дослідження
Research

НИРКИ KIDNEYS

DOI: 10.65327/kidneys.v15i1.620

Alka Katiyar[1], Munish Rastogi[2], Pradeep Kumar Tiwari[3], Dheeraj Kumar[4]*

[1]Assistant Professor, School of Health Sciences, Chhatrapati Shahu Ji Maharaj University, Kanpur, Uttar-Pradesh, INDIA 208024, mail Id:- alkaphdbiochem@gmail.com Orcid Id:- 0000-0002-3462-0609
[2]Associate Professor, Director, School of Health Sciences, Chhatrapati Shahu Ji Maharaj University, Kanpur, Uttar-Pradesh, INDIA 208024, Email Id:- munishkanuniv@gmail.com Orcid Id:- 0009-0004-5745-8853
[3]Research Scholar, Department of Education, Chhatrapati Shahu Ji Maharaj University, Kanpur, Uttar-Pradesh, INDIA 208024, Email Id:- pradeepkumartiwari23@gmail.com Orcid Id:- 0009-0004-3099-9000
[4]*Assistant Professor/ Assistant Director, School of Health Sciences, Chhatrapati Shahu Ji Maharaj University, Kanpur, Uttar-Pradesh, INDIA 208024, Email: dheeraj@csjmu.ac.in/ dheeraj199494@gmail.com, Orcid Id:- 0000-0003-4285-8104

***Corresponding Author:** Dheeraj Kumar
*Assistant Professor/ Assistant Director, School of Health Sciences, Chhatrapati Shahu Ji Maharaj University, Kanpur, Uttar-Pradesh, INDIA 208024, Email: dheeraj@csjmu.ac.in/ dheeraj199494@gmail.com, , Orcid Id:- 0000-0003-4285-8104

Pre-Analytical Errors in Renal Diagnostics: Implications for Kidney Disease Evaluation, Patient Safety, and Clinical Decision-Making

For citation: Kidneys. 2026;15(1):01-08. Acceptance- 13/12/2025 Received- 13/11/2025
doi: 10.65327/kidneys.v15i1.620

Abstract
Renal diagnostics are central to modern nephrology, guiding the evaluation, staging, and management of chronic kidney disease (CKD) and acute kidney injury (AKI). However, most laboratory errors occur in the pre-analytical phase, including patient preparation, specimen collection, labeling, handling, transport, and storage. Such upstream failures can significantly compromise the accuracy of kidney biomarkers such as serum creatinine, estimated glomerular filtration rate (eGFR), albuminuria, and electrolytes. This review examines the classification, burden, and clinical impact of pre-analytical errors in renal diagnostic testing, emphasizing their implications for kidney disease evaluation, patient safety, and evidence-based clinical decision-making. A narrative synthesis of recent nephrology and laboratory medicine literature was conducted, focusing on major categories of pre-analytical failure, including identification errors, specimen collection problems, sample interferences, transport instability, and medication- or physiology-related confounders. Specialized nephrology populations and emerging quality improvement strategies were also reviewed. Pre-analytical errors may lead to CKD misclassification, inaccurate eGFR estimation, unreliable urine albumin-to-creatinine ratio testing, and delayed AKI recognition. High-risk groups such as pediatric patients, lupus nephritis populations, oncology-associated kidney injury cases, and perioperative surgical patients are particularly vulnerable. Clinical consequences include inappropriate drug dosing, avoidable dialysis initiation, unnecessary hospital admissions, and increased healthcare resource utilization. Standardization initiatives, quality indicators, harmonization frameworks, and innovations such as artificial intelligence, delta checks, and smart sample tracking offer promising approaches to reduce preventable diagnostic variability. Strengthening pre-analytical integrity is essential for accurate renal biomarker interpretation, guideline-concordant CKD management, and improved patient outcomes.

Keywords: Pre-analytical errors; Renal diagnostics; chronic kidney disease; Patient safety; Laboratory quality assurance

1. Introduction

The modern nephrology environment relies on the laboratory diagnostics as the means to identify, classify, monitor, and treat kidney diseases. The biochemical/urinary markers (serum creatinine, estimated glomerular filtration rate, eGFR, urine albumin-to-creatinine ratio, UACR, electrolytes) are the primary points to evaluate chronic kidney disease (CKD) and acute kidney injury (AKI) assessment. The international nephrology models emphasize that adequate laboratory testing would be a valuable instrument in making sure that those affected by kidney diseases are diagnosed, staged and the risk stratified in

For correspondence: Dheeraj Kumar ,Assistant Professor/ Assistant Director, School of Health Sciences, Chhatrapati Shahu Ji Maharaj University, Kanpur, Uttar-Pradesh, INDIA 208024, Email: dheeraj@csjmu.ac.in/ dheeraj199494@gmail.com, , Orcid Id:- 0000-0003-4285-8104
Full list of authors information is available at the end of the article.

time both adults and children [1]. KDIGO 2024 clinical practice guidelines strengthen the idea that clinical decision-making, i.e., the initiation of renoprotective therapy, timing of referral, and the choice of monitoring strategies, is directly dependent on diagnostic thresholds of eGFR fall and albuminuria [2]. Simultaneously, guideline synopses emphasize the fact that nephrology care is being more reliant on laboratory-identified categories of risk, which dictate long-term management courses [3]. In immune-mediated fatalities of kidneys like lupus nephritis, laboratory diagnosis becomes even more important as the level of treatment and prognosis assessment are subject to accurate results of interpreting renal function and urine dysfunctions [4]. In addition to the diagnosis, laboratory tests are also critical in drug safety and dosing, especially the drugs that need modifications when affected by renal problems. The clinical pharmacy practice has shown that improper interpretation of renal markers can lead to the avoidable adverse effects [5]. Recent revision of NICE and implementation research shows that the laboratory observation forms the core of implementing evidence-based interventions, including sodium-glucose co-transporter-2 inhibitors in the treatment of CKD [6]. In this way, nephrology is still inseparable with laboratory medicine, and the accuracy of diagnosing patients is a fundamental pillar of patient safety and clinical excellence.

Although there have been improvements in the analytical instrumentation, most laboratory errors occur prior to the onset of the testing, during the pre-analytical phase. This stage involves the preparation of patients, collection of specimen, labeling, handling, transporting, and storing of the specimen. Extensive evidence supports the notion that pre-analytical error is by far the greatest number of errors in the overall laboratory testing process, much greater than analytical and post-analytical error [7]. Such errors are especially prone to renal diagnostics due to the extreme sensitivity of kidney biomarkers to procedure and biological variability. Hemolysis is one of the most common pre-analytical problems in clinical chemistry greatly interfering with the creatinine and electrolyte levels. Standardized ways of managing hemolyzed samples are prioritized by practical recommendations of the European working groups as they have clinical consequences on the interpretation of diagnoses [8]. Any small pre-analytical deviations can cause false hyperkalemia, incorrect diagnosis of CKD stage or incorrect emergency treatment. Greater scans of the laboratory quality improvement emphasize that diagnostic excellence is impossible without a systemic focus on pre-analytical vulnerabilities, which are not sufficiently addressed in spite of its deep-seated effects on patient outcomes [9]. Urine based testing such as albuminuria can also be distorted by pre-analytical errors, which can influence CKD staging, prognosis and referral decision. Literature review of the sources and control interventions of pre-analytical failures indicate that three reasons are prevalent to cause diagnostic delay and avoidable harm: human factors, workflow gaps, and insufficient standardization [10]. Notably, the practice of nephrology is becoming more and more reliant on laboratory-based guideline thresholds. The CKD care pathways based on KDIGO presuppose renal markers reliability, i.e. the possibility of upstream pre-analytical errors to impair the evidence-based decision-making [11]. Other diagnostic fields address the same issues, and a much more thorough review of the diagnosis type prioritizes prevention measures and systematic quality arrangements to minimize pre-analytical variability [12]. Consequently, the pre-analytical stage is one of the most significant determinants of correctness in the assessment of kidney diseases, and it has direct consequences on patient safety, clinical decision making, and medical efficiency.

This review will investigate the clinical and mental cost of pre-analytical errors in renal diagnostics in terms of their effect on kidney disease assessment, patient safety, and nephrology decision-making. It is an attempt to summarize the existing body of knowledge on the prevalent pre-analytical weaknesses of renal biomarkers, their consequences to the guideline-based care of CKD and lupus nephritis, as well as quality enhancement approaches applicable to the laboratory-nephrology interface. The importance of the standardized practices and error-prevention models to increase the reliability of the diagnosis of kidney care is given special consideration.

2. The Pre-Analytical Phase in Renal Diagnostic Testing

2.1 Definition and Components of the Pre-Analytical Process

Pre-analytical stage entails all the activities before the laboratory test that might include test requesting, patient identification, preparation, collection of sample, labeling, transportation, centrifugation and storage. These are the measures that directly affect renal biomarkers accuracy. The recent studies are focused on the notion that the workflow at this stage can be assisted by employing new technologies, such as artificial intelligence and applied machine learning to minimize errors and optimize the work process [13]. Preanalytical quality has been regarded as an important construct in quality diagnostics in the field of nephrology [14].

2.2 Frequency and Burden of Pre-Analytical Errors in Clinical Laboratories

Pre-analytical errors constitute the most common cause of failures in laboratory medicine with a high load of clinical risk and diagnostic error. The emergence of new information indicates that the problems of poor handling, delays in processing, and insufficient standardization are still prevalent in laboratories. These mistakes are closely associated with diagnostic delay and patient safety issues, which has been proven in case of referral-based clinical assessments [15]. Thus, the pre-analytical quality is a significant concern.

2.3 Pre-Analytical Vulnerabilities Unique to Renal Diagnostics

Renal testing is exquisitely susceptible to pre-analytical variability since creatinine, potassium and albuminuria

are biomarkers that are subject to hydration, hemolysis, and urine collection situation. The tests of urine albumin-to-creatinine ratios are especially urgent to optimize the CKD staging and referral decisions [16]. Wider precepts of sample integrity and international standardization as are promoted in the biomarker biobanking operations underpin austerity pre-analytical control in the nephrology diagnostics [17].

3. Classification of Pre-Analytical Errors Relevant to Kidney Testing

3.1 Patient Identification and Test Request Errors

One of the first and most grave failures in the pre-analytical period of the renal diagnostics is patient identification and test request error. Misjudgment of kidney functioning and incorrect staging of CKD might be caused by inaccurate patient labeling and incorrect requisition form or wrong choice of the test (Figure 1). These errors can result in failure to diagnose in time, redundant repeated testing or improper referral. The European harmonization efforts focus on the need to have standardized workflows and institutional guidelines to help reduce such avoidable errors within the healthcare systems [18]. In nephrology, where eGFR thresholds and albuminuria levels significantly influence the key treatment choices, a proper identification and proper ordering of tests are critical to patient safety and evidence-based management of kidney disease.

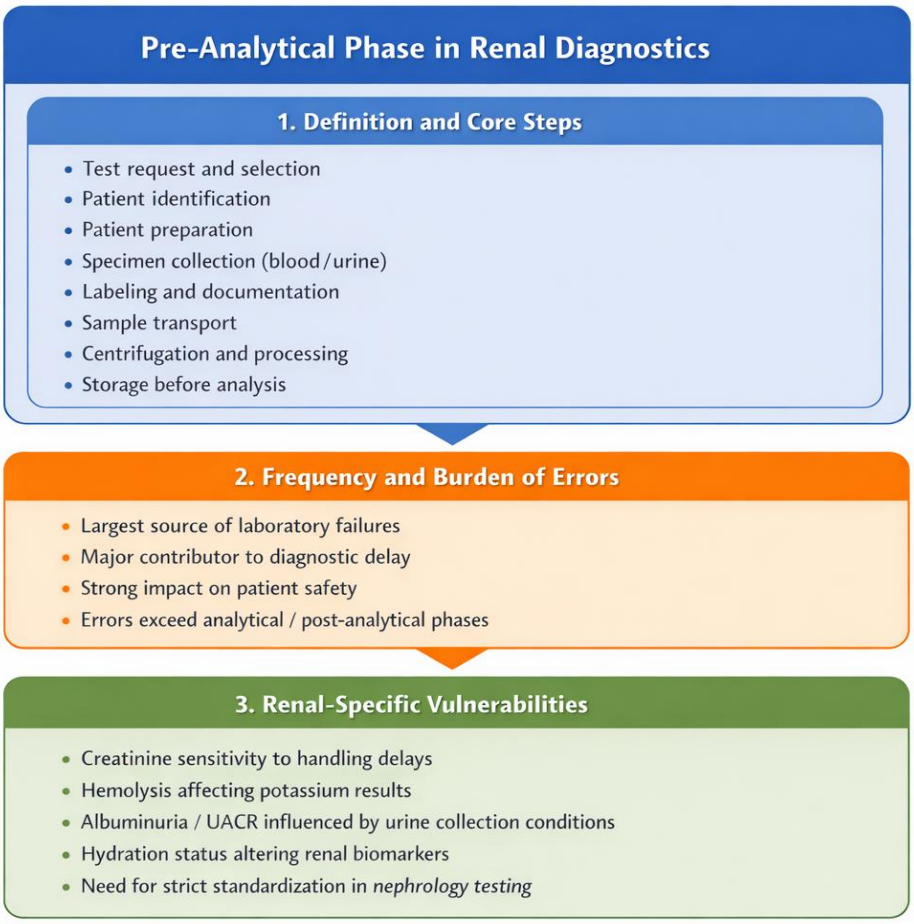

Figure 1. Key Elements of the Pre-Analytical Phase in Renal Diagnostic Testing

3.2 Specimen Collection Errors in Renal Investigations

Specimen collection errors are one of the largest causes of diagnostic mistakes in the renal investigations as kidney biomarkers are highly sensitive to conditions during the collection. The measurements of creatinine, potassium, and albuminuria may be altered because of poor venipuncture, choice of inappropriate tubes, contamination, and poor urine sampling habits. These deviations can distort the outcomes of kidney functioning and possibly enhance the idea of the acute aggravation or onset of the disease. The international laboratory safety evaluations indicate that collection failures are among the most prevalent reasons of pre-analytical error load in clinical practice [19]. These are especially worrisome in the nephrology practice because clinical judgments are premised on drug dosing, dialysis arrangements, and CKD staging that relies on the proper levels of biomarkers through properly gathered samples.

3.3 Sample Handling, Transport, and Storage Issues

Sample errors, such as mistakes in handling, transport and storage are crucial weaknesses that can undermine the reliability of renal diagnostic. The centrifugation process can be slowed down, unsuitable temperature can be exposed to, or even long transportation can lead to destruction of sample integrity and renal chemistry data could be distorted. The reason that such instability is critical is especially important to the electrolytes, urea, and urine protein markers, where the pre-analytical

conditions need to be controlled. The organized creation and application of laboratory quality indicators offers a fundamental framework of control over these weaknesses of handling and enhancement of the consistency of the diagnoses at the institutions [20]. When it comes to kidney disease diagnosis, transport logistics and timely processing must be ensured to eliminate any unnecessary delays during the process and assist in making the right clinical decision.

3.4 Hemolysis, Lipemia, and Interference in Renal Chemistry Assays

One of the most common pre-analytical threats to renal chemistry assays includes hemolysis, lipemia and other interferences with the specimen. Hemolyzed blood samples can give false high results on the potassium or creatinine, and lipemic samples can interfere with photometric measurements. Such interferences can cause improper emergency treatments, unwarranted hospitalizations, or a misclassification of severity of CKD. Suggestions towards designing and carrying out an extensive pre-analytical quality assurance programs highlight the use of standardized rejection criteria and correction procedures to ensure that unsuitable specimens are not used to affect the care of the patient [21]. Since the practice of nephrology depends on the presence of precise biochemical thresholds, it is necessary to reduce the errors associated with interference to preserve the integrity of diagnosis and patient safety.

3.5 Medication-Related and Physiological Pre-Analytical Confounders

Pharmacological factors and physiological parameters are significant pre-analytical confounders, which impact the interpretation of renal biomarkers. Hydration status, intake of protein in the diet, posture and muscle mass and recent administration of drugs can all change the creatinine concentration before the laboratory analysis (Table 1). Such deviations can cause poor estimation of eGFR, and inappropriate categorization of CKD, especially in long term renal functional monitoring. The use of creatinine-based equations in research to assess kidney function decline over a period of time has shown the impact that biological and pre-analytical variability can have on the outcome [22]. Clinical documentation of medications and patient conditions in nephrology practice should therefore be done carefully in order to make laboratory results to be interpreted under the right physiological context.

Table 1. Classification of Pre-Analytical Errors Relevant to Kidney Testing and Their Clinical Impact

Error Category	Examples in Renal Diagnostics	Potential Clinical Impact in Nephrology	Reference
Patient Identification & Test Request Errors	Wrong patient labeling, mismatched requisition forms, inappropriate renal test ordering	Misleading CKD staging, delayed diagnosis, incorrect referral decisions	[18]
Specimen Collection Errors	Poor venipuncture, wrong collection tube, contaminated urine samples	False creatinine/electrolyte results, misinterpretation of kidney function, inappropriate treatment planning	[19]
Handling, Transport & Storage Issues	Delayed centrifugation, improper temperature control, prolonged transport time	Sample degradation, distorted renal chemistry values, diagnostic delays in CKD/AKI evaluation	[20]
Hemolysis, Lipemia & Assay Interference	Hemolyzed blood causing false hyperkalemia, lipemic sample interference in photometric assays	Misclassification of CKD severity, unnecessary emergency interventions or hospital admissions	[21]
Medication-Related & Physiological Confounders	Drug interference, dehydration, posture effects, dietary protein influence on creatinine	Inaccurate eGFR estimation, inappropriate CKD staging, flawed longitudinal monitoring	[22]

4. Impact of Pre-Analytical Errors on Core Renal Biomarkers

4.1 Serum Creatinine Measurement and Analytical Distortion

Serum creatinine is the most commonly used biomarker to measure kidney performance, but it is very susceptible to pre-analytical error. Avoiding improper sample collection, delay in processing, hemolysis, and patient-related variability could pose a significant contributor to creatinine concentration preceding analysis. Due to the fact that creatinine is central to the estimation of the glomerular filtration rate, any minor pre-analytical errors can be misleading to the status of the kidney. The consideration of core nephrology curriculum underlines the fact that precise measurement of creatinine and contextual interpretation are critical components of the routine clinical practice especially when it comes to staging CKD and detecting AKI [23]. Therefore it is essential to control pre-analytical conditions in order to make diagnostic reliable.

4.2 Errors in Estimated Glomerular Filtration Rate (eGFR) Interpretation

The creatinine-based equations are used to estimate GFR, which is the basis of CKD diagnosis, prognosis and therapeutic decision-making. The possible pre-analytical errors affecting the creatinine values can directly reflect to false estimation of eGFR thus a false determination of the severity of kidney diseases. The implications of this not only in nephrology but in cardiovascular medicine are large because GFR deterioration is increasingly becoming a clinical trial endpoint, and a surrogate of systemic risk. The difficulties in reading GFR deteriorate the significance

of reducing upstream variability that can distort longitudinal measurement [24]. Pre-analytical quality control is thus relied on in order to have a reliably eGFR.

4.3 Albuminuria and Urine Albumin-to-Creatinine Ratio (UACR) Testing Challenges

Albuminuria is one of the most important indicators of kidney damage and cardiovascular risk, but because of the urine-based test, pre-analytical inconsistencies are especially likely. The results of urine collection may produce a false UACR due to variation in the time of urine collection, improper storage, contamination and incomplete sampling. These errors can produce a false impression of progression or improvement of CKD, which affects the referral decision and escalation of treatment. Research assessing GFR in estimating renal performance in younger groups is also instrumental to highlighting the greater issue of variability in biomarkers across population groups and support the need to scrutinize pre-analytical conditions in renal measurement [25]. Urine testing standardization is an urgent nephrology concern.

4.4 Pre-Analytical Factors Affecting Acute Kidney Injury Biomarkers

Biomarker interpretation is important to the early detection of acute kidney injury, and pre-analytic variability may delay the identification of renal dysfunction. Sample instability, transport delay as well as unreliable reporting of laboratory could obscure the actual kidney injury, or overstate short-lived fluctuations. The recommendation of the working group of the National Kidney Foundation to implement race-free CKD-EPI equations highlights the necessity that labs should practice the same that will help them report renal functions correctly and make appropriate clinical decisions [26]. The pre-analytical error should also be minimized in AKI settings to avoid failure to identify diagnoses and enhance early intervention.

4.5 Electrolyte and Acid–Base Measurement Errors in Renal Emergencies

Laboratory results require accuracy as they can help to identify the electrolyte imbalance and acid-base disorders typical of renal emergencies. There are pre-analytical errors like hemolysis, late analysis, or mishandling of samples that can give falsely abnormal potassium, bicarbonate, or blood gas values resulting in incorrect emergency treatment (Figure 2). The value-based laboratory medicine underlines that it is necessary to minimize the number of avoidable diagnostic errors to enhance patient-centered outcomes and prevent unwarranted interventions [27]. Pre-analytical integrity of electrolyte and acid-base testing is thus a very important aspect of patient safety in nephrology practice.

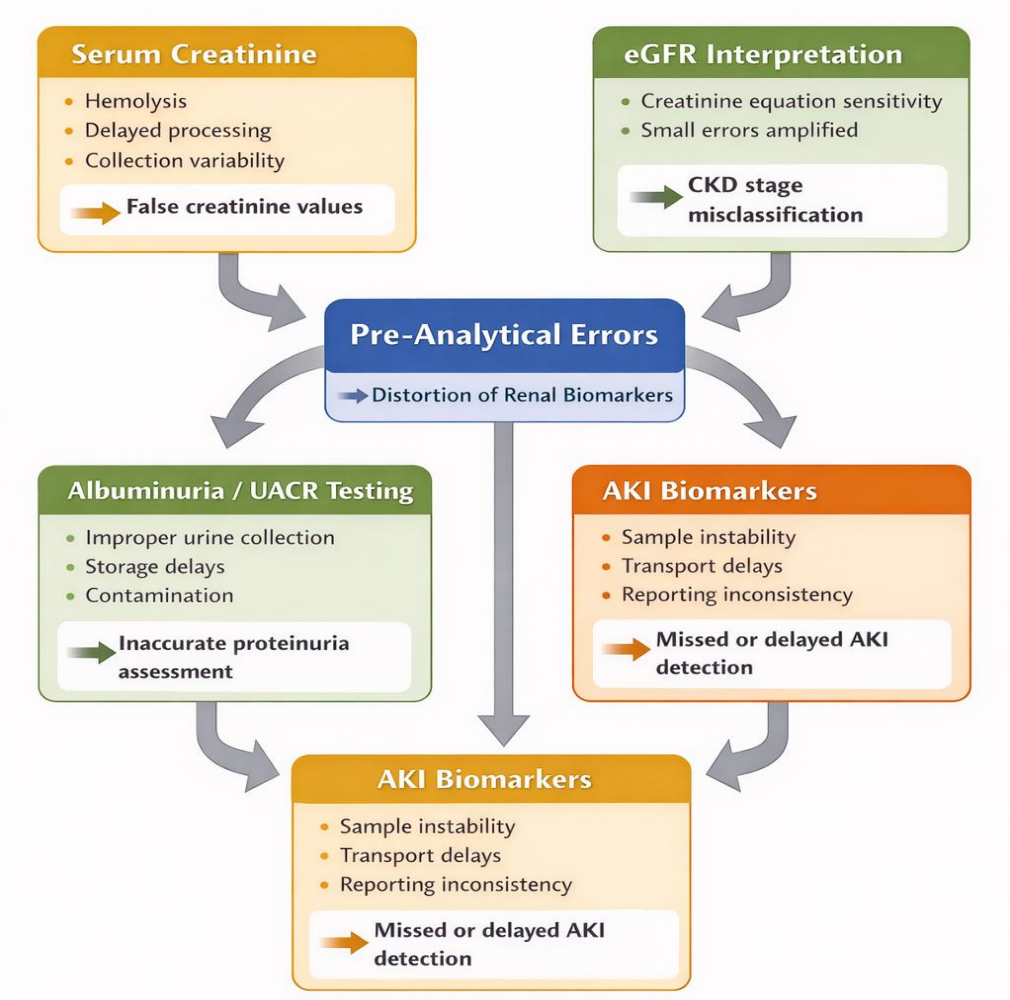

Figure 2. Impact of Pre-Analytical Errors on Core Renal Biomarkers

5. Implications for Chronic Kidney Disease Diagnosis and Staging

5.1 Alignment with KDIGO 2024 CKD Diagnostic Criteria

The proper laboratory examination is required to match CKD diagnosis with KDIGO 2024 standards that should be based on the continued eGFR decline and the presence of kidney damage, including albuminuria. Nevertheless, these thresholds may be complicated by biological and pre-analytical variation of renal biomarkers. Research proves that plasma and urinary measurements of kidney damage show high intra-individual variability, especially in individuals (those with established CKD), and thus, the importance of constant-sampling conditions is highlighted [28]. Hence, the pre-analytical control is required to be strict to allow CKD diagnosis and monitoring to be guideline-concordant.

5.2 Misclassification of CKD Stage Due to Pre-Analytical Variability

With the pre-analytical variability, the misclassification of CKD stage can be tremendous especially when slight fluctuations in the creatinine or urine biomarkers alters patients and shifts them across the diagnostic lines. This is of particular concern with vulnerable populations like pediatrics whereby early biomarkers of kidney injury are increasingly being used to detect and monitor this disease. There is evidence on the diagnostic value of urinary enzymes including N-acetyl-b-D-glucosaminidase at the early AKI detection, although they are also susceptible to pre-analytical procedures and collection issues [29]. The absence of a set of protocols can lead to late referral or ineffective intervention.

5.3 Consequences for Risk Stratification and Prognosis

Proper staging of the CKD is the key to prognostic assessment, the prediction of cardiovascular risks, and the planning of long-term care (Table 2). Pre-analytical errors that may affect biomarker values and risk stratification models include incorrect sample collection, delay in transport, and the difference in patient preparation. The pre-analytical variables reviews underline that pre-analytical variables are still a significant cause of laboratory error, and they have direct clinical decision-making and patient safety implications [30]. Such inaccuracies can cause overestimation of the disease progression, or loss of opportunities of early therapeutic intervention in CKD management.

Table 2. Implications of Pre-Analytical Variability for CKD Diagnosis, Staging, and Prognosis

Clinical Domain	Pre-Analytical Issue	Implication for CKD Evaluation	Reference
Alignment with KDIGO CKD Diagnostic Criteria	Intra-individual biological and sampling variability in plasma and urinary kidney injury markers	Difficulty applying fixed KDIGO thresholds for eGFR decline and albuminuria persistence; risk of inconsistent diagnosis	[28]
CKD Stage Misclassification	Small pre-analytical shifts in creatinine or urine biomarker levels due to handling and collection differences	Incorrect CKD staging, delayed nephrology referral, inappropriate monitoring intensity, especially in pediatrics	[29]
Risk Stratification and Prognosis	Errors from improper collection, transport delays, and patient preparation inconsistencies	Distorted prognostic models, inaccurate progression estimates, missed opportunities for early intervention	[30]

6. Pre-Analytical Errors in Specialized Nephrology Conditions

6.1 Lupus Nephritis and Immune-Mediated Kidney Disorders

Lupus nephritis is a threatening type of kidney disease that is based on an autoimmune mechanism and in which the accuracy of the diagnosis is vital to inform the immunosuppressive treatment and assess disease progression. Errors at the pre-analytical level can greatly falsify the interpretation of the biomarkers, especially in the case of proteinuria, creatinine and new inflammatory biomarkers. Poor handling of samples, slow processing of urine or contamination may result in misleading measurements of disease flare or remission. The development of precision medicine indicates the increasing significance of the biomarker-based and AI-based diagnostic strategies in lupus nephritis, yet they continue to rely on the strict pre-analytical integrity to guarantee valid predictive modeling as well as the evaluation of treatment response [31]. Thus, in the case of immune-mediated nephrology, it is essential to reduce upstream variability.

6.2 Pediatric CKD and Pre-Analytical Sensitivities in Children

CSKD in the pediatric patient is associated with some peculiarities of pre-analytical issues, the reduced blood volumes, the variability of renal biomarkers with development, and the increased sensitivity of the test to sampling variability. Creatinine-based measurements and electrolyte measurements in children could be disproportionately impacted by minor errors in collection, hemolysis or poor tube selection. Also, children may need a high frequency of monitoring, which adds up to the cumulative risk of pre-analytical variability. As something that could enhance early CKD identification and monitoring access, community-based point-of-care testing is suggested, although its impact is

highly reliant on the good quality of pre-analytical control and uniform operation practices [32]. Appropriate age diagnostic reliability is thus a necessitate in pediatric nephrology.

6.3 Oncology-Associated Kidney Injury and Biomarker Reliability

The patients with malignancies are especially susceptible of having kidney injury because of chemotherapy exposure, risk of sepsis and hemodynamic instability. The sensitive biomarkers other than serum creatinine are becoming crucial in the early diagnosis of AKI in cancer facilities. Nevertheless, these biomarkers are very prone to pre-analytical variability, such as incorrect storage, or delay in analysis or interference in the assay. The reviews of AKI biomarker development state that NGAL, KIM-1, and other markers have potential to have earlier diagnosis but their clinical utility would hinge on high standards of sample collection and processing [33]. In the process of cancer care, therefore, pre-analytical reliability is necessary to identify kidney injury correctly.

6.4 Renal Surgery and Precision Measurement of Kidney Function

Perioperative kidney function monitoring is a necessary requirement among patients of renal surgery since there can be small changes in creatinine or electrolyte balance that can be used to predict the presence of a developing injury or lack of renal reserve. Such errors in pre-analysis like fluid shifts, inconsistency of the time when samples were taken, or hemolysis may blur actual postoperative renal status (Figure 3). The proper interpretation of biomarkers in the setting of surgical nephrology will play a crucial role in preventing preventable AKI, fluid management, and monitoring of the postoperative period. Hence, adherence to standardized pre-analytical protocols is especially crucial in the perioperative kidney care as it enables safe clinical decision-making.

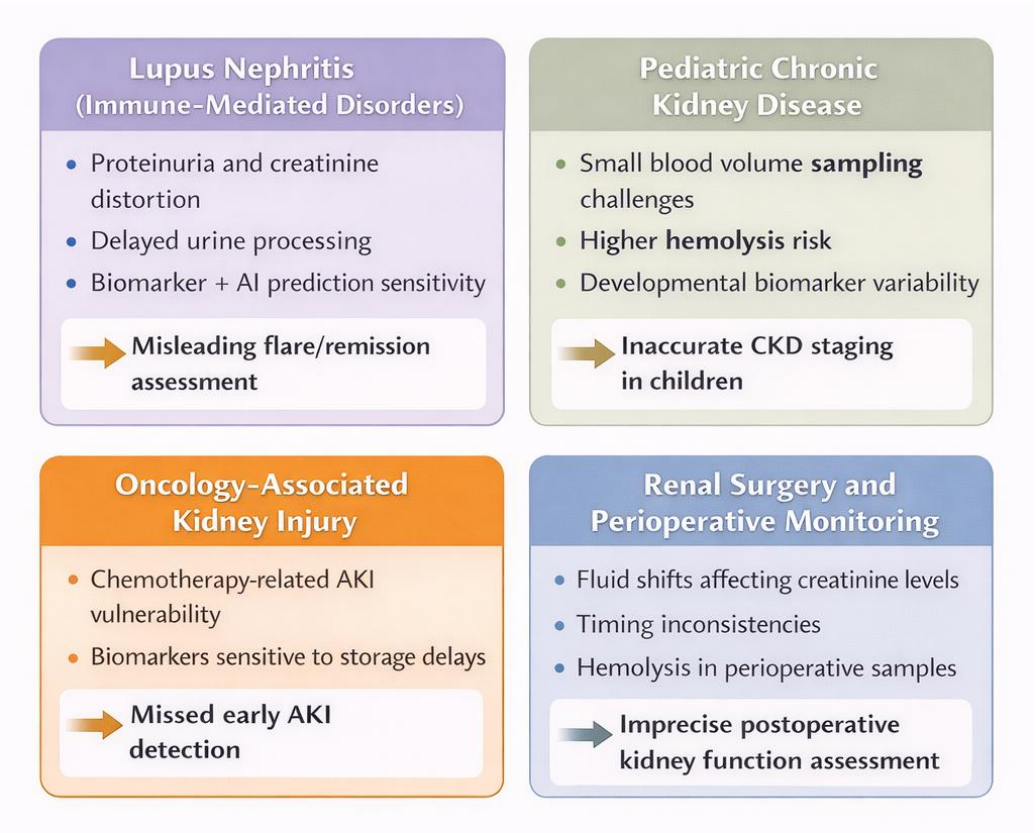

Figure 3. Pre-Analytical Errors in Specialized Nephrology Conditions

7. Patient Safety and Clinical Decision-Making Consequences

7.1 Diagnostic Delay and Inappropriate Referral Pathways

Diagnostic delay in nephrology may be directly caused by pre-analytical errors, which may be caused by poor quality of creatinine or urea results, leading to premature CKD diagnosis. One area of research has been point-of-care testing to enhance rapid renal testing, but it will be highly unreliable unless pre-analytical handling and validation are rigorous [34]. The miscarriage of justice in the entire testing procedure, in the choice of the test to be performed to misinterpreted failures during reporting can lead to late referral or unneeded specialist visits [35]. Enhancement of pre-analytical processes is thus necessary to the evaluation of kidney disease in timely manner.

7.2 Incorrect Drug Dosing in Renally Impaired Patients

Correct renal laboratory findings are essential in the administration of medications particularly drugs that

need a cut down to a patient with a compromised renal system. Mistaken creatinine or electrolyte levels may result due to pre-analytical interference such as contamination, hemolysis or disruption of the assay by drugs. Practical advice is that medication-related interferences are a significant and underappreciated cause of laboratory error, which directly creates risks of toxicity or therapeutic failure [36]. Such inaccuracies can negatively affect patient safety in the field of nephrology by making an inappropriate dosage choice.

7.3 Avoidable Dialysis Initiation or Missed AKI Detection

Pre-analytical variability in acute nephrology can lead to falsely abnormal or falsely reassuring biomarker outcome, which can be used to make high-stakes decisions, such as starting dialysis. Evidence-based laboratory medicine emphasizes that point-of-care testing can help in making decisions faster as long as pre-analytical integrity is preserved [37]. Inadequate control of the conditions of sampling may either postpone the AKI recognition or over-emphasize temporary fluctuations, which results in unnecessary interventions. Thus, to provide proper emergency kidney care, it is important to reduce instances of upstream error.

7.4 Economic Burden and Healthcare Resource Utilization

Pre-analytical failures add up a big economic pressure in the form of repeat test, long term hospital stay, and ineffective utilization of resources (Table 3). Mistakes in molecular and diagnostic work point to the lack of control in the pre-analytical stage as a factor that causes avoidable waste and low efficiency of the clinics [38]. The consequences of improper renal outcome in nephrology may include unnecessary renal imaging, inappropriate escalation of referral, or delayed treatment, which may advance the health care spending. The necessity to focus on the pre-analytical quality, therefore, manifests as a patient safety issue and not another aspect of sustainable kidney care delivery.

Table 3. Patient Safety and Clinical Decision-Making Consequences of Pre-Analytical Errors in Nephrology

Clinical Consequence	Pre-Analytical Source of Error	Impact on Kidney Care and Patient Safety	Reference
Diagnostic Delay and Inappropriate Referrals	Inaccurate creatinine/urea results, poor sample handling, unreliable POCT validation	Delayed CKD recognition, unnecessary specialist consultations, inappropriate referral pathways	[34]
Incorrect Drug Dosing in Renal Impairment	Hemolysis, contamination, medication-related assay interference	Risk of drug toxicity or therapeutic failure due to erroneous renal function estimates	[36]
Avoidable Dialysis or Missed AKI Detection	Pre-analytical variability causing false abnormal or falsely reassuring biomarker values	Inappropriate dialysis initiation, delayed AKI diagnosis, avoidable emergency interventions	[37]
Economic Burden and Resource Utilization	Repeat testing, workflow inefficiency, preventable diagnostic errors	Increased hospitalization costs, unnecessary investigations, inefficient healthcare delivery	[38]

8. Quality Indicators and Standardization Strategies in Renal Laboratory Medicine

8.1 Pre-Analytical Quality Metrics and IFCC/EFLM Recommendations

Quality indicators are an essential tool that will assist in ascertainment of the weak points of the pre-analytical phase and improving the quality of the renal diagnostics. Laboratory diagnostics is gaining popularity as an inherent goal in clinical decision making, and there is a suggestion of the need to standardize performance monitoring [39]. International programs also promote standardized pre-analytical quality measures to reduce the number of errors that can be avoided and improve patient safety. The secret behind the regular application of such recommendations in the nephrology sector where the determination of the CKD staging is made by the utilization of biomarkers such as creatinine.

8.2 Harmonization of Renal Testing Practices Across Healthcare Systems

The differences in kidney biomarkers measurement and interpretation can be harmonized to achieve similarity among institutions in the renal laboratory practices. This is particularly important in the field of transplant medicine with risk assessment systems proposing the efficacy of the diagnostic procedures to support the important stakes clinical decisions [40]. Standard practices, in their turn, increase inter-laboratory and in the provision of evidence-based nephrology care in the healthcare sectors, it also increases comparability of outcome aids.

8.3 Role of Delta Checks and Automated Surveillance Tools

Automated surveillance programs (delta check and digital monitoring programs) have gained more importance in identifying the abnormal renal biomarkers changes and diagnosing the potential pre-analytical errors. Artificial intelligence is turning out to be a groundbreaking technology in clinical labs as well, as it assists to notice the errors in the very beginning of the work and to streamline the working process [41]. The systems-based biomarker safety analyses also indicate how the best diagnostic reliability may be achieved through sophisticated monitoring [42]. New clinical recommendations also support the value of standardization of albuminuria testing as a vital bio-

marker to monitor the kidney and cardiovascular system [43].

9. Innovations and Future Directions

Renal laboratory medicine is becoming more digitally innovative and reliant on artificial intelligence to eliminate pre-analytical failures and enhance the reliability of diagnostic outcomes. New AI-based solutions will be able to assist in automated detection of inappropriate specimens, inappropriate workflow diversion, and support predictive monitoring prior to analysis. Digital decision-support systems may additionally minimize mislabeling, processing time, and unnecessary variability in reporting on renal biomarkers, in combination with intelligent sample tracking systems that are based on barcode verification, electronic ordering, and automated transport monitoring. Such developments are in line with these larger harmonization initiatives in laboratory medicine and therefore, requests, samples, measurements and reports are placed on standardized structures to promote nephrology diagnostics and patient safety [44]. At the same time, increasing point-of-care testing in nephrology is an advantage because the tests provide the rapid creatinine, electrolyte, and acid-base tests in an emergency and outpatient case, which aid in the prompt clinical decision-making process. However, POCT also incurs other risks, including discrepancies in the operators, reduced supervision in the laboratories, and pre-analytical variation. The delta check strategies that compare the present value to previous patient values provide a needed defense against the sudden change that could have been caused by sampling errors and not by a true renal failure and also improve the quality assurance of the kidney care [45].

10. Practical Recommendations for Clinicians and Laboratory Teams

10.1 Best Practices for Sample Collection in Kidney Testing

Effective sample collection practice is the key to proper assessment of kidney disease. Phlebotomy teams and clinicians need to ensure that the patient has been properly identified, the correct tube is chosen and that standard venipuncture procedures should be observed in order to minimize hemolysis and contamination. These protocols are also to be observed in the urine sampling especially in the case of albuminuria testing where timing, storage and collection procedure all play a major role in the results. Ascertainity of guidelines to the patients regarding the state of hydration on one hand, fasting on the other hand and revelation of medication also increases the credibility of diagnosis. Personnel involved in the specimen collection should be trained and periodically assessed in order to curb the unnecessary variability of the renal biomarkers.

10.2 Improving Communication Between Nephrologists and Laboratories

The emphasis on close collaboration between nephrology and laboratory specialists will result in the decrease of pre-analytic errors and improvement of clinical interpretation. Clinicians are supposed to provide relevant history of the patient including comorbidities, medications, and recreational clinical incidences that might affect the values of the biomarkers. Their role, in their turn, should be to notify in real time about an inappropriate specimen, abnormal interference of some results that need an explanation. The systematic consultation channels as an establishment would facilitate in the development of knowledge and ensure that lab information is applied in a satisfactory manner in the diagnosis, staging and treatment of kidney disease.

10.3 Institutional Protocols for Error Prevention

Healthcare institutions are recommendable to implement comprehensive measures that will target the prevention of pre-analytical errors in the context of renal diagnostic processes. These include standard procedures of specimen labeling, the schedule of transport, storage conditions and rejection of damaged specimen.. In compliance with best practices, periodic audits, enhancement programs and staff education programs are useful in ensuring compliance to best practices. Manual errors can also be minimized and traceability also be enhanced with the inclusion of electronic tracking systems and automated alerts. A culture of safety meant to be embedded within the institution will guarantee that pre-analytical quality is made a collective duty among clinical and laboratory departments.

10.4 Integrating Pre-Analytical Safety into CKD Management Guidelines

Pre-analytical safety is one of the principal parts of guideline-based CKD management. Only reliable results (laboratory) and when the diagnosis is carried out under standard conditions, are diagnostic thresholds of eGFR and albuminuria clinically meaningful. The introduction of pre-analytical information to clinical pathways, referral algorithm, and monitoring schedules enhances the use of evidence-based decisions. Nephrology expertise and laboratory quality frameworks (when offered in a multidisciplinary approach can result in a higher level of accuracy in diagnosis, less unnecessary interventions, and improve the long-term outcomes of the patients with kidney disease.

11. Conclusion

Pre-analytical errors are one of the most influential, but less known in the literature, problems in renal diagnostics, and their implications on kidney disease assessment, patient safety, and clinical decision-making are huge. Since the laboratory biomarker, including serum creatinine, eGFR, albuminuria, and electrolytes, is essential to the nephrology practice and can be used to classify the CKD stage, detect acute kidney injury in a timely manner, and provide the appropriate therapeutic interventions, the error prior to the analysis may result in the misclassification of CKD stage, the failure to identify acute kidney injury in time, and the inappropriate treatment. As noted in this review, the major causes of pre-analytical failure are patient identification errors, collection of the sample, unfavorable conditions in handling and transportation, interference of the samples like hemolysis and lipemia, and confounding factors by physiological or medication.

Significantly, diagnostic uncertainty does not just have diagnostic consequences such as incorrect drug dosage, unnecessary dialysis, unnecessary hospitalization, and unnecessary use of healthcare resources. Certain populations (such as patients with lupus nephritis, kidney disease in children, kidney disease in cancer, and kidney disease in surgery) are particularly vulnerable to pre-analytical variability and, therefore, require specific diagnostic protection. The improvement of the quality indicators, standardization schemes, and institutional guidelines are yet to be fully used in improving reliability in the pathways of renal tests. Certain new technologies such as artificial intelligence, automated surveillance, delta checks, and smart sample tracking are potentially effective solutions that will contribute to reducing the number of mistakes that can be avoided and enhance the partnership of laboratories and clinicians. Lastly, pre-analytical safety should be presented as an inseparable part of nephrology practices and guideline-based interventions into CKD care as the key that will allow improving its correct diagnosis, evidence-based treatment, and improved patient with kidney disease outcomes.

Reference

1. Lippi G, Cadamuro J, von Meyer A, Simundic AM, European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for Preanalytical Phase (WG-PRE). Practical recommendations for managing hemolyzed samples in clinical chemistry testing. Clinical Chemistry and Laboratory Medicine (CCLM). 2018 Apr 25;56(5):718-27.
2. Lin Y, Spies NC, Zohner K, McCoy D, Zaydman MA, Farnsworth CW. Pre-analytical phase errors constitute the vast majority of errors in clinical laboratory testing. Clinical Chemistry and Laboratory Medicine (CCLM). 2025 May 5(0).
3. John GK, Favaloro EJ, Austin S, Islam MZ, Santhakumar AB. From errors to excellence: the pre-analytical journey to improved quality in diagnostics. A scoping review. Clinical Chemistry and Laboratory Medicine (CCLM). 2025 Jun 26;63(7):1243-59.
4. Iatridi F, Carrero JJ, Cornec-Le Gall E, Kanbay M, Luyckx V, Shroff R, Ferro CJ. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease in Children and Adults: a commentary from the European Renal Best Practice (ERBP). Nephrology Dialysis Transplantation. 2025 Feb;40(2):273-82.
5. Madero M, Levin A, Ahmed SB, Carrero JJ, Foster B, Francis A, Hall RK, Herrington WG, Hill G, Inker LA, Kazancıoğlu R. Evaluation and management of chronic kidney disease: synopsis of the Kidney Disease: Improving Global Outcomes 2024 Clinical Practice Guideline. Annals of Internal Medicine. 2025 May;178(5):705-13.
6. Rovin BH, Ayoub IM, Chan TM, Liu ZH, Mejía-Vilet JM, Floege J. KDIGO 2024 Clinical Practice Guideline for the management of LUPUS NEPHRITIS. Kidney International. 2024 Jan 1;105(1):S1-69.
7. Awdishu L, Maxson R, Gratt C, et al. *KDIGO 2024 guideline primer for CKD management.* Am J Health-Syst Pharm. 2025
8. Matar MS, Elsheikheljanzoury AM, Hamid SI, Ahmed MM, Ali AA, Salih AM, Ahmed SB, Badi S, Yousef BA. Knowledge and Practice of Sudanese Clinical Pharmacists Towards Drugs that Require Dosage Adjustment in Renally Impaired Patients: A Cross-Sectional Study.
9. Martinez YV, Benett I, Lewington AJ, Wierzbicki AS. Chronic kidney disease: summary of updated NICE guidance. bmj. 2021 Sep 6;374.
10. Forbes AK, Hinton W, Feher MD, Elson W, Joy M, Ordóñez-Mena JM, Fan X, Cole NI, Banerjee D, Suckling RJ, de Lusignan S. Implementation of chronic kidney disease guidelines for sodium-glucose co-transporter-2 inhibitor use in primary care in the UK: a cross-sectional study. EClinicalMedicine. 2024 Feb 1;68.
11. Nordin N, Ab Rahim SN, Omar WF, Zulkarnain S, Sinha S, Kumar S, Haque M. Preanalytical errors in clinical laboratory testing at a glance: source and control measures. Cureus. 2024 Mar 30;16(3).
12. Mankar PD, Hatgaonkar K, Kohale MG, Wankhade RS, Bandre GR. Enhancing Quality in Hematology Laboratory Testing: a comprehensive review of preanalytical phase errors and prevention strategies. Journal of Applied Hematology. 2024 Apr 1;15(2):95-101.
13. Uddin MM. Artificial Intelligence and Applied Machine Learning to Improve Pre-Analytical and Post-Analytical Processes in Laboratory Medicine. Journal of Ai ML DL. 2025 Oct 5;1(1):1-0.
14. Plebani M, Scott S, Simundic AM, Cornes M, Padoan A, Cadamuro J, Vermeersch P, Çubukçu HC, González Á, Nybo M, Salvagno GL. New insights in preanalytical quality. Clinical Chemistry and Laboratory Medicine (CCLM). 2025 Aug 1;63(9):1682-92.
15. AlSahly SN, Alothiqi IA, Alzahrani NA, Halawi MY, Alharbi YA, Hazazi YA, Alqahtani SA, Alharbi SF, Garada AA. Evaluating Pre-analytical and Post-analytical Errors in Laboratory Processes and Their Impact on Diagnostic Delay and Patient Safety in Family Medicine Referrals. Vascular and Endovascular Review. 2025 Nov 25;8(13s):1-6.
16. Capelli I, De Benedictis M, Di Lenarda A, Di Maso V, Fabbrini P, Galli P, Garofalo C, Leone AM, Maiorino MI, Marengo M, Pasqualetti S. Optimizing urine albumin-to-creatinine ratio testing and referral pathways for chronic kidney disease: a nominal group technique consensus study among Italian experts. Journal of Nephrology. 2025 Nov;38(8):2067-75.
17. Teunissen CE, Tumani H, Engelborghs S, Mollenhauer B. Biobanking of CSF: international standardization to optimize biomarker development. Clinical biochemistry. 2014 Mar 1;47(4-5):288-92.

18. Cornes MP, Church S, van Dongen-Lases E, Grankvist K, Guimarães JT, Ibarz M, Kovalevskaya S, Kristensen GB, Lippi G, Nybo M, Sprongl L. The role of European Federation of Clinical Chemistry and Laboratory Medicine Working Group for Preanalytical Phase in standardization and harmonization of the preanalytical phase in Europe. Annals of clinical biochemistry. 2016 Sep;53(5):539-47.
19. Sciacovelli L, Lippi G, Sumarac Z, del Pino Castro IG, Ivanov A, De Guire V, Coskun C, Aita A, Padoan A, Plebani M. Pre-analytical quality indicators in laboratory medicine: Performance of laboratories participating in the IFCC working group "Laboratory Errors and Patient Safety" project. Clinica Chimica Acta. 2019 Oct 1;497:35-40.
20. del Rosario Dávila-Muñoz B, Parrales-Pincay IG. Desarrollo y uso de indicadores de calidad en el laboratorio clínico. MQRInvestigar. 2023 Jul 11;7(3):528-42.
21. Sanz IM, Escuer MI, Diaz MA, Meseguer NB, Kirchner MJ, Espartosa DM, Alemany MV, del Pino Castro IG, Amaro MS, Lanzarote JJ, Roselló JM. Recomendaciones para el diseño e implementación de un programa de aseguramiento de la calidad de la fase preanalítica. Revista del laboratorio clínico. 2019 Oct 1;12(4):e54-65.
22. van Rijn MH, Metzger M, Flamant M, Houillier P, Haymann JP, van den Brand JA, Froissart M, Stengel B. Performance of creatinine-based equations for estimating glomerular filtration rate changes over time. Nephrology Dialysis Transplantation. 2020 May 1;35(5):819-27.
23. Inker LA, Titan S. Measurement and estimation of GFR for use in clinical practice: core curriculum 2021. American Journal of Kidney Diseases. 2021 Nov 1;78(5):736-49.
24. Inker LA, Neuen BL, McCallum W, Vaduganathan M, Greene T, Heerspink HJ. Decline in glomerular filtration rate as an endpoint in heart failure clinical trials: challenges and solutions. European Heart Journal. 2025 Nov 7;46(42):4379-95.
25. Inker LA, Tighiouart H, Adingwupu OM, Ng DK, Estrella MM, Maahs D, Yang W, Froissart M, Mauer M, Kalil R, Torres V. Performance of GFR estimating equations in young adults. American Journal of Kidney Diseases. 2024 Feb 1;83(2):272-6.
26. Miller WG, Kaufman HW, Levey AS, Straseski JA, Wilhelms KW, Yu HY, Klutts JS, Hilborne LH, Horowitz GL, Lieske J, Ennis JL. National Kidney Foundation Laboratory Engagement Working Group recommendations for implementing the CKD-EPI 2021 race-free equations for estimated glomerular filtration rate: practical guidance for clinical laboratories. Clinical chemistry. 2022 Apr 1;68(4):511-20.
27. Plebani M. Advancing value-based laboratory medicine. Clinical Chemistry and Laboratory Medicine (CCLM). 2025 Jan 29;63(2):249-57.
28. Carter JL, Parker CT, Stevens PE, Eaglestone G, Knight S, Farmer CK, Lamb EJ. Biological variation of plasma and urinary markers of acute kidney injury in patients with chronic kidney disease. Clinical chemistry. 2016 Jun 1;62(6):876-83.
29. Bíró E, Szegedi I, Kiss C, Oláh AV, Dockrell M, Price RG, Szabó T. The role of urinary N-acetyl-β-D-glucosaminidase in early detection of acute kidney injury among pediatric patients with neoplastic disorders in a retrospective study. BMC pediatrics. 2022 Jul 20;22(1):429.
30. SK SM. Pre-analytical Variables: A Potential Source of Laboratory Error. Journal of Diabetic Association Medical College. 2023;7(1):34-9.
31. Shang S, Xia J, He G, Zheng Y, Zhang J, Lu H, Wang H, Li W, Li Q, Chen X. Advances in precision medicine for lupus nephritis: biomarker- and AI-driven diagnosis and treatment response prediction and targeted therapies. EBioMedicine. 2025 Jul 1;117.
32. Gama RM, Nebres D, Bramham K. Community Point of Care Testing in Diagnosing and Managing Chronic Kidney Disease. Diagnostics 2024, 14, 1542 [Internet]. 2024
33. Rizvi MS, Kashani KB. Biomarkers for early detection of acute kidney injury. The Journal of Applied Laboratory Medicine. 2017 Nov 1;2(3):386-99.
34. Bargnoux AS, Kuster N, Sutra T, Laroche L, Rodriguez A, Morena M, Chenine L, Chalabi L, Dupuy AM, Badiou S, Cristol JP. Evaluation of a new point-of-care testing for creatinine and urea measurement. Scandinavian Journal of Clinical and Laboratory Investigation. 2021 Jul 1;81(4):290-7.
35. Mrazek C, Lippi G, Keppel MH, Felder TK, Oberkofler H, Haschke-Becher E, Cadamuro J. Errors within the total laboratory testing process, from test selection to medical decision-making–A review of causes, consequences, surveillance and solutions. Biochemia medica. 2020 Jun 15;30(2):215-33.
36. Theab NM, Alhajri RB, Alotaibi SF, Almishrafi MF, Alomayri SS, Alsahli AB, Alenazi AK, Alosail SS, Alotaibi FM. Medication-Related Interferences in Laboratory Testing: A Practical Guide for Nursing Technicians, Clinical Pharmacists, and Laboratory Specialists. Saudi J. Med. Pharm. Sci. 2025;11:612-25.
37. Florkowski C, Don-Wauchope A, Gimenez N, Rodriguez-Capote K, Wils J, Zemlin A. Point-of-care testing (POCT) and evidence-based laboratory medicine (EBLM)–does it leverage any advantage in clinical decision making?. Critical reviews in clinical laboratory sciences. 2017 Nov 17;54(7-8):471-94.
38. Anvari MS, Gharib A, Abolhasani M, Azari-Yam A, Gharalari FH, Safavi M, Mirzaie AZ, Vasei M. Pre-analytical practices in the molecular diagnostic tests, a concise review. Iranian Journal of Pathology. 2020 Nov 10;16(1):1.
39. Agrawal B. Laboratory Diagnostics–Tools for Clinical Decision-Making and Clinical Trial Endpoints. Principles of Biomedical Sciences and

Industry: Translating Ideas into Treatments. 2022 Oct 3:357-76.
40. Mishra VC, Chandra D, Raina V. Risk Assessment in Clinical Histocompatibility Testing: Challenges, Strategies, and Future Directions. OBM Transplantation. 2025 Nov;9(4):1-2.
41. Chopra S. Artificial intelligence: A transformative role in clinical laboratory. Journal of Laboratory Physicians. 2025 Jul 4;17(2):158-63.
42. Schofield AL, Brown JP, Brown J, Wilczynska A, Bell C, Glaab WE, Hackl M, Howell L, Lee S, Dear JW, Remes M. Systems analysis of miRNA biomarkers to inform drug safety. Archives of toxicology. 2021 Nov;95(11):3475-95.
43. Beernink JM, van Mil D, Laverman GD, Heerspink HJ, Gansevoort RT. Developments in albuminuria testing: A key biomarker for detection, prognosis and surveillance of kidney and cardiovascular disease—A practical update for clinicians. Diabetes, Obesity and Metabolism. 2025 Mar 26.
44. Plebani M. Harmonization in laboratory medicine: requests, samples, measurements and reports. Critical Reviews in Clinical Laboratory Sciences. 2016 May 3;53(3):184-96.
45. Randell EW, Yenice S. Delta checks in the clinical laboratory. Critical reviews in clinical laboratory sciences. 2019 Feb 17;56(2):75-97.