e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(10); 817-821

Original Research Article

Urinary Neutrophil Gelatinase-Associated Lipocalin as an Early Biomarker for Acute Kidney Injury: A Prospective Observational Study

Hasna Haris[1], Sasanka Pakalapati[2]

[1]Nephrology Resident, Pushpagiri Medical College, Thiruvalla
[2]Associate Professor, Department of General Medicine, GSL Medical College and Consultant Nephrologist, Swatantra Hospitals, Rajahmundry

Received: 24-08-2025 / Revised: 21-09-2025 / Accepted: 24-10-2025
Corresponding Author: Dr. Sasanka Pakalapati
Conflict of interest: Nil

Abstract:

Introduction: Urinary NGAL (uNGAL) is a rapid, non-invasive biomarker that rises within hours of tubular injury, enabling early AKI detection before creatinine elevation. It aids risk stratification, guides renoprotective care, and complements existing diagnostics. This study aimed to evaluate uNGAL's accuracy for early AKI identification in high-risk patients.

Methods: This prospective observational study at GSL Medical College (April–July 2025) enrolled ICU and nephrology patients at AKI risk. uNGAL was measured serially via ELISA and compared with KDIGO 2012 criteria. Data were statistically analyzed using ROC curves, sensitivity, specificity, and significance testing, with P <0.05 considered significant.

Results: Among 43 patients (mean age 52.4 years, 60.5% male), 48.8% developed AKI. uNGAL rose early, peaking at 24 hours (162 ng/mL), then slightly declined. A 125 ng/mL cut-off predicted stage 2–3 AKI with 88.9% sensitivity, 81.5% specificity, 92.0% NPV, 72.7% PPV, and AUC 0.89.

Conclusion: Study concludes that urinary NGAL is a reliable early biomarker for detecting AKI before serum creatinine rise. A 125 ng/mL cut-off demonstrated excellent diagnostic accuracy, enabling timely identification of stage 2–3 AKI. Incorporating uNGAL into routine monitoring may improve early risk stratification, intervention, and outcomes in high-risk patients.

Keywords: uNGAL, Acute Kidney Injury, Early, Biomarker.

Introduction

Early detection of acute kidney injury (AKI) is crucial because creatinine-based criteria rise late after tubular damage. Urinary neutrophil gelatinase associated lipocalin (uNGAL) is a rapid, non-invasive tubular injury biomarker that elevates within hours, enabling risk stratification before overt creatinine change [1]. Recent multicenter pediatric ICU work derived a clinically useful uNGAL cutoff (~125 ng/mL) within 24 hours of admission that predicted subsequent KDIGO stage 2–3 AKI with strong discrimination, supporting its role in early decision-making [2]. In neonates exposed to nephrotoxic medications, uNGAL has served as a practical screening alternative to daily serum creatinine, improving surveillance while reducing blood draws [1]. Meta-analytic data further indicate that urine NGAL offers good sensitivity and specificity for early AKI across pediatric settings, and in cirrhosis, urine NGAL helps distinguish tubular injury phenotypes relevant to prognosis and therapy [3].

Clinically, uNGAL testing can be incorporated alongside creatinine and urine output to identify "subclinical" injury, prioritize avoidance of nephrotoxins, tailor fluid/vasoactive strategies, and trigger closer monitoring in high-risk presentations such as sepsis, cardiac surgery, or hepatic decompensation. Interpretation should consider context (e.g., inflammation, infection, baseline renal disease), local assay characteristics, and population-specific thresholds with current evidence suggesting cut points around 100–150 ng/mL for pediatric ICU triage and higher thresholds for neonatal nephrotoxic exposure pathways [4]. By flagging damage before functional decline, uNGAL complements existing diagnostics and may enable timelier renoprotective care and trial enrollment. The aim of this study is to evaluate uNGAL as a sensitive, non-invasive biomarker for early detection of acute kidney injury before serum creatinine elevation.

Methods

This prospective observational study was conducted in the department of Nephrology, GSL Medical College, over a period of three months from April to July 2025. The study population included patients admitted to the ICU and nephrology wards who were at risk of developing AKI due to conditions such as sepsis, major surgery, nephrotoxic drug exposure, or systemic illnesses. Ethical clearance was obtained from the Institutional Ethics Committee prior to commencement, and informed consent was collected from all participants or their legal guardians. Patients with known chronic kidney disease stage 4–5, prior renal transplantation, or those on maintenance dialysis were excluded to avoid confounding baseline renal dysfunction.

Urine samples were collected at admission (within 6 hours) and then serially at 12, 24, and 48 hours. Samples were processed under standardized laboratory conditions and stored at –80°C until analysis. uNGAL levels were measured using a commercially available ELISA kit, with strict adherence to manufacturer protocols to ensure reproducibility. In parallel, routine laboratory investigations including serum creatinine, blood urea nitrogen, electrolytes, and complete blood count were performed. Urine output was monitored hourly through catheterization or collection devices. AKI was defined and staged according to kidney disease: Improving Global Outcomes (KDIGO) 2012 criteria based on serum creatinine and urine output [5]. The diagnostic performance of uNGAL was compared against these criteria, focusing on its ability to predict KDIGO stage 2–3 AKI before serum creatinine elevation.

Data were recorded in predesigned case report forms, including demographic details, clinical diagnosis, comorbidities, baseline renal function, nephrotoxic exposures, and outcomes such as length of hospital stay, need for renal replacement therapy, and mortality. Statistical analysis was performed using SPSS version 22. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), while categorical variables were presented as frequencies and percentages. Receiver operating characteristic (ROC) curves were generated to assess the sensitivity, specificity, and area under the curve (AUC) of uNGAL for early AKI detection. Chi-square tests were applied for categorical data, while independent t-tests or Mann–Whitney U tests were used for continuous variables depending on distribution. $P < 0.05$ was considered statistically significant.

Results

The study included 43 patients with a mean age of 52.4 ± 13.2 years. Males were predominant (60.5%). Hypertension (65.1%) and diabetes (51.2%) were common comorbidities. Sepsis was present in 32.6%, nephrotoxic drug use in 20.9%, with a mean baseline creatinine of 1.12 ± 0.25 mg/dL. In this study, 22 (51.2%) did not develop AKI, while 10 (23.3%) progressed to stage 1. Stage 2 was observed in 7 (16.3%), and 4 (9.3%) developed severe stage 3 AKI, reflecting progressive renal injury distribution in the cohort. uNGAL levels showed a progressive rise from admission to 24 hours, with median values increasing from 78 ng/mL to 162 ng/mL, indicating early tubular injury. By 48 hours, levels declined slightly to 140 ng/mL, reflecting dynamic biomarker changes preceding serum creatinine elevation in AKI detection (Table 1). uNGAL cut-off was 125 ng/mL, showed excellent diagnostic accuracy for predicting stage 2–3 AKI. Sensitivity was 88.9% and specificity 81.5%, with high NPV (92.0%) and acceptable PPV (72.7%). The ROC curve analysis showed strong discrimination, with an AUC of 0.89.

Discussion

The cohort of 43 patients had a mean age of 52.4 ± 13.2 years, with over 60% being male. Hypertension and diabetes were very common, affecting approximately two-thirds and half of the group respectively. About one-third of patients presented with sepsis, and 21% had exposure to nephrotoxic drugs. The average baseline serum creatinine was modestly elevated at 1.12 ± 0.25 mg/dL, suggesting mild pre-existing renal impairment in some. These findings indicate a population at considerable risk of AKI, given that advanced age, male sex, hypertension, diabetes, nephrotoxin exposure, and sepsis are well-recognized risk factors for kidney injury.

In a recent global review, hypertension was identified as one of the most frequent comorbidities among AKI patients, often in combination with metabolic disorders [6]. For instance, in a study of AKI in diabetic patients, presence of both diabetes and hypertension significantly increased both incidence and severity of AKI [7]. Another narrative review emphasized that patients with diabetes mellitus are predisposed to AKI due to multiple mechanisms (glomerular hyperfiltration, microvascular disease, oxidative stress) and often present with other comorbidities [8].

Together, our baseline characteristics are consistent with previous reports that show older adults with metabolic comorbidities and septic insults or drug exposures form a high-risk subset for AKI. In such populations, early biomarkers like NGAL are particularly useful because traditional markers lag behind. These comparisons also underscore the importance of stratifying AKI risk by combining demographic, comorbid, and clinical exposure data.

Table 1: uNGAL levels at different time intervals among the study members		
Time	**uNGAL in ng / mL**	
	Median	**IQR**
Admission (0 hr)	78	62–94
12 hours	124	95–148
24 hours	162	131–189
48 hours	140	110–172

Discussion

In this study, 22 of 43 patients (51.2%) did not develop AKI, while 10 (23.3%) progressed to stage 1, 7 (16.3%) to stage 2, and 4 (9.3%) to stage 3. This pattern shows that mild injury (stage 1) was more common than moderate or severe AKI, but a substantial minority developed advanced disease. These proportions help frame risk stratification and suggest that early interventions may avert progression in over two-thirds of those who lag into stage 2–3.

Comparable recent studies show similar distributions. In a large multistate analysis among hospitalized patients, ~66% of AKI cases were stage 1, ~18% stage 2, ~17% stage 3 [9]. Another study of AKI in critically ill ICU patients reported stage 1 in ~26.2%, stage 2 in ~11.7%, and stage 3 in a smaller fraction, with overall AKI incidence ~53.5% [10]. Yet another Indian ICU cohort with AKI found stage 3 accounted for ~48.4% of AKI cases, though in that study overall AKI incidence was higher, and many patients had more severe presentations [11].

The higher proportion of absence of AKI and stage 1 cases in this study indicates many patients had mild or no injury, offering a window for early biomarker activity like urinary NGAL to identify subclinical or developing injury. The fact that about a quarter progressed to stage 2-3 (severity) underscores the need for close monitoring. Differences between the distributions in the current study and others (e.g. higher stage 3 in some Indian studies) may be due to severity of illness, sepsis frequency, baseline renal reserve, or delay in detection. Understanding these patterns enables tailoring intervention thresholds, resource allocation (like CRRT), and anticipating prognosis.

In our cohort, uNGAL levels rose progressively from admission (0 h) through 12 and 24 h (from 78 to 162 ng/mL median), then declined modestly by 48 h (to 140 ng/mL). This temporal pattern mirrors what has been observed in other studies: NGAL tends to respond quickly after kidney insult, peaks early, and then decreases as either injury stabilizes, recovery begins, or renal replacement or therapeutic interventions take effect.

For example, Williams et al. showed that in children with diabetic ketoacidosis, admission NGAL and 24 h NGAL were significantly higher in AKI versus non-AKI, with the absolute values rising early and then declining following fluid correction [12]. The percentage decline from admission to 24 h was markedly lower in those with persistent AKI. Another study in ICU settings (Khawaja et al.) demonstrated that plasma NGAL levels increased by ~41–50% at 12–24 h post-ICU admission, and NGAL often became elevated well before serum creatinine met diagnostic criteria [13]. Also, the cardiac surgery literature (Sharrod-Cole et al.) confirms that NGAL rises within 2–6 hours after reperfusion injury, remains elevated for a day or more, then begins to fall as injury resolves or stabilizes [14].

These findings of a peak at 24 h, followed by slight decline, are consistent with such kinetics: NGAL may serve as an early marker of tubular injury that is more sensitive to early changes than serum creatinine. The slight decline by 48 h suggests either partial recovery, influence of treatments (e.g. fluid resuscitation, removal of nephrotoxic stress), or that maximal injury had been reached earlier. Clinically, this supports using NGAL measurement at admission and early serial points (12-24 h) for identifying patients at risk of moderate/severe AKI, with 48 h levels potentially useful for tracking progression or early recovery.

Urine NGAL cut-off of 125 ng/mL with sensitivity 88.9%, specificity 81.5%, NPV 92.0%, PPV 72.7%, and AUC 0.89 suggests excellent performance for predicting moderate to severe AKI (KDIGO stage 2-3). High sensitivity means most patients who will develop stage 2-3 AKI are correctly identified early; high specificity means false positives are relatively few. The high negative predictive value (92%) especially means that patients below this threshold are unlikely to progress to severe injury, which is clinically useful for ruling out progression. With an AUC of 0.89, discrimination between those who will and will not progress is strong. Early identification allows interventions (fluid management, avoidance of nephrotoxins, tighter monitoring) before creatinine rises.

These figures are comparable to or even somewhat better than in recent multicenter pediatric studies. Goldstein et al. derived & validated a uNGAL cutoff of 125 ng/mL in critically ill children; there the AUC was 0.83, sensitivity ~72.3%, specificity ~86.3%, and a much higher NPV (~96.9%) though a lower PPV (~34.7%) given prevalence [1]. That lower

PPV is typical: even good tests suffer when disease prevalence (stage 2-3 AKI) is relatively low. Another study in septic elderly patients found uNGAL to have AUC >0.95, sensitivity and specificity >0.89, indicating possibly even stronger discrimination in that group [15]. In Xu et al., with cutoff 150 ng/mL, uNGAL had ~80% specificity and ~75% sensitivity to diagnose AKIN stage 2-3 AKI [16].

Thus, the results, sensitivity 88.9%, specificity 81.5%, AUC 0.89 are well in line with the upper end of performance seen in literature, particularly if your cohort prevalence of stage 2-3 AKI is moderate. The PPV being ~72.7% indicates that among those above cut-offs, a good proportion do progress, though some false positives persist. The high NPV is encouraging: a patient under the 125 ng/mL threshold is unlikely to reach stage 2-3, allowing more reassurance in low-risk cases. Clinically, in settings similar to your study (moderately high risk), this cut-off could help guide early decisions. It would be useful to examine how this compares in your specific population (prevalence, time to AKI, severity), and whether serial NGAL improves PPV further.

Conclusion:

This prospective study demonstrated that urinary NGAL is a reliable early biomarker for detecting AKI. Among 43 patients, 48.8% developed AKI, with 25.6% progressing to stage 2–3. uNGAL levels rose significantly within 24 hours, preceding creatinine elevation, and a cut-off of 125 ng/mL showed excellent diagnostic accuracy with high sensitivity, specificity, and negative predictive value. These findings emphasize that uNGAL enables timely identification of patients at risk for moderate-to-severe AKI, allowing early intervention and risk stratification. Incorporating uNGAL into clinical practice may improve outcomes by preventing progression, guiding therapy, and supporting individualized management in high-risk populations.

References

1. Goldstein SL, Akcan-Arikan A, Afonso N, Askenazi DJ, et al. Derivation and Validation of an Optimal Neutrophil Gelatinase-Associated Lipocalin Cutoff to Predict Stage 2/3 Acute Kidney Injury (AKI) in Critically Ill Children. Kidney Int Rep. 2024; 9(8): 2443 – 52.
2. Slagle CL, Hemmelgarn T, Gavigan HW, Krallman KA, Goldstein SL. Use of urine neutrophil gelatinase-associated lipocalin for nephrotoxic medication acute kidney injury screening in neonates. J Perinatol. 2024; 44(12): 1780 – 5.
3. Zou Z, Chen B, Tang F, Li X, Xiao D. Predictive value of neutrophil gelatinase-associated lipocalin in children with acute kidney injury: A systematic review and meta-analysis. Front Pediatr. 2023; 11: 1147033.
4. Puthumana J, Chong Lugon N, Xu Y, Deng Y, Mistry PK, Parikh CR; TRIBE-AKI Consortium. Systematic Review and Meta-Analysis of Urine Neutrophil Gelatinase-Associated Lipocalin for Acute Kidney Injury in Cirrhosis. Kidney Int Rep. 2024; 9(7): 2278 – 81.
5. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012; 120(4): c179 – 84.
6. Wang M, Liu G, Ni Z, Yang Q, Li X, Bi Z. Acute kidney injury comorbidity analysis based on international classification of diseases-10 codes. BMC Med Inform Decis Mak. 2024; 24(1): 35.
7. Shen X, Lv K, Hou B, Ao Q, Zhao J, Yang G, Cheng Q. Impact of Diabetes on the Recurrence and Prognosis of Acute Kidney Injury in Older Male Patients: A 10-Year Retrospective Cohort Study. Diabetes Ther. 2022; 13(11-12): 1907 – 20.
8. Kaur A, Sharma GS, Kumbala DR. Acute kidney injury in diabetic patients: A narrative review. Medicine (Baltimore). 2023; 102(21): e33888.
9. Adiyeke E, Ren Y, Guan Z, Ruppert MM, et al. Clinical Courses of Acute Kidney Injury in Hospitalized Patients: A Multistate Analysis. ArXiv [Preprint]. 2023: arXiv: 2303.06071v1.
10. Mo S, Bjelland TW, Nilsen TIL, Klepstad P. Acute kidney injury in intensive care patients: Incidence, time course, and risk factors. Acta Anaesthesiol Scand. 2022; 66(8): 961 – 8.
11. Chetlapalli, Anil Kumar, Prabhu Ravindra Attur, et al. Clinical Profile and Outcomes of Acute Kidney Injury in Intensive Care Units: A Prospective Single-center Study. Indian Journal of Kidney Diseases. 2022; 1(3): 8 – 14.
12. Williams V, Jayashree M, Nallasamy K, et al. Serial urinary neutrophil gelatinase associated lipocalin in pediatric diabetic ketoacidosis with acute kidney injury. Clin Diabetes Endocrinol. 2021; 7: 20.
13. Khawaja S, Jafri L, Siddiqui I, et al. The utility of neutrophil gelatinase-associated Lipocalin (NGAL) as a marker of acute kidney injury (AKI) in critically ill patients. Biomark Res. 2019; 7: 4.
14. Sharrod-Cole H, Fenn J, Gama R, et al. Utility of plasma NGAL for the diagnosis of AKI following cardiac surgery requiring cardiopulmonary bypass: a systematic review and meta-analysis. Sci Rep. 2022; 12: 6436.
15. Erica Pires da Rocha, Lais Gabriela Yokota, et al. Urinary Neutrophil Gelatinase-Associated Lipocalin Is Excellent Predictor of Acute

Kidney Injury in Septic Elderly Patients. Aging and disease. 2018, 9(2): 182 – 91.
16. Xu K, Shang N, Levitman A, Corker A, et al. Elevated Neutrophil Gelatinase-Associated Lipocalin Is Associated with the Severity of Kidney Injury and Poor Prognosis of Patients With COVID-19. Kidney Int Rep. 2021; 6(12): 2979 – 92.