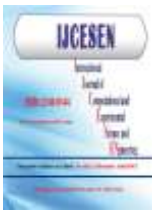
International Journal of Computational and Experimental Science and ENgineering (IJCESEN)

Vol. 10-No.4 (2024) pp. 2909-2916
http://www.ijcesen.com



ISSN: 2149-9144

Research Article

Early Detection of Acute Kidney Injury: The Combined Role of Nursing Monitoring and Laboratory Biomarkers

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Article Info:

DOI: 10.22399/ijcesen.4341
Received : 02 March 2024
Accepted : 30 March 2024

Keywords

Acute kidney injury,
early detection,
nursing monitoring,
laboratory biomarkers,
serum creatinine,
neutrophil gelatinase-associated lipocalin

Abstract:

Early detection of acute kidney injury (AKI) is crucial in minimizing potential complications and improving patient outcomes. The combined efforts of nursing monitoring and laboratory biomarkers play a pivotal role in this early identification process. Nurses are often the first line of observation in clinical settings, routinely assessing vital signs, urine output, and patient symptoms. Their ability to recognize subtle changes can provide critical insights that may indicate the onset of AKI. In parallel, advances in laboratory biomarkers, such as serum creatinine levels and novel urinary markers like neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1), enhance diagnostic accuracy. These biomarkers can detect kidney injury earlier than traditional methods, allowing for prompt intervention and treatment. The integration of nursing vigilance and laboratory biomarkers establishes a comprehensive approach to AKI management. Nurses equipped with knowledge of specific risk factors and signs of AKI can initiate further investigations rapidly, benefiting from the timely results of laboratory tests. This synergy enhances early diagnostic capabilities, enabling healthcare providers to implement targeted therapies sooner. Research has shown that a multidisciplinary approach involving nursing staff and laboratory technology not only facilitates early detection but also contributes to the overall quality of care, ultimately reducing hospital stays and improving patient safety. Thus, fostering a collaborative environment in which nursing monitoring and laboratory biomarker analysis coexist is essential in the fight against acute kidney injury.

1. Introduction

Acute Kidney Injury (AKI) transcends the definition of a simple disease; it is a complex and dynamic clinical syndrome that represents a critical failure of the renal system's homeostatic functions. It manifests as a rapid—occurring over hours to days—decline in kidney function, fundamentally compromising the organ's vital roles in filtering blood, regulating fluid and electrolyte balance, maintaining acid-base equilibrium, and excreting waste products of metabolism, most notably urea and creatinine [1]. This abrupt loss of function disrupts the internal milieu of the entire body, creating a cascade of physiological derangements that can precipitate multi-organ dysfunction and failure. AKI does not occur in isolation; it is a frequent and formidable complication that shadows the clinical course of a vast spectrum of illnesses, affecting patients within hospitals and, increasingly, those residing in the community, presenting a significant diagnostic and therapeutic challenge across all healthcare settings [2].

The pathophysiological landscape of AKI is traditionally categorized into three etiological domains: prerenal, intrinsic renal, and postrenal. Prerenal AKI, the most common form, arises from inadequate blood flow to the kidneys, often due to volume depletion (e.g., hemorrhage, dehydration), heart failure, or systemic vasodilation as seen in sepsis. Intrinsic renal AKI involves direct damage to the kidney's structures, primarily the renal tubules (acute tubular necrosis), glomeruli, or interstitium. Postrenal AKI results from obstruction of the urinary outflow tract, such as from an enlarged prostate, stones, or tumors [3]. Despite this classification, in clinical practice, these categories often overlap, creating a complex picture. For instance, prolonged prerenal azotemia can evolve into intrinsic acute tubular necrosis, and sepsis can cause a combination of prerenal and intrinsic injury through a combination of hypotension, inflammatory mediators, and microvascular thrombosis [4]. This complexity underscores that AKI is not a single entity but a final common pathway for a multitude of insults.

The global incidence of AKI is substantial and represents a major public health concern. It affects millions of individuals worldwide each year, with estimates suggesting a steady increase in its prevalence, partly due to an aging population with more comorbidities and more complex medical and surgical interventions [5]. The burden is not uniformly distributed; it disproportionately affects low- and middle-income countries, where limited access to healthcare, a high prevalence of infectious diseases like malaria and leptospirosis, and delayed presentations contribute to higher incidence and mortality rates [6]. Within hospitals, AKI is a ubiquitous challenge, but its incidence peaks in high-acuity environments. In the Intensive Care Unit (ICU), AKI is a hallmark of critical illness, complicating the course of over 50% of patients in some cohorts, and its severity is a powerful predictor of mortality in this vulnerable population [7]. The rising incidence is a testament to the syndrome's intimate link with modern medical care, often occurring as a complication of treatments for other life-threatening conditions.

The patient populations at highest risk for developing AKI are well-characterized. These include individuals with pre-existing chronic

conditions that render the kidneys more vulnerable, such as Chronic Kidney Disease (CKD), diabetes mellitus, hypertension, and heart failure [8]. Advanced age is a significant non-modifiable risk factor, as the aging kidney experiences a natural decline in functional reserve and regenerative capacity. Furthermore, specific clinical scenarios dramatically elevate risk. Patients undergoing major cardiac surgery, especially those requiring cardiopulmonary bypass, are exposed to periods of ischemia-reperfusion injury and hemolysis, placing them at considerable peril [9]. Similarly, the use of nephrotoxic agents—ranging from intravenous contrast media for computed tomography scans to certain antibiotics (e.g., aminoglycosides, vancomycin), chemotherapeutic drugs, and non-steroidal anti-inflammatory drugs (NSAIDs)—is a common and often preventable cause of AKI in both inpatient and outpatient settings [10]. The recognition of these high-risk profiles is the first step in any preventive strategy.

The repercussions of an AKI episode extend far beyond the immediate dysfunction of the kidneys, casting a long shadow over a patient's health trajectory. In the short term, AKI is an independent risk factor for mortality. Numerous studies have demonstrated a dose-response relationship between the severity of AKI, as staged by the KDIGO criteria, and the risk of death [3]. Alarmingly, even small, transient increases in serum creatinine that were historically dismissed as insignificant are now known to be associated with a markedly higher risk of in-hospital mortality [11]. The reasons for this are multifactorial, relating not only to the complications of AKI itself—such as life-threatening hyperkalemia, metabolic acidosis, and fluid overload—but also to its role as a marker of overall physiological reserve and severity of the underlying illness.

For those who survive the initial insult, the consequences do not end with the recovery of renal function. A single episode of AKI initiates a cascade of long-term sequelae that can permanently alter a patient's health. Most notably, AKI is now firmly established as a potent catalyst for the development and acceleration of Chronic Kidney Disease (CKD) and its progression to end-stage renal disease (ESRD), necessitating lifelong dialysis or kidney transplantation [4]. The pathophysiological link between AKI and CKD involves maladaptive repair processes, including capillary rarefaction, persistent inflammation, and fibrotic pathways that are activated during the injury phase and fail to resolve [12]. This creates a vicious cycle, often termed the "AKI-CKD continuum," where pre-existing CKD increases the risk of AKI, and an episode of AKI increases the risk of progressive CKD [13]. This long-term legacy imposes a substantial and growing public health burden, creating a population of patients requiring ongoing nephrological care and facing increased risks of cardiovascular events and premature death.

The economic impact of AKI is as profound as its clinical toll, placing a heavy strain on healthcare systems globally. The costs are driven by multiple factors. Patients with AKI experience significantly prolonged hospital lengths of stay, consuming more resources in terms of nursing care, monitoring, and diagnostic tests [14]. The management of severe AKI frequently requires renal replacement therapy (RRT), such as intermittent or continuous dialysis, which is one of the most resource-intensive therapies in modern medicine, involving specialized equipment, dedicated nursing staff, and consumables [15]. Furthermore, AKI is a strong independent predictor of hospital readmission, often related to unresolved complications, ongoing CKD, or infections associated with dialysis catheters [16]. The cumulative direct medical costs for a patient with severe AKI are exponentially higher than for a matched patient without AKI. Beyond the direct costs, there are substantial indirect costs related to lost productivity, disability, and long-term care needs, creating a significant economic ripple effect that extends far beyond the hospital walls.

2. Traditional Diagnostic Criteria

The KDIGO criteria, while providing a valuable and standardized framework for defining and staging AKI, are fundamentally retrospective. Serum creatinine, a byproduct of muscle metabolism, is an indirect and imperfect marker of glomerular filtration rate (GFR). Its levels are influenced by numerous non-renal factors, including age, gender, muscle mass, nutritional status, and certain medications [5]. More critically, a significant reduction in GFR must occur before a detectable rise in serum creatinine is observed, creating a diagnostic lag of 24 to 48 hours or more after the initial kidney injury [6]. This delay means that by the time a patient is formally diagnosed with AKI, a substantial amount of irreversible renal damage may have already occurred. Similarly, while oliguria is a sensitive sign of renal dysfunction, it is non-specific. It can be influenced by hypovolemia, hemodynamic status, and medications, and its monitoring in non-catheterized patients is often inaccurate [7]. Therefore, the dependence on these conventional markers means that clinicians are often treating established injury rather than preventing its progression. This

diagnostic inertia underscores the necessity for a more dynamic and anticipatory approach to AKI management.

3. Proactive Nursing Monitoring and Assessment

At the forefront of patient care, nurses occupy a unique and indispensable position in the early recognition of patients at risk for or in the nascent stages of AKI. Their continuous presence at the bedside enables the synthesis of clinical data into a coherent picture of impending deterioration long before laboratory values become abnormal. This proactive surveillance is the first critical pillar in the early detection framework.

Vigilant Hemodynamic Monitoring and Fluid Status Assessment. The kidneys are highly sensitive to perfusion pressures. Nurses are responsible for the meticulous and frequent assessment of hemodynamic parameters. This includes tracking blood pressure trends, with a particular focus on identifying and reporting hypotension, even if transient, as well as a narrowing pulse pressure, which can indicate reduced stroke volume [8]. Tachycardia is often an early compensatory mechanism for hypovolemia or low cardiac output and is a key vital sign to monitor. Perhaps the most nuanced nursing skill is the comprehensive assessment of fluid status. This involves daily weights, which are the most reliable indicator of fluid balance; careful measurement of all intake and output; and systematic physical examination for signs of hypovolemia (e.g., dry mucous membranes, poor skin turgor, sunken eyes) or hypervolemia (e.g., peripheral edema, pulmonary crackles, elevated jugular venous pressure) [9]. Identifying a negative fluid balance or the onset of oliguria provides a crucial real-time clinical clue that precedes a rise in serum creatinine.

Systematic Risk Factor Identification and Patient Profiling. Not all patients possess an equal risk of developing AKI. A core nursing function is to perform a thorough admission and ongoing assessment to identify those at highest risk. This involves recognizing predisposing conditions such as pre-existing CKD, diabetes, heart failure, and advanced age [10]. Furthermore, nurses must maintain a high index of suspicion for nephrotoxic insults. This includes vigilant monitoring of patients receiving intravenous contrast for imaging studies, aminoglycoside antibiotics, vancomycin, or non-steroidal anti-inflammatory drugs (NSAIDs) [11]. The nursing role extends to advocating for medication dose adjustments based on changing renal function and collaborating with pharmacists to monitor drug levels. In the perioperative setting, nurses monitor for periods of hypotension, significant blood loss, or sepsis, all of which are potent triggers for AKI [12]. By creating a risk-aware culture, nursing surveillance transforms the clinical approach from one of diagnosis to one of prediction.

Clinical Recognition of Systemic Illnesses Linked to AKI. AKI is frequently a manifestation of a broader systemic pathology. Nurses are often the first to detect the subtle signs of sepsis, a leading cause of AKI, by noting changes in mental status, fever or hypothermia, and tachypnea [13]. They also monitor for clinical signs of conditions like rhabdomyolysis (e.g., muscle pain, tea-colored urine) or hepatorenal syndrome (e.g., jaundice, ascites), which have specific implications for renal function. The nurse's holistic assessment, which integrates the patient's subjective complaints with objective findings, creates a clinical context that guides the judicious ordering of diagnostic tests, including the novel biomarkers discussed below.

4. The Emergence of Novel Biomarkers:

The limitations of serum creatinine have catalyzed an intensive search for more sensitive and specific biomarkers of AKI. These novel biomarkers, often detectable in blood or urine, reflect various pathophysiological processes within the nephron, including tubular injury, cell cycle arrest, and inflammation. Their introduction into clinical practice marks the second pillar of early AKI detection, offering a objective means to diagnose injury before functional impairment becomes evident.

Neutrophil Gelatinase-Associated Lipocalin (NGAL): A Rapid Responder to Tubular Damage.NGAL is one of the most extensively studied and promising biomarkers for AKI. It is a protein massively upregulated and released by distal tubular cells in response to various injurious stimuli, such as ischemia or sepsis [14]. Notably, NGAL levels in both plasma and urine rise sharply within 2 to 6 hours following the renal insult, far preceding any significant increase in serum creatinine [15]. This early signal makes it an invaluable tool for risk stratification in high-acuity settings like the emergency department, cardiac surgery, and ICU. Elevated NGAL levels have been consistently shown to predict the subsequent development and severity of AKI, the need for renal replacement therapy, and even mortality [16]. Its utility is particularly pronounced in specific populations, such as pediatric cardiac surgery patients, where it can guide early fluid and inotropic management [17].

Tissue Inhibitor of Metalloproteinase-2 (TIMP-2) and Insulin-like Growth Factor-binding Protein 7 (IGFBP7): Markers of Cellular Stress. The combination of TIMP-2 and IGFBP7 represents a paradigm shift in biomarker technology. These two markers are involved in G1 cell cycle arrest, a protective mechanism enacted by renal tubular cells when they encounter significant stress or damage [18]. By temporarily halting the cell cycle, the kidney attempts to prevent the division of damaged cells and allow for repair. The urinary measurement of [TIMP-2]•[IGFBP7] provides a functional readout of this cellular stress response. The FDA-approved NephroCheck® test measures this product and has been validated for use in critically ill patients to assess their risk for progressing to moderate or severe AKI within the subsequent 12 hours [19]. This provides an incredibly narrow window for intervention, enabling clinicians to implement kidney-protective strategies proactively.

Other Promising Biomarkers in the Arsenal. The biomarker landscape is rich and diverse, with several other molecules showing significant diagnostic potential. Kidney Injury Molecule-1 (KIM-1) is a transmembrane protein that is not detectable in healthy kidneys but is highly expressed on the apical membrane of proximal tubular cells after ischemic or toxic injury [20]. It is highly specific for AKI and has also been implicated in the prognosis and progression of injury. Interleukin-18 (IL-18) is a pro-inflammatory cytokine that is cleaved and released in the urine following activation of the inflammasome pathway in proximal tubular cells, making it a specific marker for ischemic AKI [21]. Furthermore, Cystatin C, a protease inhibitor produced by all nucleated cells, is a superior functional marker compared to creatinine. It is less influenced by muscle mass, age, or sex, and its serum levels rise earlier than creatinine following a reduction in GFR, providing a more sensitive gauge of glomerular filtration changes [22].

5. Synergistic Integration:

The true power in the early detection of AKI lies not in choosing between nursing assessment and biomarkers, but in their strategic integration. Biomarkers should not replace clinical acumen; rather, they should augment and validate it. This synergy creates a powerful, two-tiered detection system that is greater than the sum of its parts.

Triggering Biomarker Testing Based on Clinical Cues. In this model, the nurse's clinical assessment acts as the primary trigger for deeper investigation. For instance, a nurse caring for a post-operative patient who identifies a persistent, subtle hypotension despite fluid resuscitation, or a progressive decline in urine output, would not only document these findings but also initiate a specific communication with the physician to suggest checking a novel biomarker like NGAL or [TIMP-2]•[IGFBP7]. This moves the diagnostic process from a passive wait for a creatinine rise to an active search for subclinical injury. Similarly, in a patient receiving a known nephrotoxic agent, the nurse's vigilance for early signs of toxicity can prompt pre-emptive biomarker testing to detect injury before it becomes severe and irreversible [23].

Interpreting Biomarker Results within the Clinical Context. Conversely, an elevated biomarker level must always be interpreted within the full clinical picture provided by the nursing assessment. A positive [TIMP-2]•[IGFBP7] test in a hemodynamically unstable, septic patient carries a different weight and demands a different intervention than the same result in a stable patient with no apparent risk factors. The nurse's comprehensive understanding of the patient's volume status, hemodynamic profile, and medication exposure is essential for correctly attributing the meaning of the biomarker result and for guiding the subsequent management steps. This collaborative interpretation prevents the over-treatment of false positives and ensures that a positive biomarker leads to a meaningful clinical action [24].

Guiding and Monitoring Kidney-Specific Interventions. Once the combined clinical and biomarker profile identifies a patient with early or high-risk AKI, the focus shifts to targeted management. Here, the role of the nurse becomes even more critical. Biomarker levels can help guide the intensity of nursing interventions. For example, a patient with elevated NGAL and clinical signs of hypovolemia would mandate a more aggressive and carefully monitored fluid resuscitation protocol, with the nurse meticulously tracking the hemodynamic response and urine output [25]. In a patient with elevated [TIMP-2]•[IGFBP7] indicating high stress, the nursing focus might shift to avoiding any further nephrotoxic insults, maintaining strict glycemic control, and ensuring optimal oxygenation—all core components of a "KDIGO bundle" of care [26]. Furthermore, serial measurement of biomarkers can provide the nursing and medical team with feedback on the effectiveness of their interventions, with decreasing levels suggesting a positive response to therapy.

6. Implications for Patient Management and Clinical Outcomes

The shift towards a combined detection model has profound implications for patient management, moving the field from a one-size-fits-all approach to a personalized, precision medicine paradigm.

Facilitating Timely and Personalized Therapeutic Strategies. Early diagnosis enables early, and therefore more effective, intervention. The goal is to prevent the transition from initial injury to established, functional AKI. Interventions at this stage are more supportive and preventive rather than rescue-oriented. They can include optimized fluid management guided by dynamic parameters or point-of-care ultrasound; discontinuation or adjustment of nephrotoxic medications; initiation of vasopressor support to maintain renal perfusion pressure in shock states; and tighter metabolic control [27]. By personalizing care based on the individual's specific risk and injury profile, clinicians can maximize benefit and minimize harm.

Impact on Morbidity, Mortality, and Healthcare Economics. The ultimate goal of early detection is to improve hard clinical outcomes. There is growing evidence that biomarker-guided strategies can lead to a reduction in the severity of AKI, a lower rate of progression to higher KDIGO stages, and a decreased need for renal replacement therapy [28]. By mitigating the severity of renal injury, this approach can directly impact mortality, as the risk of death is strongly correlated with the stage of AKI [29]. From an economic perspective, although biomarker testing adds a direct cost, it is likely highly cost-effective. The potential savings from preventing a single case of severe AKI requiring dialysis—through avoided ICU days, dialysis costs, and complications—are substantial [30]. Furthermore, by reducing the long-term risk of CKD, early detection and intervention confer a lifelong health economic benefit.

7. Challenges and Future Directions:

Despite the clear promise, the widespread implementation of this combined model faces several challenges. The cost and availability of novel biomarker assays can be a barrier, especially in resource-limited settings [31]. There is a need for further large-scale, randomized controlled trials to conclusively demonstrate that biomarker-guided management strategies improve patient-centered outcomes across diverse populations [32]. Furthermore, successfully integrating this approach requires a significant educational effort to ensure that all members of the healthcare team, from bedside nurses to intensivists, understand the interpretation and clinical application of these new tools [33].

Future directions in this field are exciting. Research is focusing on biomarker panels that combine multiple markers to improve diagnostic and prognostic accuracy for specific etiologies of AKI, such as sepsis-induced versus ischemic AKI [34]. The integration of biomarker data with electronic health records to create "AKI sniffer" algorithms and clinical decision support systems is another promising avenue [35]. These systems can automatically flag high-risk patients based on their clinical data and suggest biomarker testing or specific care bundles to the clinical team. The development of point-of-care testing devices for biomarkers could further revolutionize management by providing results at the bedside within minutes, dramatically shortening the time to intervention [36].

8. Conclusion:

The battle against Acute Kidney Injury is being transformed by a dual-front strategy that synergistically combines the irreplaceable human element of expert nursing surveillance with the objective, predictive power of novel laboratory biomarkers. Nurses, with their continuous presence and holistic assessment, provide the essential clinical context and are the first line of defense in identifying at-risk patients. Novel biomarkers like NGAL and [TIMP-2]•[IGFBP7] offer an unprecedented, objective glimpse into the subclinical phase of renal injury, breaking free from the diagnostic constraints of serum creatinine. It is the thoughtful integration of these two domains—where clinical suspicion triggers biomarker testing and biomarker results inform and intensify clinical care—that holds the key to true early detection. This paradigm shift from a reactive to a proactive and preventive model of AKI management is the most promising pathway toward reducing the significant mortality, morbidity, and economic burden associated with this devastating syndrome. The future of nephroprotection lies in this collaborative, vigilant, and biomarker-informed approach to patient care.

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
- **Conflict of interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

- **Acknowledgement:** The authors declare that they have nobody or no-company to acknowledge.
- **Author contributions:** The authors declare that they have equal right on this paper.
- **Funding information:** The authors declare that there is no funding to be acknowledged.
- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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