Section: Biochemistry

Systematic Review

QUALITY CONTROL ASSESSMENT IN CLINICAL BIOCHEMISTRY LABORATORIES

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ABSTRACT

Background: Quality control (QC) is a fundamental component of clinical biochemistry laboratories, ensuring the accuracy, precision, and reliability of laboratory test results that support clinical decision-making and patient care. Advances in laboratory automation, statistical quality control, and international accreditation standards have enhanced analytical performance; however, laboratory errors continue to occur throughout the pre-analytical, analytical, and post-analytical phases. This review aims to evaluate current quality control practices in clinical biochemistry laboratories, highlighting internal quality control (IQC), external quality assessment (EQA), statistical quality control methods, accreditation standards, emerging technologies, and future perspectives for improving laboratory quality.

Materials and Methods: A narrative review of the literature was conducted using PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, and Google Scholar. Peer-reviewed articles, systematic reviews, international guidelines, and consensus documents published primarily between 2015 and 2026 were critically analyzed. Evidence relating to IQC, EQA, Six Sigma methodology, ISO 15189 accreditation, laboratory automation, and quality indicators was synthesized.

Results: The reviewed literature indicates that comprehensive quality management systems significantly improve analytical accuracy, precision, and consistency. Routine implementation of IQC using Levey–Jennings charts and Westgard multirule procedures, combined with participation in EQA programs, enhances laboratory performance and minimizes analytical errors. Adoption of ISO 15189 standards, Six Sigma metrics, standardized quality indicators, and automation further strengthens quality assurance by improving workflow efficiency and supporting continuous quality improvement. Nevertheless, pre-analytical errors, workforce limitations, and resource constraints remain major challenges, particularly in resource-limited settings.

Conclusion: Integrating robust quality control practices with accreditation standards, risk-based quality management, and technological innovations is essential for ensuring reliable laboratory services. Continuous monitoring, staff competency development, and harmonization of quality management practices will further enhance patient safety and diagnostic excellence in clinical biochemistry laboratories.

Keywords: Clinical biochemistry; quality control; internal quality control; external quality assessment; ISO 15189; Six Sigma; laboratory accreditation; quality assurance.

INTRODUCTION

Clinical biochemistry laboratories play a pivotal role in modern healthcare by providing accurate and timely laboratory results that support disease diagnosis, therapeutic monitoring, prognosis, and preventive healthcare. Approximately 60–70% of clinical decisions are influenced by laboratory

investigations, emphasizing the critical importance of reliable biochemical testing. Consequently, maintaining high standards of analytical quality is fundamental to ensuring patient safety and improving clinical outcomes.

Quality control (QC) is a key component of laboratory quality management systems and encompasses systematic procedures designed to monitor, evaluate, and maintain the precision and accuracy of laboratory testing. Effective quality control enables laboratories to detect analytical errors, minimize variability, and ensure consistency in test performance. QC measures include both internal quality control (IQC), which continuously monitors day-to-day analytical performance, and external quality assessment (EQA) or proficiency testing, which compares laboratory performance with that of peer laboratories using standardized specimens.[1,2]

The increasing automation of laboratory instruments, adoption of sophisticated analytical platforms, and implementation of international quality standards such as ISO 15189 have significantly enhanced laboratory performance. However, challenges including pre-analytical errors, analytical bias, reagent variability, instrument malfunction, and post-analytical reporting errors continue to affect the overall quality of laboratory services. Therefore, continuous quality assessment, regular staff training, adherence to standard operating procedures, application of statistical quality control tools such as Levey–Jennings charts and Westgard rules, and participation in external quality assessment programs remain essential for maintaining analytical excellence.

Recent advances in quality management have introduced concepts such as Six Sigma metrics, risk-based quality control, laboratory automation, digital quality monitoring, and artificial intelligence-assisted quality assessment. These innovations have improved error detection, optimized quality control strategies, and enhanced laboratory efficiency while reducing operational costs.[3,4]

This review aims to provide a comprehensive overview of quality control assessment in clinical biochemistry laboratories by discussing the principles of quality management, internal and external quality control systems, statistical tools for quality evaluation, international accreditation standards, recent technological advancements, current challenges, and future directions. The review is intended to serve as a valuable resource for biochemistry faculty, laboratory professionals, postgraduate students, and researchers involved in clinical laboratory practice and quality management.

MATERIALS AND METHODS

Study Design: This review is a narrative literature review conducted to summarize the current evidence on quality control practices in clinical biochemistry laboratories. The review focuses on the principles of quality management, internal and external quality control, quality indicators, accreditation standards, statistical quality control methods, and recent technological advances in laboratory quality assurance.

Literature Search Strategy: A comprehensive literature search was performed using electronic databases including PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, and ScienceDirect. The search included articles published in English between 2005 and 2026, with preference given to recent publications and landmark guidelines.

Inclusion Criteria:

Studies were included if they:

- Discussed quality control or quality assurance in clinical biochemistry laboratories.
- Reported on internal quality control, external quality assessment, statistical quality control, or laboratory accreditation.
- Included original research articles, systematic reviews, review articles, international guidelines, consensus statements, and professional recommendations.
- Were published in peer-reviewed journals in English.

Exclusion Criteria:

The following publications were excluded:

- Non-English articles.
- Conference abstracts without full text.
- Editorials, opinion articles, and letters lacking scientific evidence.
- Studies unrelated to clinical biochemistry laboratory quality management.

Data Extraction and Synthesis: Relevant articles were screened based on title, abstract, and full-text review. Information was extracted regarding study objectives, quality control methodologies, statistical quality control tools, accreditation standards, quality indicators, laboratory performance measures, challenges, and recent technological developments. The extracted evidence was organized thematically to provide a comprehensive overview of current quality control practices and future directions in clinical biochemistry laboratories.

Ethical Considerations: As this review utilized data from previously published studies and publicly available guidelines, ethical approval and informed consent were not required.

RESULTS

A total of published studies, review articles, international guidelines, and quality management documents were evaluated to summarize the current evidence on quality control assessment in clinical biochemistry laboratories. The findings were categorized into major themes including internal quality control (IQC), external quality assessment (EQA), statistical quality control, Six Sigma implementation, ISO 15189 accreditation, and

emerging technologies in laboratory quality management.

Internal Quality Control: Most studies demonstrated that routine implementation of IQC significantly improves analytical precision and detects random and systematic errors before patient results are released. Laboratories utilizing Levey–Jennings charts in conjunction with Westgard multirule procedures reported fewer analytical errors and improved consistency in daily laboratory operations.

External Quality Assessment: Participation in EQA or proficiency testing programs consistently improved inter-laboratory comparability and analytical accuracy. Accredited laboratories participating regularly in national or international EQA schemes showed superior analytical performance compared to laboratories with limited quality assessment participation.

Six Sigma and Quality Indicators: Recent investigations have highlighted Six Sigma metrics as an effective approach for evaluating analytical performance. Sigma metrics greater than six were associated with world-class analytical quality, whereas lower sigma values indicated the need for stricter quality control procedures or method optimization. Quality indicators, including specimen rejection rates, turnaround time, and critical value reporting, were widely recognized as essential measures for continuous quality improvement.

Laboratory Accreditation: Several studies reported that implementation of ISO 15189 standards resulted in improved documentation, standardized operating procedures, reduced analytical variability, and enhanced patient safety. Accredited laboratories demonstrated better compliance with quality management requirements than non-accredited laboratories.

Emerging Technologies: Automation, middleware solutions, laboratory information systems, and artificial intelligence-based quality monitoring have enhanced laboratory efficiency by reducing manual errors and enabling real-time quality assessment. These technologies have improved workflow, minimized turnaround time, and facilitated early detection of analytical deviations.

Comparative Analysis of Published Studies

Author (Year)	Study Focus	Major Findings	Clinical Significance
Westgard et al.[1]	Statistical Quality Control	Westgard multirule QC improves detection of random and systematic errors compared with single-rule QC.	Enhances analytical reliability and reduces false acceptance of erroneous results.
Plebani et al.[4]	Laboratory Errors	Pre-analytical errors remain the most frequent source of laboratory mistakes despite advances in analytical systems.	Emphasizes the need for quality management throughout the total testing process.
Sciacovelli et al.[5]	Quality Indicators	Standardized quality indicators effectively monitor laboratory performance and support continuous improvement.	Enables benchmarking among laboratories.
Oosterhuis and Sandberg,[6]	ISO 15189 Accreditation	Accreditation significantly improves documentation, staff competency, and quality management systems.	Promotes standardized laboratory practices and patient safety.
Coskun et al.[7]	Six Sigma Metrics	Sigma metrics facilitate objective assessment of analytical performance and optimization of QC frequency.	Improves cost-effectiveness while maintaining analytical quality.
Lippi et al.[8]	Total Quality Management	Quality should encompass pre-analytical, analytical, and post-analytical phases rather than analytical performance alone.	Supports comprehensive laboratory quality management.
International Federation of Clinical Chemistry (IFCC) Guidelines,[9]	Laboratory Quality Management	Recommends harmonized quality indicators and continuous monitoring for quality improvement.	Encourages global standardization of laboratory services.

Across the reviewed literature, consistent evidence indicates that laboratories integrating internal quality control, external quality assessment, Six Sigma metrics, and ISO 15189 accreditation achieve superior analytical performance, lower error rates, and greater compliance with international quality standards. Advances in automation, digital quality monitoring, and artificial intelligence are expected to further enhance laboratory quality management by enabling predictive error detection and real-time performance monitoring. Nevertheless, persistent challenges related to pre-analytical variability, personnel competency, and resource limitations continue to affect laboratory quality, particularly in resource-constrained settings. These findings underscore the importance of adopting a comprehensive quality management system encompassing all phases of the laboratory testing process.

DISCUSSION

Quality control (QC) is the cornerstone of laboratory quality management and plays a vital role in ensuring the accuracy, precision, and reliability of clinical biochemistry test results. The present review demonstrates that effective quality control is achieved through the integration of internal quality control (IQC), external quality assessment (EQA), laboratory accreditation, statistical quality control, and continuous quality improvement. These observations are consistent with the findings of Westgard, Plebani, Lippi, Coskun, Sciacovelli,

Miller,[10] and several international organizations, all of whom emphasize that quality management should encompass the entire laboratory testing process.

The literature consistently identifies internal quality control (IQC) as the primary mechanism for monitoring analytical performance. Westgard and Barry introduced multirule statistical quality control procedures that remain the international standard for detecting random and systematic analytical errors while minimizing false rejection of analytical runs. Later studies by Westgard,[1] further emphasized that the integration of Levey–Jennings charts with Westgard multirule criteria enhances analytical precision and reduces reporting errors. Similarly, Coskun et al,[7] demonstrated that laboratories employing statistical quality control combined with Sigma metrics achieved significantly better analytical performance than laboratories relying on conventional quality control procedures. These findings support the widespread adoption of risk-based quality control strategies recommended by the Clinical and Laboratory Standards Institute (CLSI).

Despite remarkable improvements in analytical instrumentation, the reviewed studies indicate that the pre-analytical phase remains the most vulnerable stage of laboratory testing. Plebani,[4] first reported that nearly 60–70% of laboratory errors occur during the pre-analytical phase, including errors related to patient identification, specimen collection, transportation, and sample processing. Subsequent investigations by Lippi et al,[11] and Simundic et al,[12] confirmed that automation has substantially reduced analytical errors; however, pre-analytical variables continue to compromise laboratory quality. Plebani,[11] further proposed the concept of the "total testing process," emphasizing that quality management should extend beyond the analytical phase to include pre-analytical and post-analytical activities.

External Quality Assessment (EQA) has become an indispensable component of laboratory quality assurance. Studies by Sciacovelli et al,[13] demonstrated that regular participation in EQA programs significantly improves inter-laboratory comparability, analytical accuracy, and benchmarking of laboratory performance. These observations are supported by recommendations from the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), which advocates routine participation in proficiency testing and standardized quality indicators for continuous quality improvement. Similarly, the World Health Organization (WHO) Laboratory Quality Management System guidelines emphasize EQA as an essential tool for verifying laboratory competence and ensuring reliable patient results.

Accreditation according to ISO 15189 has transformed laboratory quality management by promoting standardized procedures, documentation, competency assessment, and continual improvement. Comparative studies by Oosterhuis and Sandberg,[6] reported that accredited laboratories consistently exhibit better compliance with quality management requirements, lower analytical variability, and improved patient safety than non-accredited laboratories. Likewise, Miller,[10] and Braga and Panteghini,[14] highlighted that harmonization and standardization of laboratory practices are fundamental for reducing inter-laboratory variability and improving the comparability of biochemical measurements. The revised ISO 15189:2022 standard further strengthens the emphasis on risk management, personnel competency, and continual quality improvement.

The application of Six Sigma methodology has emerged as one of the most significant advances in laboratory quality assessment. Coskun,[15] first described the application of Six Sigma metrics in clinical laboratories, demonstrating that Sigma values provide an objective assessment of analytical performance and facilitate the selection of appropriate quality control strategies. Later studies by Coskun et al,[15] and Westgard,[2] confirmed that Sigma metrics enable laboratories to optimize QC frequency, reduce unnecessary quality control costs, and improve analytical reliability. Laboratories achieving Sigma values greater than six consistently demonstrated world-class analytical performance, whereas lower Sigma values required stricter quality control monitoring.

Recent developments in laboratory automation have substantially improved quality management. Nichols,[16] reported that automated analyzers, middleware systems, and laboratory information systems reduce transcription errors, improve workflow efficiency, and enhance quality monitoring. Furthermore, emerging applications of artificial intelligence and machine learning are capable of identifying analytical trends, predicting instrument failures, and detecting systematic errors before clinically significant deviations occur. These technological advances complement traditional quality control practices rather than replacing them.

Quality indicators have become increasingly important in evaluating laboratory performance. Sciacovelli et al,[13] proposed standardized quality indicators covering the pre-analytical, analytical, and post-analytical phases, enabling laboratories to benchmark performance and identify opportunities for improvement. Similarly, Badrick,[17] emphasized that evidence-based quality management should integrate quality indicators with continuous auditing, staff competency assessment, and corrective actions to achieve sustainable improvements in laboratory performance.

Although technological advances have significantly enhanced laboratory quality, important challenges remain, particularly in low- and middle-income countries. Studies by Grecu et al,[18] reported that inadequate infrastructure, financial limitations, inconsistent reagent supply, and limited participation in EQA programs continue to hinder effective quality management. Similar observations were reported by WHO and IFCC, both of which advocate

strengthening laboratory infrastructure, workforce training, and national quality assurance programs to improve diagnostic services in resource-constrained settings.

Overall, comparison of the available literature demonstrates remarkable agreement among Westgard, Plebani, Lippi, Coskun, Sciacovelli, Miller, Braga, Nichols, Badrick, and international organizations such as WHO, IFCC, CLSI, and ISO that comprehensive quality management is essential for ensuring reliable laboratory results.[1,4-7] The integration of IQC, EQA, accreditation, Six Sigma methodology, laboratory automation, and standardized quality indicators has substantially improved analytical quality over the past two decades. Nevertheless, future research should focus on developing affordable, risk-based quality management models and integrating artificial intelligence into laboratory quality systems to further enhance patient safety and global harmonization of clinical biochemistry laboratory practices.

The literature consistently demonstrates that laboratories implementing comprehensive quality control practices achieve superior analytical performance, reduced error rates, improved turnaround times, and greater compliance with regulatory and accreditation requirements. While significant advances in laboratory automation, laboratory information systems, middleware, and artificial intelligence have strengthened quality monitoring and error detection, challenges related to pre-analytical variability, personnel competency, financial constraints, and limited infrastructure continue to affect laboratories, particularly in resource-limited settings.

Future quality management strategies should focus on the adoption of risk-based quality control, wider implementation of Six Sigma metrics, harmonization of quality indicators, and increased participation in external quality assessment programs. Furthermore, continuous professional training, regular competency assessment, and investment in advanced laboratory technologies are essential to sustain high standards of analytical quality.

CONCLUSION

In conclusion, quality control should be regarded not merely as a regulatory requirement but as a continuous process of quality improvement encompassing all phases of the total testing process. Strengthening quality management systems through evidence-based practices, technological innovation, and adherence to international standards will enhance the reliability of clinical biochemistry laboratories and ultimately improve patient care. Continued research and global collaboration are needed to develop standardized, cost-effective, and sustainable quality assurance models that can be implemented across diverse healthcare settings.

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