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Preanalytical Errors in Clinical Biochemistry: A Focused Review of Current Challenges and Solutions

Dr. Mohamed Amri

Laboratory Department - Habib Bayar Hospital - Tunisia

Abstract: ***The preanalytical phase is a critical yet often overlooked component of clinical biochemistry diagnostics. Studies (1,2) indicate that 60% to 70% of laboratory errors occur before sample analysis. This review synthesizes findings from 29 publications published between 2020 and 2025, focusing on common sources of preanalytical errors such as sample collection, transport, storage, and identification. These errors can lead to misdiagnoses and inappropriate treatments, posing substantial risks to patient safety. Proposed solutions include standardized training, automation, and robust quality control systems. Integrating these measures is essential for improving laboratory reliability and ensuring accurate diagnostic outcomes.***

Keywords: preanalytical phase, laboratory errors, sample collection, specimen handling, quality control.

1. Introduction

Modern clinical biochemistry has made impressive progress in analytical precision, with automated systems now capable of producing highly accurate results. However, this technical excellence is often contrasted by ongoing errors in the preanalytical phase (3). This phase, encompassing all steps from test ordering to analysis, is a recognized weak point in the diagnostic process, as recent meta-analyses have shown (4,5). A prospective study (6) revealed that up to 14% of results were affected by preanalytical errors, with direct clinical consequences. These statistics are particularly alarming given the key role of laboratory testing in medical decision-making, where diagnoses often rely on these tests (7). This review examines preanalytical errors by integrating 29 of the most relevant publications from 2020 to 2025. We take a practical, clinically focused approach, emphasizing challenges in different care settings and solutions proposed in the literature. This review aims to identify and analyze the main sources of preanalytical errors in clinical biochemistry, as well as to evaluate proposed solutions for improving sample handling and laboratory reliability. It also underscores the critical role of these processes in ensuring diagnostic accuracy and patient safety, advocating for systemic improvements across laboratory and clinical practices.

2. Methodology

For this review, we searched PubMed, Scopus, and Web of Science using MeSH terms such as "preanalytical phase," "laboratory error," "sample collection", and "specimen handling". We included only English or French articles published from January 2020 to July 2025, with the final search conducted on July 15, 2025. PRISMA guidelines (8) were followed for article selection. Of the 214 articles identified, 29 were chosen based on relevance and methodological quality. Inclusion criteria focused on prospective studies, studies reporting error statistics with corrective actions, meta-analyses, and guidelines from professional societies.

3. Results

3.1 Main Sources of Preanalytical Errors

3.1.1 Biological Sample Collection Errors

The collection of samples is a major source of preanalytical errors. Lima-Oliveira (9) demonstrated that venipuncture technique directly impacts sample quality; a randomized controlled trial involving 1,500 samples found that using small-gauge needles (less than 21G) significantly increased the risk of hemolysis. This confirms the CLSI recommendations (10) to use needles of 21G or larger for routine collection. The stability of analytes and the precision of laboratory tests can be affected by tube walls, rubber stoppers, anticoagulants, and separator gels (11). Tourniquet application time also warrants attention (12). Underfilled anticoagulant tubes continue to be a problem, leading to the adoption of automated volume control systems in reference centers (4, 13) that have documented reductions in errors.

3.1.2 Transport and Storage Issues

Although the impact of transport conditions on sample quality has long been known, compliance remains inconsistently monitored (14). Temperature fluctuations, undetectable without continuous monitoring, can alter results for sensitive analytes such as ACTH (15). Sample stability during air transport is especially important. Jukić et al. (14) evaluated the effects of cabin pressurization on blood specimen quality. Their comprehensive multidisciplinary research indicates the significant impact of transport conditions and microclimate on blood samples, thereby justifying the need for specific protocols for long-distance transport. In vitro glycolysis continues to pose significant challenges for glucose testing. An international dual-center study (16) that compared collection systems found that insufficient glycolysis inhibition systematically leads to lower glucose levels. This supports the American Diabetes Association (17) recommendations for mandatory use of inhibitor tubes in diagnosing and monitoring diabetes.

3.1.3 Identification and Traceability Errors

Misidentification remains a major patient outcomes concern (18). Data from the College of American Pathologists show an average misidentification rate of 0.45% across 1,800 labs, with a wide range (0.1 to 1.2%). Misidentification rates are three times higher in emergencies (1.32%) compared to routine care (0.44%) due to time pressures and other challenges. To address this, the Korean Society for Laboratory Medicine (19) recommends using at least two identifiers, such as the patient's name and either the medical record number or the date of birth. New technologies, such as radio frequency identification (RFID) and narrow band–Internet of Things (NB-IoT), have been shown to be effective in minimizing these preanalytical errors (20).

3.2 Improvement Strategies

3.2.1 Automation and Artificial Intelligence

In a risk assessment study (21), the authors used Failure Mode, Effects, and Criticality Analysis (FMECA) to identify critical phases in the preanalytical process, finding that human-controlled steps - such as manual acceptance of test orders, patient identification, tube labeling, and sample collection - had the highest risk indices. The study concludes that automation is crucial to replace, support, or extend human contributions in the preanalytical phase, leading to reduced errors and improved patient safety.

Algorithmic models have been developed to detect hemolysis with high sensitivity, surpassing experienced technicians' performance. Integrated into modern analyzers, these systems can now automatically reject non-conforming samples with high specificity (22). Unrecognized interferences, such as those from icterus (23) and lipemia (24), can lead to misinterpretations. Because interferences are specific to each analyte and can differ from the manufacturer's data, individual laboratories should perform their own evaluations and establish preanalytical recommendations to ensure accurate results.

3.2.2 Training and Quality Control

Staff training is essential. Delianu et al. (25) evaluated a standardized program (comprising e-learning, workshops, and audits) that significantly reduced collection errors within six months. A study on quality practices in laboratory workers (26) found that while most were knowledgeable about preanalytical quality management, improper procedures can still lead to specimen rejection and wasted resources. This highlights the critical role of a robust Quality Management System in minimizing errors before analysis. The European Federation for Clinical Chemistry and Laboratory Medicine (EFLM) argues that enhancing the quality of laboratory testing depends on more than just internal laboratory procedures (7, 27). The EFLM emphasizes that improving the preanalytical phase - which includes test selection, sample collection, and transport - is an interdisciplinary effort requiring participation from all involved professions.

4. Discussion

Despite ongoing efforts to standardize preanalytical processes, significant variations in definitions and laboratory practices persist. Most current research comes from academic or well-funded institutions, which limits its broader applicability. Furthermore, few studies directly link preanalytical errors to patient outcomes, instead focusing on analytical consequences. However, findings confirm that preanalytical errors remain a widespread and impactful issue (28). Even high-performing laboratories face persistent preanalytical challenges (29), contradicting the assumption that automation alone solves the problem. Improvement requires integrated strategies that include addressing human factors, effective training, and ongoing quality initiatives.

5. Conclusion

Preanalytical errors remain a critical challenge in clinical biochemistry, directly influencing diagnostic reliability and patient safety. While automation and technological advancements offer promising solutions, success requires a holistic approach that includes standardized protocols, staff training, and continuous quality monitoring. Future research should prioritize linking preanalytical errors to clinical outcomes to highlight their true cost in patient care.

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