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Urinary Neutrophil Gelatinase-Associated Lipocalin as a Complementary Biomarker for Acute Kidney Injury Detection and Severity Stratification : A Prospective Diagnostic Cohort Study

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Title Page

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Urinary Neutrophil Gelatinase-Associated Lipocalin as a Complementary Biomarker for Acute Kidney Injury Detection and Severity Stratification : A Prospective Diagnostic Cohort Study

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Abstract

Introduction: AKI is associated with substantial morbidity and mortality, yet early diagnosis remains challenging because serum creatinine is a delayed marker of kidney dysfunction. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) has emerged as a promising biomarker of structural kidney injury. This study evaluated the diagnostic and prognostic utility of uNGAL in hospitalized adults with AKI.

Study Design: Prospective diagnostic cohort study with 90-day follow-up.

Methods: Adults admitted between June and December 2024 were prospectively enrolled. The cohort included 215 patients with AKI defined according to KDIGO criteria and 173 hospitalized controls without AKI. u-NGAL was measured at enrollment using the Abbott Alinity i Urine NGAL assay. Receiver operating characteristic (ROC) analyses were performed to evaluate diagnostic performance for AKI detection and severity stratification. AKI patients were followed for renal recovery and hemodialysis initiation.

Results: A total of 388 participants were included. For AKI detection, uNGAL demonstrated moderate diagnostic accuracy with an area under the ROC curve (AUC) of 0.736 ($p = 0.001$). At a cutoff of 90.2 ng/mL, sensitivity was 56.7% and specificity was 80.3%. Diagnostic performance improved with AKI severity, with AUCs of 0.696 for stage 1 AKI and 0.785 for stage 3 AKI. At a cutoff of >158.9 ng/mL, uNGAL achieved 87.5% sensitivity and 95.8% negative predictive value for identifying stage 3 AKI. Higher uNGAL concentrations were associated with hemodialysis initiation in unadjusted analyses but not after multivariable adjustment. No significant association was observed between uNGAL and renal recovery.

Conclusions: uNGAL demonstrated moderate diagnostic accuracy for AKI detection and good performance for identifying severe AKI. Although not independently associated with renal recovery or hemodialysis initiation, its ability to detect structural kidney injury and stratify AKI severity supports its role as a complementary biomarker alongside conventional measures of kidney function.

Keywords: Acute kidney injury; uNGAL; biomarker; diagnostic accuracy; KDIGO; hemodialysis.

Urinary Neutrophil Gelatinase-Associated Lipocalin as a Complementary Biomarker for Acute Kidney Injury Detection and Severity Stratification : A Prospective Diagnostic Cohort Study

Introduction

Acute kidney injury (AKI) is a rapid decline in kidney function that impairs waste elimination, fluid balance, electrolyte regulation, and acid–base homeostasis. It is associated with high morbidity, mortality, prolonged hospitalization, and progression to chronic kidney disease (CKD) or end-stage kidney disease (ESKD)(Kellum et al., 2021; Ostermann et al., 2025a). Globally, AKI remains a major public health challenge, with the greatest burden occurring in low- and middle-income countries, where delayed recognition, limited nephrology services, and fragmented care pathways contribute to poor outcomes (Francis et al., 2024; Gameiro et al., 2025; Sengthavisouk et al., 2020).

Current AKI diagnosis relies mainly on serum creatinine and urine output, as recommended by KDIGO criteria. However, these conventional markers have important limitations because serum creatinine may rise only after substantial functional impairment has occurred and can be affected by hydration status, muscle mass, medications, and baseline kidney function. As a result, AKI may remain clinically silent and undetected during its early phase, delaying timely intervention and increasing the risk of disease progression (KDIGO, 2012; Wilson et al., 2023).

Novel kidney injury biomarkers have been proposed to overcome the well-recognized limitations of traditional AKI diagnostic markers. Among these, neutrophil gelatinase-associated lipocalin (NGAL) has emerged as one of the most extensively investigated and clinically validated biomarkers of renal tubular injury. Unlike serum creatinine, which reflects delayed changes in glomerular filtration and may not increase until substantial kidney dysfunction has occurred, NGAL is rapidly released from injured tubular epithelial cells and can become detectable within hours of ischemic, inflammatory, or nephrotoxic renal injury (Ostermann et al., 2025a; Schrezenmeier et al., 2017). Consequently, NGAL may identify kidney damage before conventional functional markers become abnormal, allowing earlier recognition of AKI and potentially facilitating timely therapeutic intervention.

Beyond its diagnostic role, accumulating evidence suggests that NGAL provides important prognostic information. Elevated NGAL concentrations have been associated with increased AKI severity, persistent kidney dysfunction, need for renal replacement therapy, prolonged hospitalization, and mortality across diverse clinical settings (Albeladi & Algethamy, 2017; Côté et al., 2022; Lumlertgul et al., 2020). Furthermore, international consensus reports and recent reviews have highlighted NGAL as a key component of the evolving paradigm that integrates structural biomarkers with conventional functional measures to improve AKI phenotyping, risk stratification, and clinical decision-making (Koyner et al., 2020; Ostermann et al., 2025a). Therefore, NGAL may serve not only as an early biomarker for AKI detection but also as a

valuable tool for severity stratification and prediction of adverse outcomes, including AKI progression, dialysis initiation, and mortality.

In Palestine, kidney disease represents a growing clinical and economic challenge. More than 3,500 patients are currently dependent on renal replacement therapy, and the number of dialysis cases has increased by over 100% during the past (Palestinian Ministry of Health, 2023). The absence of a national renal registry, a limited nephrology workforce, and the lack of standardized follow-up pathways for patients at risk of AKI further compound the burden on the healthcare system. Combined with annual dialysis costs exceeding US$16,000 per patient (Younis et al., 2015), these challenges underscore the human and financial consequences of delayed AKI recognition and progression to advanced kidney disease. In this context, practical diagnostic tools that facilitate earlier detection and risk stratification are urgently needed. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) has emerged as a promising biomarker of structural kidney injury that complements conventional functional markers such as serum creatinine. Although extensively investigated in selected populations, evidence regarding its real-world clinical utility in resource-limited healthcare settings remains limited. Therefore, this prospective study aimed to evaluate the diagnostic and prognostic performance of uNGAL among hospitalized adults with acute kidney injury (AKI) in a Palestinian governmental hospital and to determine its complementary value for AKI detection and severity stratification alongside conventional laboratory markers.

Methods

Study Design and Setting

This prospective diagnostic cohort study was conducted at Beit-Jala Governmental Hospital, Palestine, between June and December 2024. The study evaluated the diagnostic and severity-stratification performance of urinary neutrophil gelatinase-associated lipocalin (u-NGAL) among hospitalized adults with acute kidney injury (AKI). Eligible patients were prospectively enrolled and followed for 90 days after AKI diagnosis. To assess diagnostic accuracy, an age and sex matched cohort of hospitalized adults without AKI was recruited during the same study period.

Study Population

Adult patients aged ≥18 years admitted to the medical, surgical, coronary care, or intensive care units between June 2024 and December 2024 were screened for eligibility. Patients were included in the AKI cohort if they fulfilled the Kidney Disease: Improving Global Outcomes (KDIGO) criteria for acute kidney injury (AKI) based on serum creatinine and/or urine output measurements. Patients with end-stage kidney disease requiring chronic dialysis, previous kidney transplantation, or pregnancy were excluded. Patients with pre-existing chronic kidney disease were included provided they met KDIGO criteria for AKI based on changes in serum creatinine and/or urine output. Consequently, the cohort included patients with acute-on-chronic kidney injury(AKI on the top of CKD).

To evaluate the diagnostic performance of urinary neutrophil gelatinase-associated lipocalin (u-NGAL), an age and sex matched reference cohort of hospitalized adults without AKI was recruited from the same hospital during the study period. Eligible controls were required to have normal kidney function tests, no evidence of AKI according to KDIGO criteria, and complete biomarker measurements. Detailed clinical and comorbidity data were not systematically collected for control participants because the control cohort was recruited solely for diagnostic accuracy analyses.

The final biomarker cohort comprised 388 hospitalized adults, including 215 patients with AKI and 173 hospitalized controls without AKI. A complete 1:1 matching strategy was not feasible because the uNGAL assay availability was limited by financial constraints, procurement costs, and logistical challenges associated with importing and laboratory processing of assay kits. Consequently, controls were selected pragmatically from eligible hospitalized adults during the same study period.

Patients in the AKI cohort were prospectively followed from enrollment for up to 90 days via the Avicenna Hospital Information System (HIS) to ascertain clinical outcomes, including renal recovery and dialysis initiation. The non-AKI control cohort was used exclusively for diagnostic accuracy analyses and was not included in longitudinal outcome assessments. Baseline clinical characteristics of the AKI cohort are presented in Table 1.

Sample size

Because this study represented the first prospective evaluation of u-NGAL among hospitalized adults at our institution, all eligible patients with available u-NGAL measurements during the study period were included. The number of participants was partly determined by the availability of u-NGAL assay kits and funding constraints related to biomarker testing. Consequently, a convenience sample was used rather than a formally calculated sample size. The final cohort comprised 215 patients with AKI and 173 non-AKI controls, which was considered adequate for estimation of diagnostic accuracy measures.

AKI Definition and Classification

Acute kidney injury was defined and staged according to the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline (Figure 1). Patients were classified according to the highest KDIGO stage reached during hospitalization.

Biomarker Measurements

Urinary NGAL concentrations were measured using the Alinity i Urine NGAL assay (Abbott Diagnostics, Abbott Park, IL, USA), a chemiluminescent microparticle immunoassay performed on the Abbott Alinity analyzer platform.

Urine samples were collected during routine clinical assessment and processed according to manufacturer recommendations. Internal quality control and calibration procedures were performed throughout the study period.

Conventional renal biomarkers, including serum creatinine, urine protein concentration, and urine protein-to-creatinine ratio (PCR), were also measured and evaluated comparatively.

Outcomes

The primary outcome was the diagnostic performance of u-NGAL for differentiating AKI from non-AKI patients and for stratifying AKI severity according to KDIGO stages.
Secondary analyses evaluated the association between u-NGAL levels measured at baseline (i.e., at the time of AKI diagnosis or initial clinical assessment) and clinically relevant outcomes, including initiation of hemodialysis and renal recovery. Patients in the AKI cohort were prospectively followed for up to 90 days after enrollment.

Statistical Analysis

Statistical analyses were performed using SPSS version 28 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation or median with interquartile range, depending on distribution.
Receiver operating characteristic curve analysis was used to evaluate the diagnostic performance of uNGAL, serum creatinine, urine protein, and protein-to-creatinine ratio for distinguishing AKI from non-AKI participants and for stratifying AKI severity according to KDIGO stages. Sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve were calculated. Optimal cutoff values were determined using Youden's index.
Associations between biomarkers and clinical outcomes were evaluated using logistic regression for hemodialysis initiation and Cox proportional hazards regression for renal recovery. Variables with $p < 0.20$ in univariable analyses were considered eligible for inclusion in multivariable models to avoid premature exclusion of potentially important predictors and confounders. Candidate variables included demographic characteristics, comorbidities, AKI severity, laboratory biomarkers, and other clinically relevant variables associated with the outcome. Odds ratios (ORs) and hazard ratios (HRs) were reported with 95% confidence intervals (CIs). A two-sided p-value <0.05 was considered statistically significant. There were no missing data for the variables included in the analyses.

Results

A total of 388 hospitalized adults were included in the biomarker cohort, comprising 215 patients with AKI and 173 age- and sex-matched non-AKI controls. Table 1 illustrates the Baseline Characteristics of Patients with Acute Kidney Injury.

Table 1. Baseline Characteristics of Patients with Acute Kidney Injury (n = 215)

Characteristic	Value
Age, mean ± SD (years)	66.5 ± 15.0
Male sex, n (%)	116 (54.0)
Female sex, n (%)	99 (46.0)
Sepsis, n (%)	116 (54.0)
Critical illness, n (%)	196 (91.2)
Circulatory shock, n (%)	72 (33.5)
Chronic kidney disease, n (%)	136 (63.3)
Hypertension, n (%)	155 (72.1)
Diabetes mellitus, n (%)	126 (58.6)
Heart disease, n (%)	171 (79.5)

Lung disease, n (%)	102 (47.4)
Anemia, n (%)	143 (66.5)
Urinary NGAL, median (IQR), ng/mL	119.6 (37.1–753.4)
Serum creatinine, median (IQR), mg/dL	2.04 (1.68–3.27)

Data are presented as mean ± SD, median (IQR), or n (%). AKI, acute kidney injury; NGAL, neutrophil gelatinase-associated lipocalin; SD, standard deviation; IQR, interquartile range.

Diagnostic performance for AKI detection

Urinary NGAL demonstrated moderate diagnostic accuracy for distinguishing AKI from non-AKI patients, with an AUC of 0.736 (p = 0.001). Serum creatinine showed the highest discriminatory performance (AUC = 0.992), followed by PCR (AUC = 0.773) and proteinuria (AUC = 0.768). Detailed diagnostic accuracy measures, including optimal cutoff values, sensitivity, specificity, positive predictive value, and negative predictive value, are presented in Table 2. The corresponding ROC curves are shown in Figure 2.

Table 2. Diagnostic Performance of Biomarkers for AKI Detection

Biomarker	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	P-value
uNGAL, ng/mL	90.2	56.74	80.34	77.71	60.59	0.736	0.001
Serum creatinine, mg/dL	1.13	98.60	100.00	100.00	98.34	0.992	<0.001
Proteinuria, mg/day	49.43	62.33	83.71	82.21	64.78	0.768	0.003
PCR	0.59	65.58	78.65	78.77	65.42	0.773	0.002

Table 2 Diagnostic accuracy parameters were calculated from ROC curve analyses. Cutoff values represent optimal thresholds determined by the Youden index. AKI, acute kidney injury; AUC, area under the receiver operating characteristic curve; uNGAL, urinary neutrophil gelatinase-associated lipocalin; PCR, urine protein-to-creatinine ratio; PPV, positive predictive value; NPV, negative predictive value.

Diagnostic Performance Across AKI Severity

Diagnostic performance varied according to AKI severity. For stage 1 AKI, uNGAL demonstrated moderate discriminatory ability (AUC = 0.696, p < 0.001), whereas serum creatinine showed the highest diagnostic accuracy (AUC = 0.785). No biomarker demonstrated meaningful diagnostic performance for stage 2 AKI.

For stage 3 AKI, uNGAL showed good diagnostic performance (AUC = 0.785, p < 0.001), with high sensitivity and negative predictive value for identifying severe AKI. Serum creatinine remained the strongest diagnostic marker (AUC = 0.873). Detailed diagnostic performance metrics are presented in Table 3, and the corresponding ROC curves for KDIGO stage 1 and stage 3 AKI are shown in Figures 3 and 4, respectively.

Table 3. Diagnostic Performance of Biomarkers for AKI Severity Stratification

Biomarker	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	P-value
AKI Stage 1							
uNGAL (ng/mL)	≤101	58.33	74.65	82.4	46.9	0.696	<0.001
Serum creatinine (mg/dL)	≤2.56	77.78	67.61	83.0	60.0	0.785	<0.001
Urine creatinine (mg/dL)	≤80.7	71.53	45.07	72.5	43.8	0.567	0.115
Proteinuria (mg/day)	≤129.9	68.06	53.52	74.8	45.2	0.610	0.008
Protein-to-creatinine ratio (PCR)	≤0.39	31.94	83.10	79.3	37.6	0.567	0.102
AKI Stage 2							
uNGAL (ng/mL)	>22.3	96.77	17.39	16.5	97.0	0.501	0.981
Serum creatinine (mg/dL)	>1.71	90.32	31.52	18.2	95.1	0.552	0.261
Urine creatinine (mg/dL)	>100	32.26	77.17	19.2	87.1	0.510	0.862
Proteinuria (mg/day)	≤26.34	38.71	77.72	22.6	88.3	0.561	0.292
Protein-to-creatinine ratio (PCR)	≤5.44	96.77	23.37	17.5	97.7	0.571	0.176

AKI Stage 3							
uNGAL (ng/mL)	>158.9	87.50	65.71	36.8	95.8	0.785	<0.001
Serum creatinine (mg/dL)	>2.69	87.50	78.86	48.6	96.5	0.873	<0.001
Urine creatinine (mg/dL)	>109.8	35.00	84.00	33.3	85.0	0.590	0.090
Proteinuria (mg/day)	>66.79	85.00	53.14	29.3	93.9	0.711	<0.001
Protein-to-creatinine ratio (PCR)	>0.40	97.50	33.14	25.0	98.3	0.655	0.001

Table 3 :PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the curve, Statistical significance for the test at P-value<0.05. PCR: Protein creatinine ratio.

3.4 Pairwise AUC comparisons

Pairwise ROC comparisons demonstrated that serum creatinine had significantly higher AUCs than uNGAL for both stage 1 AKI (AUC difference = 0.089, p = 0.029) and stage 3 AKI (AUC difference = 0.088, p = 0.039). For stage 1 AKI, uNGAL performed significantly better than proteinuria (AUC difference = 0.086, p = 0.044). For stage 3 AKI, uNGAL showed significantly greater discriminatory performance than PCR (AUC difference = 0.130, p = 0.011). Additional significant differences were observed among other biomarker pairs, particularly those involving serum creatinine, which consistently demonstrated the highest discriminatory performance across comparisons. Complete pairwise AUC comparisons are presented in Table 4.

Table 4. Comparison of AUCs for Significant Biomarkers

Comparison	Difference in AUC	P-value
KDIGO Stage 1 AKI		
uNGAL vs Serum Creatinine	0.089	0.029
uNGAL vs Proteinuria	0.086	0.044
Serum Creatinine vs Proteinuria	0.175	<0.001
KDIGO Stage 3 AKI		
uNGAL vs Serum Creatinine	0.088	0.039
uNGAL vs Proteinuria	0.074	0.112
uNGAL vs PCR	0.130	0.011
Serum Creatinine vs Proteinuria	0.162	<0.001
Serum Creatinine vs PCR	0.218	<0.001
Proteinuria vs PCR	0.056	0.014

Table 4 AUC: Area under the curve, Statistical significance at P-value<0.05

Association between u-NGAL and renal recovery

In Cox regression analysis, urinary NGAL was not significantly associated with renal recovery over time (HR = 0.9999, 95% CI: 0.9997–1.0001, p = 0.382). This suggests that baseline u-NGAL was not an independent predictor of recovery among AKI patients.

Association between u-NGAL and hemodialysis initiation

In univariate logistic regression analysis, as expressed in Table 5, higher u-NGAL concentration was significantly associated with hemodialysis initiation (OR = 1.001, 95% CI: 1.0001–1.001, p = 0.011). However, this association did not remain significant after multivariable adjustment (adjusted OR = 1.0001, 95% CI: 0.999–1.001, p = 0.790). In contrast, serum creatinine remained independently associated with hemodialysis initiation (adjusted OR = 2.46, 95% CI: 1.48–4.09, p = 0.001).

Table 5. Prognostic Associations of u-NGAL with Clinical Outcomes

Outcome	Unadjusted estimate	P-value	Adjusted estimate	P-value
Renal recovery	HR = 0.9999 (0.9997–1.0001)	0.382	Not included	—

Hemodialysis initiation	OR = 1.001 (1.0001–1.001)	0.011	OR = 1.0001 (0.999–1.001)	0.790

Table 5:Hazard ratio, CI: Confidence interval, Statistical significance at P-value<0.05

Discussion

The present study evaluated the diagnostic and prognostic utility of u-NGAL among hospitalized adults with AKI in a Palestinian governmental hospital. The findings demonstrated that u-NGAL exhibited moderate diagnostic accuracy for overall AKI detection and good discriminatory performance for severe AKI (KDIGO stage 3). Although serum creatinine remained the strongest overall diagnostic marker, u-NGAL provided clinically meaningful complementary information regarding structural kidney injury and severity stratification. Furthermore, while u-NGAL was associated with dialysis initiation in univariate analyses, it was not independently associated with renal recovery or dialysis after adjustment for clinical covariates.

For overall AKI detection, u-NGAL achieved an AUC of 0.736, indicating moderate discriminative ability. Diagnostic performance improved considerably for severe AKI (AUC = 0.785), suggesting that u-NGAL becomes increasingly informative as tubular injury progresses. This observation is biologically plausible because u-NGAL is rapidly released by injured renal tubular epithelial cells following ischemic, inflammatory, or nephrotoxic insults. Consequently, u-NGAL reflects structural tubular damage rather than delayed changes in glomerular filtration, and greater elevations are expected in advanced stages characterized by more extensive epithelial injury (Schrezenmeier et al., 2017; Ostermann et al., 2025a).

Our findings agree with previous investigations demonstrating that urinary NGAL correlates with AKI severity and adverse renal outcomes. Albeladi and Algethamy (2017) reported excellent predictive performance of u-NGAL for renal replacement therapy among critically ill patients, while Brogi et al. (2024) demonstrated very high sensitivity for AKI detection at ICU admission. Likewise, Lumlertgul et al. (2020) showed that elevated urinary NGAL predicted persistent AKI and major adverse kidney events. Although the diagnostic performance observed in the present study was more modest, this likely reflects the heterogeneous hospitalized population studied under routine clinical conditions rather than highly selected ICU cohorts, thereby enhancing the external validity and real-world applicability of our findings.

A particularly important observation was the high negative predictive value of u-NGAL for KDIGO stage 3 AKI (95.8%). Clinically, biomarkers with high negative predictive values are especially useful for excluding severe disease, allowing clinicians to identify patients at relatively low risk of progression. This characteristic may be particularly valuable in resource-limited healthcare systems where nephrology services are scarce, and prioritization of high-risk patients is essential.

Serum creatinine demonstrated superior diagnostic performance for both stage 1 and stage 3 AKI. This finding was expected because serum creatinine constitutes part of the KDIGO diagnostic and

staging criteria and therefore benefits from incorporation bias when used as the reference standard (KDIGO, 2012).

However, the value of u-NGAL should not be interpreted simply in comparison with serum creatinine because these biomarkers represent different pathophysiological processes. Serum creatinine primarily reflects kidney function, whereas u-NGAL reflects structural tubular injury. Contemporary ADQI recommendations emphasize that structural and functional biomarkers should be interpreted together rather than viewed as competing diagnostic tests (Ostermann et al., 2020).

This distinction is clinically important because structural injury frequently precedes measurable reductions in glomerular filtration. Consequently, patients may demonstrate elevated u-NGAL despite preserved serum creatinine concentrations, a condition referred to as subclinical AKI (Schrezenmeier et al., 2017). Increasing evidence indicates that these patients remain at increased risk of adverse renal outcomes despite not fulfilling conventional creatinine-based diagnostic criteria.

Consistent with this concept, u-NGAL outperformed proteinuria-based indices in several analyses and demonstrated particularly strong discriminatory performance for severe AKI. Collectively, these findings support the growing consensus that structural biomarkers provide clinically relevant information beyond conventional functional markers (Ostermann et al., 2025a).

The present findings should be interpreted within the broader evolution of AKI diagnostics. Current KDIGO criteria rely primarily on serum creatinine and urine output; however, both markers have well-recognized limitations. Serum creatinine is a delayed functional marker influenced by muscle mass, hydration status, nutritional status, liver disease, and medications, whereas urine output may be affected by fluid administration, diuretic therapy, and monitoring inaccuracies (Ostermann et al., 2025). Consequently, both measures may fail to identify early or subclinical kidney injury.

A growing body of evidence supports the incorporation of structural biomarkers into AKI diagnosis. Besides u-NGAL, biomarkers such as kidney injury molecule-1 (KIM-1), liver-type fatty acid-binding protein (L-FABP), interleukin-18 (IL-18), and the cell-cycle arrest markers TIMP-2·IGFBP7 have demonstrated the ability to detect kidney injury before substantial declines in glomerular filtration occur (Hatton et al., 2020; Neyra et al., 2019; Zou et al., 2022). These biomarkers improve identification of subclinical AKI and facilitate differentiation between transient functional changes and intrinsic tubular injury (Schrezenmeier et al., 2017).

Accordingly, the objective of biomarker implementation is not to replace serum creatinine but to complement conventional functional assessment. Contemporary AKI frameworks increasingly advocate integrating structural biomarkers, functional markers, and clinical risk assessment to improve diagnostic precision throughout the AKI continuum (Albert et al., 2020; Ostermann et al., 2020). The present study contributes further evidence supporting this integrated approach.

Beyond diagnosis, the present study evaluated the prognostic significance of u-NGAL for dialysis initiation, renal recovery, and mortality. Although higher u-NGAL concentrations were associated with dialysis initiation in univariate analyses, these relationships were no longer statistically

significant after adjustment for demographic variables, comorbidities, AKI severity, and conventional laboratory findings.

Similarly, baseline NGAL concentrations were not independently associated with renal recovery or mortality. These findings suggest that although u-NGAL reflects the presence and severity of tubular injury, its independent prognostic value may be limited when established clinical predictors are simultaneously considered.

This observation is consistent with previous studies demonstrating that biomarkers perform optimally when incorporated into multivariable prediction models rather than used in isolation. Lumlertgul et al. (2020) reported improved prediction of persistent AKI after combining NGAL with clinical variables, while Côté et al. (2022) demonstrated superior prognostic performance using multimarker prediction models. These findings support future development of integrated clinical prediction tools rather than reliance on individual biomarkers.

Most evaluations of u-NGAL have been conducted in highly specialized centres within high-income countries. Evidence from low- and middle-income countries remains comparatively limited despite bearing a substantial proportion of the global burden of AKI (Ostermann et al., 2025a).

The present study, therefore, provides important evidence from Palestine, where AKI remains associated with considerable morbidity and mortality. Previous Palestinian studies have reported substantial mortality and incomplete renal recovery among hospitalized patients with AKI (Damin Abukhalil et al., 2024), while Nazzal et al. (2022) demonstrated markedly increased mortality among oncology patients who developed AKI.

Within this context, earlier identification of patients at risk of severe AKI could facilitate timely intervention, more appropriate nephrology referral, and improved allocation of limited healthcare resources. Rather than replacing conventional assessment, selective incorporation of u-NGAL into structured clinical pathways alongside serum creatinine, clinical evaluation, and electronic alert systems represents a pragmatic strategy that aligns with contemporary KDIGO and ADQI recommendations (Ostermann et al., 2020; Ostermann et al., 2025).

Strengths and Limitations

This study has several strengths. It represents one of the first prospective evaluations of urinary neutrophil gelatinase-associated lipocalin (uNGAL) among hospitalized patients in Palestine and provides real-world evidence from a governmental hospital operating in a resource-limited healthcare setting. The inclusion of matched non-AKI controls enabled robust assessment of diagnostic accuracy, while comparison with conventional laboratory markers, including serum creatinine, urine protein, and protein-to-creatinine ratio, provided clinically relevant benchmarking. In addition, the prospective study design and standardized application of KDIGO criteria strengthened the validity of the findings.

Several limitations should be acknowledged. First, this was a single-center study with a relatively modest sample size, largely determined by the availability and cost of uNGAL assay kits, which may have limited statistical power for prognostic analyses despite being adequate for evaluating

diagnostic performance. Second, AKI classification relied on the KDIGO criteria incorporating serum creatinine, introducing unavoidable incorporation bias. Third, serial uNGAL measurements were unavailable, precluding assessment of biomarker kinetics over time. Fourth, inflammatory conditions such as sepsis, infection, and chronic kidney disease may independently increase uNGAL concentrations and reduce diagnostic specificity. Finally, only uNGAL was evaluated; other established urinary biomarkers, such as kidney injury molecule-1 (KIM-1), interleukin-18 (IL-18), liver-type fatty acid-binding protein (L-FABP), and the cell-cycle arrest biomarkers TIMP-2 and IGFBP7, were not available for direct comparison. Therefore, larger multicenter prospective studies incorporating multiple urinary biomarkers are warranted to validate these findings and further define the complementary role of uNGAL in AKI diagnosis and risk stratification.

Conclusion

Urinary NGAL demonstrated moderate diagnostic accuracy for AKI detection and good discriminatory performance for severe AKI among hospitalized adults. Although serum creatinine remained the strongest overall diagnostic marker, u-NGAL provided valuable complementary information regarding structural tubular injury and disease severity. The high negative predictive value observed for stage 3 AKI suggests potential utility as a rule-out biomarker, particularly in resource-limited healthcare settings. These findings support further evaluation of uNGAL as a complementary biomarker within multimodal AKI assessment strategies. Larger multicenter studies incorporating multiple urinary biomarkers are warranted before widespread clinical implementation.

Author statement's

Ethical Approval

This study is part of a broader doctoral research thesis titled "Enhancing Acute Kidney Injury Management in Southern Palestinian Governmental Hospitals: Impact of Risk Triage, Novel Biomarkers, and Electronic Health Alerts," which comprises three components: a quantitative study, a qualitative study, and a published systematic review (WCN25-3547, DOI: 10.1016/j.ekir.2024.11.184) and qualitative study also published (DOI: 10.1186/s12882-025-04449-w). Ethical approval was obtained from the Institutional Review Board (IRB) at the School of Public Health, Al-Quds University (Approval No: 5/24, dated 13 February 2024), and from the Scientific Research Unit at the Palestinian Ministry of Health (Approval dated 28 February 2024). The study was conducted in accordance with the Declaration of Helsinki and applicable national and institutional ethical guidelines. Written informed consent was obtained from all participants before their enrolment in the study. Participants were informed about the study procedures, their voluntary participation, their right to withdraw at any time without consequences, and the confidentiality of their information.

Clinical trial number

Not applicable.

Consent for Publication

Not applicable. This study does not include any identifiable personal data, images, or other information requiring individual consent for publication.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to confidentiality agreements with participants, but are available from the corresponding author on reasonable request.

Authors' Contributions

The authors conceptualized and designed the study, conducted interviews, analyzed the data, drafted the manuscript, and approved the final submission.

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The study was self-funded.

Competing interests

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.

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Figure Legends

Figure 1

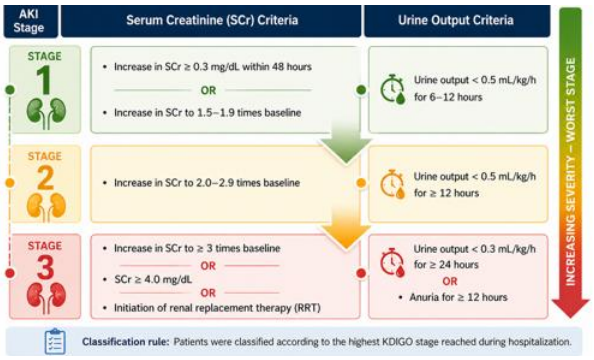


Figure 1KDIGO Definitions and classifications of Aute Kidney Injury

Figure 2

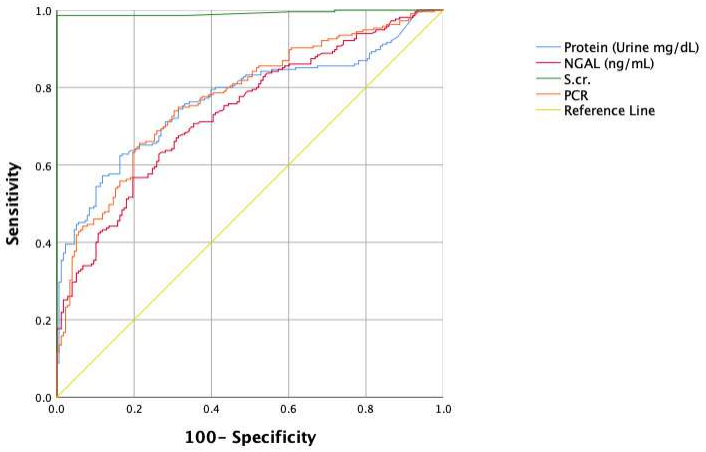


Figure 4: ROC curves of u-NGAL, serum creatinine, urine protein, and PCR for discriminating AKI from non-AKI

Figure 3

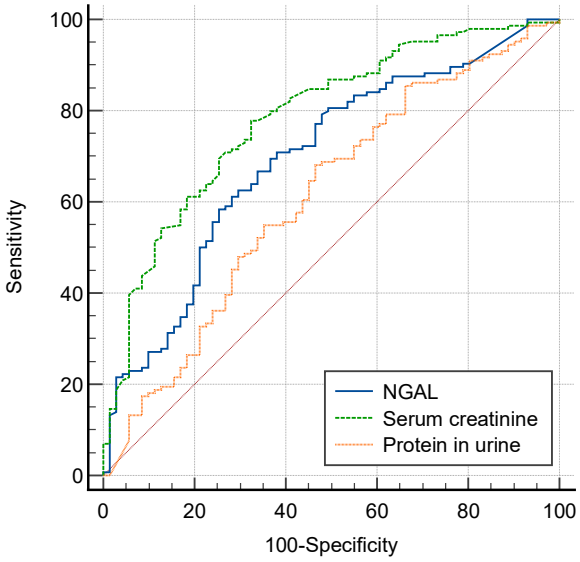


Figure 3: Comparison of ROC curves of significant indices for the prediction of AKI stage 1

Figure 4

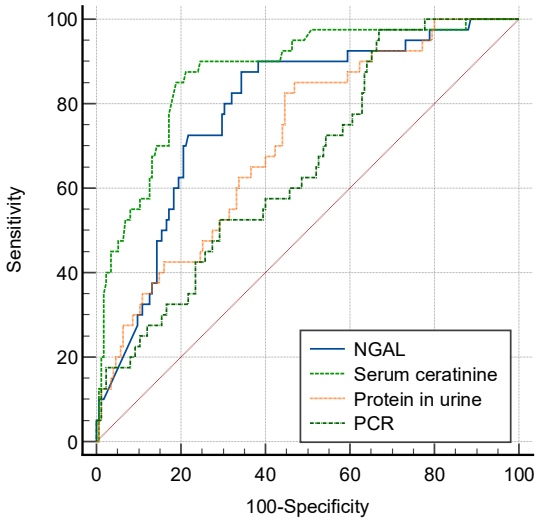


Figure 4: Comparison of ROC curves of significant indices for the prediction of AKI stage 3