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Original Article

Early Prediction of Post-Cardiac-Surgery Acute Kidney Injury: Urinary NGAL versus Serum Creatinine

Lubna Sarfraz[1], Anum Iftikhar[2], Sara Reza[1] & Absara Tanveer[3]
[1]Quaid-e-Azam Medical College, Bahawalpur, Pakistan
[2]Bahawalpur Medical and Dental College, Bahawalpur, Pakistan
[3]CMH Institute of Medical Sciences, Bahawalpur, Pakistan

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Abstract

Background: Acute Kidney Injury (AKI) is a common and serious complication following cardiac surgery, associated with adverse outcomes and increased healthcare costs. Early identification of AKI is critical for timely intervention and improved prognosis. However, serum creatinine—the traditional biomarker for renal function—lacks sensitivity in the early stages due to its delayed rise. Neutrophil Gelatinase-Associated Lipocalin (NGAL) has emerged as a promising early biomarker.
Objective: This study aimed to compare the diagnostic performance of urinary NGAL versus serum creatinine for early prediction of AKI in post-cardiac surgery patients.
Methodology: This descriptive cross-sectional study was conducted from May 2023 to June 2024 and included 123 patients aged 40–70 years undergoing elective cardiac surgery. Patients with pre-existing chronic kidney disease or recent urological procedures were excluded. Urinary NGAL levels were measured 2 hours postoperatively, while serum creatinine was assessed at 48 hours. Diagnostic performance was evaluated in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy.
Results: Urinary NGAL demonstrated superior diagnostic accuracy with a sensitivity of 92.0%, specificity of 81.25%, PPV of 88.46%, NPV of 86.67%, and overall accuracy of 87.80% in predicting AKI. In comparison, serum creatinine exhibited lower diagnostic metrics, reinforcing the early predictive value of NGAL.
Conclusion: Urinary NGAL outperforms serum creatinine as an early biomarker for AKI following cardiac surgery. Incorporating urinary NGAL testing into routine postoperative care may enhance early detection and improve clinical outcomes. Further large-scale, multicenter studies are warranted to validate these findings across diverse populations.

Keywords: Acute Kidney Injury, Biomarker, Cardiac Surgery, Neutrophil Gelatinase-Associated Lipocalin, Serum Creatinine.

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Corresponding Author:
Dr. Sara Reza
Assistant Professor,
Department of Pathology,
Quaid-e-Azam Medical and Dental College, Bahawalpur, Pakistan.
sara_qmc@gmail.com

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Introduction

Acute Kidney Injury (AKI), previously referred to as acute renal failure (ARF), is a significant clinical condition that encompasses a broad spectrum of acute renal impairments, ranging from mild declines in kidney function to complete renal failure [1]. AKI is associated with considerable morbidity, mortality, and financial burden due to increased demands for intensive care and prolonged hospital stays [2]. Early recognition and timely intervention are crucial for improving outcomes and reducing the risk of long-term renal complications.

Cardiac surgery-associated acute kidney injury (CSA-AKI) is one of the most frequent and serious postoperative complications, defined by a sudden decline in renal function, often reflected by a reduction in glomerular filtration rate (GFR). AKI following cardiac surgery has been reported in approximately 30% of patients, contributing to prolonged hospitalization and increased mortality [3]. In severe cases requiring renal replacement therapy, the prevalence of CSA-AKI decreases to approximately 4% [4]. Even minimal increases in serum creatinine (sCr) postoperatively (0.3–0.5 mg/dL) have been associated with significantly elevated mortality within the first 30 days. For example, while the mortality rate for patients undergoing open-heart surgery without AKI is less than 8%, it increases fourfold in those who develop AKI [5].

The adverse consequences of CSA-AKI are compounded by the limitations of currently used biomarkers. Serum creatinine, the standard indicator of renal function, is a late marker and often rises only after substantial kidney damage has occurred [6,7]. This delay in detection limits the clinician's ability to intervene early and mitigate further injury, thereby underscoring the need for more sensitive and specific early biomarkers.

Neutrophil Gelatinase-Associated Lipocalin (NGAL) has emerged as one of the most promising biomarkers for the early detection of AKI. Initially identified as a 25-kDa protein bound to neutrophil gelatinase, NGAL is now known to be released in large quantities from renal tubular cells in response to ischemic or nephrotoxic injury [8]. Its diagnostic and prognostic utility in both plasma and urine has been well-documented [9]. NGAL has also demonstrated potential in identifying patients at risk of progression to chronic kidney disease (CKD) [10]. Specifically, in the context of cardiac surgery, elevated NGAL levels within hours postoperatively have been correlated with the onset of AKI, offering an early warning that precedes the rise in serum creatinine [11].

A previous study reported a 36.26% prevalence of AKI following cardiac surgery and found urinary NGAL to have a sensitivity of 87.9% and specificity of 71.7% for AKI prediction [12]. While these findings are promising, they are largely based on research conducted in Western populations. Variations in genetic makeup, environmental exposures, and healthcare infrastructure suggest the need to validate these findings in local populations. Therefore, the objective of this study is to evaluate and compare the diagnostic efficacy of urinary NGAL and serum creatinine in detecting AKI among adult patients undergoing elective cardiac surgery in our regional setting. By doing so, we aim to generate locally relevant evidence to inform clinical practice and improve patient care.

Methodology

Study Design

This study was designed as a cross-sectional analytical study aimed at evaluating the diagnostic performance of urinary neutrophil gelatinase-associated lipocalin (NGAL) in predicting acute kidney injury (AKI) following cardiac surgery. The cross-sectional design allowed for the measurement of urinary NGAL and serum creatinine at predetermined postoperative intervals in a cohort of patients undergoing elective cardiac surgery.

Ethics

Prior to the initiation of the study, ethical approval was obtained from the Institutional Ethical Review Committee of Bahawal Victoria Hospital, Bahawalpur. All participants provided written

informed consent after a thorough explanation of the study objectives, procedures, potential risks, and benefits. Confidentiality and anonymity of patient data were strictly maintained throughout the study.

Setting

The study was conducted in the Department of Pathology at Bahawal Victoria Hospital, a tertiary care teaching hospital located in Bahawalpur, Pakistan. The hospital is equipped with modern diagnostic facilities and serves a large population from Southern Punjab.

Participants

The study population consisted of patients aged 40 to 70 years scheduled to undergo elective cardiac surgery during the one-year period from May 10, 2023, to June 10, 2024. Participants were recruited using a non-probability consecutive sampling method. Eligibility criteria included patients classified as American Society of Anesthesiologists (ASA) physical status class I or II. Both male and female patients were included. Patients with pre-existing chronic kidney disease, small echogenic kidneys on ultrasound, or those who had undergone recent urological procedures were excluded to minimize confounding related to baseline renal function.

Variables

The primary variable of interest was the development of acute kidney injury post-cardiac surgery, defined according to serum creatinine criteria. The main predictor variable was urinary NGAL levels measured two hours postoperatively. Additional demographic and clinical variables, such as age, gender, ASA classification, and type of cardiac surgery, were also recorded.

Data Sources/Measurement

Urinary NGAL levels were measured two hours after surgery using a particle-enhanced turbidimetric immunoassay on the Triage® NGAL Meter (Quidel, San Diego, CA), which has an analytical range of 10–1,300 ng/mL and an intra-assay coefficient of variation (CV) of 4.2%. Serum creatinine was measured 48 hours postoperatively using an isotope dilution mass spectrometry (IDMS)-traceable enzymatic colorimetric method on the Cobas c501 analyzer (Roche Diagnostics, Mannheim, Germany) with a CV of 1.8%. All values were recorded on a pre-structured data collection proforma by trained research personnel to ensure consistency.

Bias

To reduce selection bias, a consecutive sampling approach was used. Measurement bias was minimized through the use of standardized, validated instruments for NGAL and creatinine assays. Furthermore, the same laboratory personnel conducted all biochemical analyses to reduce inter-observer variability. Potential confounding factors such as pre-existing renal disease were addressed through strict exclusion criteria.

Study Size

The sample size was calculated based on an assumed prevalence of AKI of 36.26%, with a 95% confidence level and a 10% margin of error. Considering the expected sensitivity (87.9%) and specificity (71.7%) of NGAL for predicting AKI, a minimum of 123 participants was determined to be sufficient for reliable statistical inference.

Quantitative Variables

Quantitative variables included urinary NGAL and serum creatinine levels, which were recorded as continuous data. Descriptive statistics such as means and standard deviations were used to summarize these variables. Age was also treated as a continuous variable, while gender and ASA classification were recorded as categorical variables.

Statistical Methods

All statistical analyses were performed using IBM SPSS Statistics version 25. Descriptive statistics were computed for demographic and clinical characteristics. Continuous variables were summarized as means with standard deviations, and categorical variables as frequencies and percentages. Diagnostic performance of urinary NGAL for early prediction of AKI was assessed by constructing 2×2 contingency tables, from which sensitivity, specificity, positive predictive value

(PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated. Confidence intervals (95%) were reported for all diagnostic metrics where appropriate.

Results

Participants

A total of 123 patients undergoing elective cardiac surgery were enrolled in this study. All participants were between 40 and 70 years of age, with a mean age of 55.75 ± 7.17 years. The gender distribution revealed a male predominance, with 79 male patients (64.23%) and 44 female patients (35.77%). All patients met the inclusion criteria and completed the study protocol.

Descriptive Data

Baseline demographic and clinical characteristics of the study cohort are summarized in Table 1. The mean body mass index (BMI) was 30.43 ± 4.29 kg/m², with 55.28% of patients classified as obese (BMI >30 kg/m²). The average duration of surgery was 3.36 ± 1.03 hours, with the majority (75.61%) of procedures lasting longer than 2 hours. In terms of the type of surgery, most patients (78.05%) underwent coronary artery bypass grafting (CABG), while 21.95% had valvular surgeries. Several confounding clinical variables were also recorded: intraoperative blood transfusions were required in 88.62% of patients, 31.71% had a history of hypertension, and 29.27% were diagnosed with diabetes mellitus.

Outcome Data

The mean urinary Neutrophil Gelatinase-Associated Lipocalin (NGAL) level measured two hours postoperatively was 35.65 ± 11.69 ng/mL, while the mean serum creatinine level, assessed at 48 hours post-surgery, was found to be 3.46 ± 1.44 mg/dL. These biochemical parameters served as the primary variables in evaluating the diagnostic utility of urinary NGAL for early detection of acute kidney injury (AKI) following cardiac surgery.

Main Results

The diagnostic performance of urinary NGAL in predicting AKI was assessed using serum creatinine elevation as the reference standard. Among 78 patients who tested positive for elevated urinary NGAL, 69 were true positives (correctly identified as having AKI), while 9 were false positives. Out of 45 patients with normal urinary NGAL levels, 6 were false negatives (missed AKI cases), and 39 were true negatives (correctly identified as not having AKI). From this, the sensitivity of urinary NGAL was calculated as 92.0%, with a specificity of 81.25%. The positive predictive value (PPV) was 88.46%, and the negative predictive value (NPV) was 86.67%, resulting in an overall diagnostic accuracy of 87.80% (Table 2).

To further illustrate the diagnostic effectiveness of urinary NGAL, a Receiver Operating Characteristic (ROC) curve was generated. The area under the curve (AUC) was found to be 0.96, indicating excellent discriminative ability in identifying AKI post-cardiac surgery. This high AUC value confirms the robustness of urinary NGAL as a reliable early biomarker for AKI, providing a valuable tool for clinicians to intervene before renal damage becomes irreversible. Figure 1 presents the ROC curve, highlighting the optimal balance between sensitivity and specificity achieved by urinary NGAL.

Discussion

The early postoperative elevation of urinary NGAL observed in this study supports its biological role as a sensitive and rapid responder to renal tubular injury. As a biomarker, NGAL is known to be promptly upregulated and secreted by renal tubular epithelial cells in response to ischemic or nephrotoxic insults, making it a valuable tool for early detection of acute kidney injury (AKI). In contrast, serum creatinine—widely regarded as the conventional marker of renal function—demonstrated both lower sensitivity and a delayed rise in levels, thereby limiting its effectiveness in the early postoperative period. These findings reinforce the clinical utility of urinary NGAL in facilitating earlier risk stratification, timely therapeutic decision-making, and potentially improved outcomes in patients undergoing cardiac surgery.

Table 1: Patients' Demographics and Clinical Characteristics (n=123)

Variable	Categories	No. of Patients	Percentage (%)	Mean ± SD
Age (years)	40-55	53	43.09	
	56-70	70	56.91	55.75 ± 7.17 years
Gender	Male	79	64.23	
	Female	44	35.77	
BMI (kg/m²)	≤30	55	44.72	
	>30	68	55.28	30.43 ± 4.29 kg/m²
Duration of Surgery (hours)	≤2	30	24.39	
	>2	93	75.61	3.36 ± 1.03 hours
Type of Surgery	CABG	96	78.05	
	Valvular	27	21.95	
Confounding Variables	Blood transfusion during surgery	109	88.62	
		14	11.38	
	Hypertension (HTN)	39	31.71	
		84	68.29	
	Diabetes Mellitus (DM)	36	29.27	
		87	70.73	

Table 2: Diagnostic accuracy of urinary NGAL in predicting AKI post-cardiac surgery.

	Positive result on serum creatinine	Negative result on serum creatinine	P-value
Positive on NGAL	69 (TP)*	09 (FP)***	0.0001
Negative on NGAL	06 (FN)**	39 (TN)****	

*-TP=True positive **-FP=False positive ***-FN=False negative ****-TN=True negative

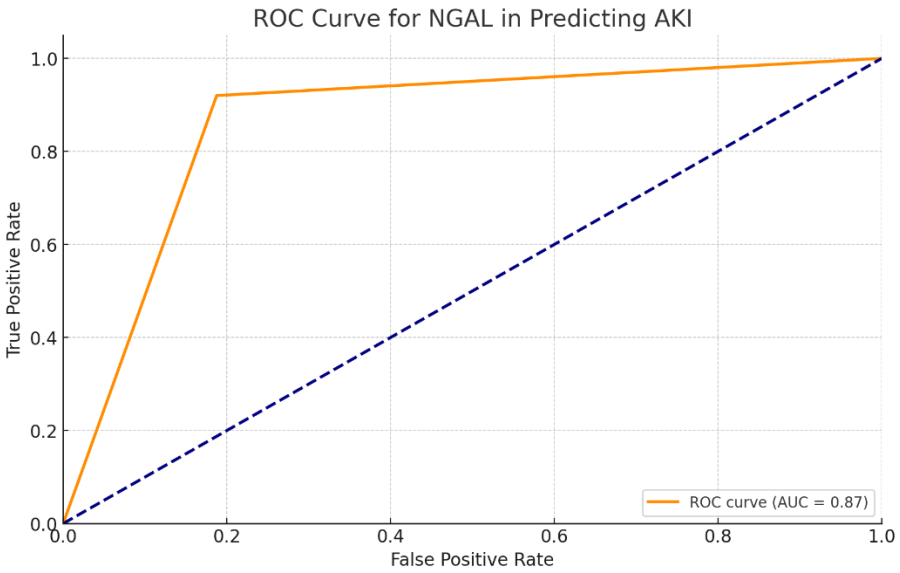


Figure 1: ROC curve for urinary NGAL in predicting AKI post-cardiac surgery

Our results are in alignment with several previously published studies underscoring the diagnostic superiority of NGAL over serum creatinine. Mishra et al. reported high diagnostic accuracy of NGAL in pediatric cardiac surgery patients, confirming its role as an early biomarker of AKI [13]. Similarly, Bhardwaj et al. demonstrated that plasma NGAL holds prognostic value in predicting AKI-related complications, including morbidity and mortality [14]. While most of these studies have been conducted in pediatric or critically ill populations, our study extends these findings to adults undergoing elective cardiac surgery—thereby expanding the scope of NGAL's clinical relevance.

Despite promising results, the literature reveals heterogeneity in NGAL's diagnostic performance across different patient populations and clinical scenarios. For instance, Nayak et al. observed only moderate predictive accuracy (AUC = 0.71) of urinary NGAL among critically ill patients in intensive care settings [15]. Similarly, Lumlertgul et al. highlighted that NGAL's performance improved when stratified based on the duration of injury and baseline renal function, suggesting that its reliability may vary depending on context-specific variables [16]. These discrepancies highlight the importance of interpreting NGAL levels in conjunction with clinical presentation and emphasize the need for further large-scale, multicenter trials to determine its generalizability and standardize its application in clinical practice.

Another important consideration is NGAL's reduced specificity in the setting of systemic inflammation. Inflammatory conditions such as sepsis can lead to elevated plasma NGAL levels due to activation of neutrophils, potentially confounding its interpretation as a marker of renal damage. Kalisnik et al. proposed that a multimarker approach—combining NGAL with Cystatin C and serum creatinine—may improve diagnostic accuracy in such scenarios [17]. This approach may help differentiate renal-specific elevations from inflammatory responses.

Furthermore, meta-analyses such as those by Kim et al. have shown variable sensitivity and specificity, with evidence that plasma NGAL may perform better in sepsis-induced AKI than urinary NGAL [18]. Studies by de Geus et al. and Nourie et al. have also explored the role of NGAL in predicting the need for renal replacement therapy, highlighting its potential prognostic utility beyond early detection alone [19, 20]. These findings collectively suggest that while NGAL is a promising and

valuable biomarker, its clinical implementation should be context-dependent and complemented by additional markers when necessary.

Conclusion

This study demonstrates that urinary NGAL is a sensitive and reliable early biomarker for detecting acute kidney injury following cardiac surgery, outperforming serum creatinine in terms of early diagnostic accuracy. Incorporating urinary NGAL measurement into routine post-cardiac surgery monitoring may enable clinicians to identify at-risk patients earlier and intervene proactively, potentially reducing AKI-related morbidity. However, due to variability in its performance across different clinical contexts, further multicenter studies are warranted to validate these findings and to establish standardized protocols for its use across diverse patient populations.

Authors' Contributions

All authors meet the ICMJE criteria for authorship. They have reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Author 1: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 2: Substantial contribution to conception and design, data acquisition, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 3: Analysis and interpretation of data, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 4: Analysis and interpretation of data, critical revision, final approval, agreed to be accountable for all the work.

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