTQC system maintained an extremely low false alarm rate of <1.5%, making specificity evaluation an important feature of this study. In laboratory medicine, "alarm fatigue" is a major issue; a system with high sensitivity but low specificity is unusable

Analytes	Sample runs	PBRTQC		IQC		Mann-Whitney U Statistics	p-value
		Median	Interquartile range	Median	Interquartile range		
Albumin (g/dL)	181	4.51	0.06	4.36	0.19	5691	<0.001
ALP (IU/L)	181	95.54	3.44	94.21	9.04	13565	0.012
ALT (IU/L)	181	31.53	1.58	29.39	3.90	6480	<0.001
AST (IU/L)	181	24.69	2.11	23.59	2.41	11429	<0.001
Chloride (mEq/L)	181	100.99	0.26	100.49	0.58	4284	<0.001
Potassium (mEq/L)	181	4.27	0.07	4.23	0.08	7517	<0.001
Sodium (mEq/L)	181	139.92	0.36	139.47	0.53	3918	<0.001
Total protein (g/dL)	181	7.14	0.11	7.09	0.16	12330	<0.001
Creatinine (mg/dL)	181	0.998	0.018	0.997	0.025	14413	0.101

[Table/Fig-2]: Comparative analysis of descriptive statistics and Mann-Whitney U test results between Patient-Based Real-Time Quality Control (PBRTQC) and Internal Quality Control (IQC) for nine analytes.
AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; Mann-whitney U test applied



[Table/Fig-3]: Comparison of analyte concentration distributions between PBT-TQC and IQC. Boxplots represent the median (central line), interquartile range (box edges), and range (whiskers) for: a) Albumin; b) ALP; c) ALT; d) AST; e) Chloride; f) Potassium; g) Sodium; h) Total Protein; and i) Creatinine. PBRTQC displays tighter clustering for electrolytes compared to IQC, while enzyme distributions show expected variability..

Parameters	PBRTQC median	CLIA (TEa goal)	Lower control limit	Upper control limit
Albumin	4.51 g/dL	+ or - 8%	4.15 g/dL	4.87 g/dL
ALP	95.54 IU/L	+ or - 20%	76.43 IU/L	114.65 IU/L
ALT	31.53 IU/L	+ or - 15%	26.80 IU/L	36.26 IU/L
AST	24.69 IU/L	+ or -15%	20.99 IU/L	28.39 IU/L
Creatinine	0.998 mg/dL	+ or - 10%	0.898 mg/dL	1.098 mg/dL
Chloride	100.99 mEq/L	+ or - 5%	95.94 mEq/L	106.04 mEq/L
Potassium	4.27 mEq/L	+ or - 0.5 mEq/L	3.77 mEq/L	4.77 mEq/L
Sodium	139.92 mEq/L	+ or - 4 mEq/L	135.92 mEq/L	143.92 mEq/L
Total protein	7.14 g/dL	+ or - 8%	6.57 g/dL	7.71 g/dL

[Table/Fig-4]: Establishment of PBRTQC control limits based on CLIA TEa goals. CLIA: Clinical laboratory improvement amendments; AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; PBRTQC: Patient based real time quality control

Parameters	Positive bias	No. of samples to detect the error (N-S-D)	Negative bias	No. of samples to detect the error (N-S-D)
Albumin	+8%	5	-8%	No error found
ALP	+20%	5	-20%	No error found
ALT	+15%	No error found	-15%	5
AST	+15%	5	-15%	No error found
Creatinine	+10%	4	-10%	No error found
Chloride	+5%	5	-5%	No error found
Potassium	+0.5 mEq/L	5	-0.5 mEq/L	5
Sodium	+4 mEq/L	5	-4 mEq/L	No error found
Total Protein	+ 8%	5	-8%	No error found

[Table/Fig-5]: Efficiency analysis of PBRTQC using number of samples to detect (N-S-D).

Parameters	Bias introduced	PBRTQC outcome	IQC outcome	False alarm rates
Albumin	+8%	Detected	Missed	0%
ALP	+20%	Detected	Missed	0%
ALT	+15%	Missed	Missed	0%
ALT	-15%	Detected	Detected	0%
AST	+15%	Detected	Missed	0%
Creatinine	+10%	Detected	Missed	<1.5%
Chloride	+5%	Detected	Missed	0%
Potassium	+0.5 mEq/L	Detected	Missed	0%
Potassium	-0.5 mEq/L	Detected	Detected	0%
Sodium	+4 mEq/L	Detected	Missed	0%
Total protein	+8%	Detected	Missed	0%

[Table/Fig-6]: Performance comparison between PBRTQC and IQC regarding error detection efficiency, sensitivity, and specificity.

[13]. The specificity results are consistent with those reported by Cembrowski GS and Westgard JO, who said that well-defined truncation limits are critical for filtering out physiological outliers and boosting PBRTQC stability [7,19]. By guaranteeing that only clinically important shifts based on CLIA goals raise an alarm, PBRTQC demonstrated that it is a robust instrument and did not unnecessarily disturb everyday laboratory operations [20]. Crucially, the study achieved an exceptionally low false alarm rate (<1.5%), proving high specificity and resistance to alarm fatigue. Finally, quantifying efficiency through the N-S-D demonstrates that the PBRTQC system can identify 89% of errors within just 4-5 samples, significantly reducing the risk of reporting erroneous data compared to traditional batch-based IQC.

The study also examined the "matrix effect" on IQC materials. The retrospective analysis indicated statistically significant discrepancies between PBRTQC and IQC data for eight of the nine analytes. In the retrospective error simulation, PBRTQC identified numerous biases that IQC missed, most likely because patient samples provide a commutable, native matrix that commercially generated controls cannot always match. This conclusion is consistent with Miller's work, which stated that non-commutable QC materials can fail to detect clinically relevant biases, reducing the reliability of results [5]. However, the present study did highlight that creatinine showed no statistically significant difference (p=0.101), suggesting comparable performance, though formal equivalence testing was not conducted.

Finally, the therapeutic impact of applying a PBRTQC methodology based on a SMA is significant. By detecting 89% of errors in five samples, the laboratory can considerably reduce the chance of providing erroneous data to doctors. The incorporation of CLIA TEa goals into the PBRTQC framework ensures that the quality criteria are not just statistically calculated, but also clinically relevant to patient diagnosis and treatment. These findings support the inclusion

of PBRTQC as a helpful supplement to standard QC procedures, as advocated by Hoffmann RG and Waid ME, to improve overall analytical dependability [2,6].

Limitation(s)

The limitations of this study primarily stem from its retrospective and simulated nature. While the use of historical patient data allowed for robust baseline modelling, the introduction of systematic bias was a mathematical simulation rather than a real-time instrument malfunction. Consequently, the findings may not fully capture the complexity of random instrument errors or multifactor analytical drifts. The study used only a single type and lot of IQC material, limiting the generalisability of matrix effects to other QC brands. Reference method or external quality assurance data were excluded, preventing evaluation of absolute accuracy. Lastly, while PBRTQC excelled in detecting systematic shifts, it is not designed to replace IQC for detecting individual "random" errors, suggesting a need for a hybrid QC approach.

CONCLUSION(S)

The current study demonstrates that PBRTQC significantly outperforms traditional IQC in the detection of systematic analytical errors. By applying CLIA TEa targets to a SMA algorithm, PBRTQC successfully detected 89% of positive systematic biases, identifying significant shifts within just 4 to 5 patient samples (N-S-D). These findings highlight the ability of PBRTQC to provide rapid, continuous monitoring of the native patient matrix, effectively mitigating the risk of error propagation during the intervals between IQC measurements. Consequently, it is recommended that PBRTQC should not replace, but rather be integrated into a hybrid QC model. This approach combines the real-time sensitivity of PBRTQC with the established stability of IQC, ensuring a robust, patient-centric quality assurance framework that enhances overall analytical reliability.

REFERENCES

[1] Westgard JO. Internal quality control: Planning and implementation strategies. Ann Clin Biochem. 2003;40(Pt 6):593-611.
[2] International Organization for Standardization. Medical laboratories- requirements for quality and competence (ISO 15189:2022). Geneva: ISO; 2022. Available from: https://www.iso.org/obp/ui/en/#iso:std:iso:15189:ed-4:v1:en.
[3] Parvin CA. Assessing the impact of the frequency of quality control testing on the quality of reported patient results. Clin Chem. 2008;54(12):2049-54. Doi: 10.1373/clinchem.2008.113639. Epub 2008 Oct 16. PMID: 18927244.
[4] Miller WG, Jones GR, Horowitz GL, Weykamp C. Proficiency testing/external quality assessment: Current challenges and future directions. Clin Chem. 2011;57(12):1670-80.
[5] Miller WG. Specimen materials, target values and commutability for external quality assessment (proficiency testing) schemes. Clin Chim Acta. 2003;327:25-37. Available from: https://doi.org/10.1016/S0009-8981(02)00370-4.
[6] Hoffmann RG, Waid ME. The "average of normals" method of quality control. Am J Clin Pathol. 1965;43:134-41.
[7] Cembrowski GS, Chandler EP, Westgard JO. Assessment of "Average of Normals" quality control procedures and guidelines for implementation. Am J Clin Pathol. 1984;81(4):492-99.
[8] Badrick T, Bietenbeck A, Cervinski MA, Katayev A, van Rossum HH, Loh TP; International Federation of Clinical Chemistry and Laboratory Medicine Committee on Analytical Quality. Patient-based real-time quality control: Review and recommendations. Clin Chem. 2019;65(8):962-71. Doi: 10.1373/clinchem.2019.305482. PMID:31263035.
[9] Loh T, Bietenbeck A, Cervinski M, van Rossum H, Katayev A, Badrick T, on behalf of the International Federation of Clinical Chemistry and Laboratory Medicine Committee on Analytical Quality. Recommendation for performance verification of patient-based real-time quality control. Clinical Chemistry and Laboratory Medicine (CCLM). 2020;58(8):1205-13. Available from: https://doi.org/10.1515/cclm-2019-1024.
[10] van Rossum HH, Kemperman H. Optimization and validation of moving average quality control procedures using bias detection curves and moving average validation charts. Clin Chem Lab Med. 2017;55(2):218-24. Doi: 10.1515/cclm-2016-0270. PMID:27522620.
[11] Centers for Medicare & Medicaid Services. Medicare, Medicaid, and CLIA programs: Laboratory requirements; total allowable error. Washington (DC): US Department of Health and Human Services; 2024.
[12] Duan X, Badrick T, Shao W, Bietenbeck A, Tan X, Zhu J, et al. Improving the efficiency of quality control in clinical laboratory with an integrated PBRTQC system based on patient risk. Clin Chem Lab Med. 2025;63(9):1716-27. Doi: 10.1515/cclm-2025-0163. PMID: 40178342.
[13] Ng D, Polito FA, Cervinski MA. Optimization of a moving averages program using a simulated annealing algorithm: The goal is to monitor the process not the patients. Clin Chem. 2016;62(10):1361-71.
[14] Ma C, Zhang Q, Hu Y, Ding W, Xia L, Qiu L. Application and insights on patient-based real-time quality control: Detecting undetected errors in internal quality control through daily antibody positivity rate analysis. Biochem Med (Zagreb). 2025;35(2):020801. Doi: 10.11613/BM.2025.020801. Epub 2025 Apr 15. PMID: 40469568; PMCID: PMC12131385.
[15] van Rossum HH. Moving average quality control: Principles, practical application and performance. Clin Chem Lab Med. 2009;47(3):289-96. Doi: 10.1515/CCLM.2009.061.
[16] Lukić V, Ignjatović S. Moving average procedures as an additional tool for real-time analytical quality control: Challenges and opportunities of implementation in small-volume medical laboratories. Biochem Med (Zagreb). 2022;32(1):010705.
[17] Lukić V, Ignjatović S. Optimizing moving average control procedures for small-volume laboratories: Can it be done? Biochem Med (Zagreb). 2019;29(3):030710.
[18] Badrick T, Bietenbeck A, Katayev A, van Rossum HH, Loh TP, Cervinski MA. Implementation of patient-based real-time quality control. Crit Rev Clin Lab Sci. 2020;57(8):532-47. Doi: 10.1080/10408363.2020.1765731.
[19] Cembrowski GS, Westgard JO. Quality control of multichannel hematology analyzers: Evaluation of Bull's algorithm. Am J Clin Pathol. 1985;83(3):337-45. Doi: 10.1093/ajcp/83.3.337. PMID: 3976570.
[20] Fleming JK, Katayev A. Changing the paradigm of laboratory quality control through implementation of real-time test results monitoring: For patients by patients. Clin Biochem. 2015;48(7-8):508-13. Doi: 10.1016/j.clinbiochem.2014.12.016. Epub 2014 Dec 27. PMID: 25549976.

PARTICULARS OF CONTRIBUTORS:
1. Tutor, Department of Biochemistry, KAHER's Jawaharlal Nehru Medical College, Belagavi, Karnataka, India.
2. Professor, Department of Biochemistry, KAHER's Jawaharlal Nehru Medical College, Belagavi, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Subhasish Nayak,
Tutor, Department of Biochemistry, KAHER's Jawaharlal Nehru Medical College, Nehru Nagar, Belagavi, Karnataka, India.
E-mail: subhasish1993nayak@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Dec 12, 2025
- Manual Googling: Mar 17, 2026
- iThenticate Software: Mar 19, 2026 (1%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Dec 08, 2025**
Date of Peer Review: **Jan 12, 2026**
Date of Acceptance: **Mar 21, 2026**
Date of Publishing: **Jun 01, 2026**