Laboratory Specimen Rejection: Pre-Analytical Errors, Trends, Quality Indicators, and Improvement Strategies – A Comprehensive Review

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Abstract*—Background: Clinical laboratory results are central to clinical decision-making and patient management. Although analytical technologies have advanced considerably, errors occurring in the pre-analytical phase continue to pose significant challenges to laboratory quality systems. Specimen rejection remains a critical quality indicator reflecting failures in patient identification, sample collection, labeling, transport, storage, and processing. Objectives: This review aims to consolidate evidence from international and regional studies on laboratory specimen rejection, focusing on its causes, trends, clinical impact, and quality improvement strategies, with particular emphasis on specimen referral networks in resource-limited settings and the application of Six Sigma metrics.Methods: A narrative review of published literature was conducted, including studies, surveillance reports, and guidelines addressing specimen rejection rates, pre-analytical errors, and laboratory quality management. Emphasis was placed on evidence related to referral laboratories and the use of Six Sigma methodology for performance evaluation. Results: The reviewed literature consistently identifies pre-analytical errors as the leading cause of specimen rejection, with improper labeling, hemolysis, insufficient sample volume, and transport-related issues being most frequent. High rejection rates were associated with delayed diagnosis, repeated phlebotomy, increased healthcare costs, and compromised patient safety. Studies employing Six Sigma metrics demonstrated improved standardization and benchmarking of laboratory performance. Discussion: Specimen rejection reflects systemic weaknesses in pre-analytical workflows, particularly in resource-limited and high-volume referral settings. The adoption of standardized quality indicators, staff training, improved referral systems, and Six Sigma-based monitoring can significantly reduce rejection rates and enhance overall laboratory efficiency. Conclusion: Specimen rejection remains a preventable yet persistent challenge in clinical laboratories. Strengthening pre-analytical practices through evidence-based interventions and integrating Six Sigma metrics into laboratory quality management systems are essential for minimizing errors, improving patient safety, and ensuring reliable diagnostic services.

***Index Terms*—Specimen rejection; Pre analytical errors; Laboratory quality indicators; Six Sigma; Referral laboratory** systems

I. INTRODUCTION

Clinical laboratory services are indispensable to modern healthcare systems, providing objective data that underpin diagnosis, prognosis, disease monitoring, and therapeutic decision-making. It is estimated that nearly 70% of clinical decisions rely directly or indirectly on laboratory test results, emphasizing the critical role of laboratory medicine in patient safety and quality of care [2,9,13]. Consequently, any error occurring within the laboratory testing process can have serious implications, including misdiagnosis, delayed treatment, inappropriate clinical interventions, and increased morbidity and mortality [9,10].

The total testing process (TTP) in laboratory medicine comprises three interdependent phases: pre-analytical, analytical, and post analytical [12,13]. Among these, the pre-analytical phase is consistently reported as the most error-prone, accounting for approximately 60–70% of all laboratory errors [3,9,10]. This vulnerability arises because many pre-analytical activities such as test ordering, patient identification, specimen collection, labeling, storage,

and transportation are performed outside the direct supervision of laboratory professionals [3,11,12]. Variations in staff training, workload, adherence to standard operating procedures, and infrastructure further exacerbate the risk of errors during this phase [1,5].

One of the most measurable and clinically relevant consequences of pre-analytical errors is laboratory specimen rejection. Specimens may be rejected due to hemolysis, clotting, insufficient volume, improper blood-to-anticoagulant ratio, use of inappropriate containers, labeling discrepancies, transport delays, or failure to maintain required environmental conditions [3,12,15,16]. While specimen rejection serves as a protective mechanism to prevent the release of unreliable results, it is also a marker of underlying deficiencies in laboratory processes and clinical–laboratory interfaces [6,21].

The impact of specimen rejection extends beyond laboratory workflow inefficiencies. Rejected specimens frequently necessitate repeat phlebotomy, leading to patient discomfort, dissatisfaction, and loss of confidence in healthcare services [6,14]. In critical and emergency settings, rejection-related delays can compromise timely clinical decision-making and adversely affect patient outcomes [6,10]. Furthermore, specimen rejection contributes to increased healthcare costs due to repeated testing, additional consumables, extended hospital stays, and increased staff workload [15,16]. These consequences are particularly pronounced in resource-limited settings, where laboratory infrastructure and referral systems already face substantial constraints [4,7].

Specimen referral networks play a vital role in expanding access to specialized diagnostic services, especially in low- and middle-income countries [7,18]. However, referral systems are inherently susceptible to pre-analytical errors because of multiple handover points, transportation challenges, and inconsistent adherence to quality standards across facilities [4,17]. Monitoring specimen rejection trends within referral networks is therefore essential for identifying systemic gaps and guiding targeted quality improvement initiatives [5,7].

In recent years, the use of quality indicators and Six Sigma metrics has gained prominence as an objective and standardized approach for evaluating laboratory performance [8,19,20]. Unlike conventional percentage-based error reporting, Six Sigma methodology enables laboratories to quantify defects in terms of defects per million opportunities (DPMO), facilitating benchmarking, trend analysis, and continuous quality improvement [8,19]. Incorporating such data-driven frameworks into routine laboratory practice is increasingly recommended by international accreditation and quality assurance bodies [1,5,20].

Given the significant clinical, operational, and economic implications of specimen rejection, a comprehensive synthesis of existing evidence is essential. This review aims to consolidate current knowledge on the magnitude, causes, trends, and consequences of laboratory specimen rejection, with particular emphasis on pre-analytical errors, referral laboratory systems, and quality improvement strategies [3,4,6]. By highlighting best practices and identifying persistent gaps, this review seeks to support laboratories in strengthening quality management systems and improving patient-centered outcomes [1,5,21].

II. METHODOLOGY:

This review was conducted through a comprehensive evaluation of published scientific literature focusing on laboratory specimen rejection and pre analytical errors in clinical laboratory practice [3,9,13]. Relevant articles were identified from peer reviewed journals, international laboratory quality guidelines, and reports issued by recognized health and accreditation organizations, including ISO and WHO publications [1,5]. Emphasis was placed on studies that examined specimen rejection trends, underlying causes, quality indicators, and improvement strategies in hospital-based and referral laboratory settings [4,6,8]. The selection criteria included original research articles, systematic reviews, quality improvement studies, and guideline documents published in English [3,11]. Studies conducted in both high-income and resource-limited settings were considered to ensure a balanced and globally relevant perspective [7,18]. Particular attention was given to research from low- and middle-income countries, where specimen referral networks and pre-analytical challenges are more pronounced [4,17].

The extracted information was qualitatively analyzed and synthesized under thematic headings, including

sources of pre-analytical errors, common causes of specimen rejection, clinical and operational impacts, and quality improvement frameworks such as Six Sigma metrics [8,19,20]. Findings from multiple studies were compared to identify consistent patterns, variations, and gaps in existing practices [9,10]. This narrative synthesis approach was adopted to provide a comprehensive understanding of specimen rejection as a quality indicator in laboratory medicine [1,21].

Pre-Analytical Phase and Sources of Error

The pre-analytical phase encompasses all processes from test ordering to sample preparation prior to analysis [12,13]. Errors during this phase arise from improper test requests, inadequate patient preparation, incorrect specimen collection techniques, inappropriate containers, labeling errors, and transportation or storage issues [3,12]. Studies consistently demonstrate that more than 60–70% of laboratory errors occur during this phase, highlighting the need for targeted quality interventions [9,10]. The pre analytical phase represents the first and most complex segment of the total testing process and includes all steps from test request initiation to the preparation of specimens for analysis [12]. This phase encompasses patient identification, test ordering, patient preparation, specimen collection, labeling, storage, and transportation [3,11]. Due to the involvement of multiple healthcare professionals and processes that occur outside the direct control of the laboratory, the pre-analytical phase is particularly vulnerable to errors [9,13].

Numerous studies have demonstrated that a majority of laboratory errors arise during the pre-analytical phase, often exceeding 60% of all documented laboratory mistakes [3,9,10]. These errors may result from inadequate training, heavy workload, poor communication between clinical and laboratory staff, non-adherence to standard operating procedures, and limitations in infrastructure or logistics [1,5,11]. Inconsistent practices in specimen collection techniques, use of inappropriate containers, and improper handling during transport further contribute to error occurrence [12,15].

In referral laboratory systems, pre-analytical errors are amplified by additional challenges such as prolonged transport times, exposure to unsuitable environmental conditions, and inadequate cold chain maintenance [4,7,18]. These issues highlight the importance of robust pre-analytical quality management, continuous staff education, and the implementation of standardized procedures to ensure specimen integrity and reliable test results [1,5,17].

Causes of Laboratory Specimen Rejection

Laboratory specimen rejection occurs when a submitted sample fails to meet predefined acceptability criteria necessary to ensure accurate and reliable test results [1,3]. The most frequently reported causes of specimen rejection are directly linked to pre-analytical errors and vary depending on specimen type and test requirements [3,9]. Hemolysis and clotting are among the leading causes of rejection in blood samples, often resulting from improper venipuncture techniques, delayed processing, or incorrect mixing of anticoagulants [15,16].

Insufficient specimen volume and inappropriate blood-to-additive ratios are also common reasons for rejection, particularly in pediatric and critically ill patients where sample collection may be challenging [12,16]. Labeling errors, including missing, mismatched, or illegible patient identifiers, represent a significant administrative cause of rejection and pose serious risks to patient safety [6,9]. Additional factors such as the use of incorrect specimen containers, contamination, transport delays, and failure to maintain required temperature conditions further contribute to specimen rejection rates [3,12,17].

While specimen rejection is a necessary quality safeguard to prevent the reporting of unreliable results, persistently high rejection rates indicate systemic weaknesses in pre-analytical processes and quality management systems [1,21]. Identifying the most common causes of rejection allows laboratories to implement targeted corrective actions, including focused staff training, standardization of procedures, and enhanced monitoring using quality indicators [5,8]. Reducing specimen rejection not only improves laboratory efficiency but also enhances patient comfort, supports timely clinical decision-making, and contributes to overall healthcare quality [6,11].

Clinical and Economic Impact of Specimen Rejection

Laboratory specimen rejection has far-reaching clinical and operational consequences that extend beyond the laboratory environment [6,15]. From a patient care perspective, rejected specimens

frequently necessitate repeat sample collection, which can cause physical discomfort, anxiety, and dissatisfaction, particularly among pediatric, elderly, and critically ill patients [6,14]. Re-collection also contributes to delays in the availability of test results, which may adversely affect diagnostic accuracy and the timely initiation or modification of treatment, especially in emergency and intensive care settings [6,10].

In addition to clinical implications, specimen rejection imposes a significant economic burden on healthcare systems [15,16]. Repeat testing increases the consumption of reagents, collection materials, and staff time, while prolonged turnaround times may lead to extended hospital stays and inefficient utilization of clinical resources [15]. Several studies have demonstrated that poor specimen quality and pre-analytical errors account for a measurable proportion of overall hospital operating costs [15,16]. Therefore, reducing specimen rejection rates is not only a patient safety priority but also a cost-containment strategy that supports sustainable and efficient healthcare delivery [5,11].

Specimen Rejection in Referral Laboratory Systems

Referral laboratory systems play a crucial role in improving access to specialized diagnostic services, particularly in low- and middle-income countries where advanced laboratory testing is often centralized [7,18]. Through these networks, specimens collected at peripheral health facilities are transported to referral laboratories for analysis. While this model enhances diagnostic coverage and equity, it also introduces additional risks during the pre-analytical phase [4,17].

Multiple points of specimen handling, prolonged transportation times, inadequate packaging, and inconsistent adherence to standard operating procedures contribute to higher rates of specimen rejection within referral systems [4,7]. Variability in staff training, infrastructure, and resource availability across referring facilities further compounds these challenges [17,18]. Evidence from Ethiopian and other African referral laboratories have reported specimen rejection rates ranging from 0.5% to 2%, highlighting persistent gaps in pre-analytical quality assurance [4,17]. Strengthening referral systems through standardized protocols, targeted training, improved logistics, and continuous performance monitoring is therefore essential to ensure specimen integrity and reliable test results [1,5,7].

Quality Indicators and Application of Six Sigma Metrics

Quality indicators are essential tools for monitoring and improving laboratory performance, with specimen rejection rate being one of the most widely used indicators of pre-analytical quality [1,3]. Traditional reporting of rejection rates as simple percentages provides a general overview of laboratory performance but may fail to adequately reflect process variability or enable meaningful benchmarking across laboratories and healthcare systems [8,19].

Six Sigma methodology offers a more robust and standardized framework for evaluating laboratory performance by expressing errors as defects per million opportunities (DPMO) and corresponding Sigma values [8,19]. This approach allows laboratories to objectively assess process capability, identify areas requiring improvement, and monitor performance trends over time [19,20]. The application of Six Sigma metrics in laboratory medicine has gained increasing recognition as a valuable strategy for transforming quality improvement efforts from reactive problem-solving to proactive, data-driven decision-making [8,20].

Strategies to Reduce Specimen Rejection

Reducing specimen rejection requires a multifaceted approach that addresses both technical and organizational factors within the pre-analytical phase [5,11]. Continuous education and competency-based training of phlebotomists, nursing staff, and other healthcare workers involved in specimen collection are fundamental to improving pre-analytical practices and minimizing human error [3,11]. The implementation of clear, standardized operating procedures, supported by the use of checklists, helps ensure consistency and adherence to best practices across clinical settings [1,5].

Technological interventions, including barcode-based patient and specimen identification systems, laboratory information systems, and automated sample handling processes, have demonstrated effectiveness in reducing labeling errors and improving specimen traceability [12,20]. Strengthening communication between clinical units

and laboratory personnel, combined with regular audit and feedback using established quality indicators, supports sustained improvement and fosters a culture of quality and accountability within healthcare institutions [8,21].

III. CHALLENGES AND FUTURE DIRECTIONS

Despite increased awareness of pre-analytical quality issues, several challenges continue to limit progress in reducing specimen rejection rates [9,21]. Resource constraints, high workload, staff shortages, frequent personnel turnover, and inadequate infrastructure remain significant barriers, particularly in resource-limited settings [4,7,18]. Inconsistent data recording practices and limited use of standardized quality metrics further complicate performance evaluation and benchmarking across laboratories [8,19].

Future research should focus on developing and validating context-specific interventions that address local challenges while aligning with international quality standards [1,5]. The integration of digital health technologies, expansion of multicenter benchmarking studies, and broader adoption of Six Sigma and other quality management frameworks represent promising directions for advancing pre-analytical quality [19,20]. Strengthening collaborative efforts between clinicians, laboratory professionals, and policymakers will be essential for achieving sustainable improvements in laboratory services and patient-centered outcomes [5,21].

IV. CONCLUSION

Specimen rejection remains a critical challenge in clinical laboratories, predominantly driven by pre analytical errors. Monitoring rejection trends using standardized quality indicators and Six Sigma metrics provides valuable insights into laboratory performance. Strengthening training programs, standardizing procedures, and enhancing referral systems are key to reducing rejection rates and improving patient care. Sustained commitment to quality management is essential for achieving reliable and timely laboratory services.

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