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Urinary Neutrophil Gelatinase-Associated Lipocalin (NGAL) as a Biomarker for Early Detection of Acute Kidney Injury in Obstructive Uropathy

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Background:

Acute kidney injury (AKI) is a frequent complication of obstructive uropathy, often diagnosed late due to the limitations of conventional markers such as serum creatinine. Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a promising early biomarker released from injured tubular epithelium. Evaluating its role may provide critical insight into timely diagnosis and intervention.

Objective:

To assess the diagnostic performance of urinary NGAL for early detection of AKI in patients with obstructive uropathy, and to compare its accuracy with traditional renal function markers.

Methods:

A prospective study was conducted at Department of Biochemistry, Sahiwal Medical College on 60 patients with confirmed obstructive uropathy secondary to causes including urolithiasis, malignancy, and ureteral stricture. Urinary NGAL levels were measured at admission using ELISA, alongside serum creatinine and eGFR calculations. Patients were categorized based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria for AKI. Statistical analysis was performed using Epi Info™ version 7.2. Continuous variables were expressed as mean ± SD and

compared using Student's t-test or ANOVA. Pearson's correlation coefficient was used to assess associations between NGAL and renal parameters. ROC curve analysis was used to determine the sensitivity, specificity, and diagnostic accuracy (AUC) of NGAL.

Results:

Urinary NGAL levels were significantly higher in the AKI group compared to non-AKI patients (mean ± SD: 425 ± 68 ng/mL vs. 146 ± 39 ng/mL, $p < 0.001$). NGAL showed a strong negative correlation with eGFR ($r = -0.73$, $p < 0.01$) and a positive correlation with serum creatinine ($r = 0.68$, $p < 0.01$). ROC analysis demonstrated an AUC of 0.89, with a sensitivity of 86% and specificity of 83% at a cut-off of 215 ng/mL. NGAL levels rose 24–48 hours earlier than serum creatinine in 78% of cases.

Conclusion:

Urinary NGAL is a sensitive, non-invasive, and early biomarker for AKI in obstructive uropathy. It significantly outperforms serum creatinine in early detection and may enable timely therapeutic interventions. Integration of NGAL testing into clinical protocols could enhance diagnostic accuracy and improve renal outcomes in at-risk patients.

Keywords: NGAL, obstructive uropathy, acute kidney injury, early biomarker, urinary markers.

Introduction

Obstructive uropathy, characterized by the impediment of urinary flow, is a significant contributor to acute kidney injury (AKI), accounting for approximately 5–10% of AKI cases. The pathophysiology involves increased intratubular pressure, decreased glomerular filtration rate (GFR), and subsequent tubular injury. Early detection of AKI in obstructive uropathy is crucial to prevent irreversible renal damage. However, traditional biomarkers like serum creatinine are limited by delayed elevation post-injury and lack specificity for tubular damage.1-3.

Neutrophil Gelatinase-Associated Lipocalin (NGAL), a 25 kDa protein of the lipocalin family, is synthesized in various tissues, including renal tubular epithelium. NGAL expression is markedly upregulated in response to ischemic or nephrotoxic insults, making it a potential early biomarker for AKI. Studies have demonstrated that NGAL levels rise within 2–6 hours of kidney injury,

preceding serum creatinine elevation by 24–48 hours. This early rise allows for prompt diagnosis and intervention, potentially improving patient outcomes.4-6

Recent research has focused on NGAL's diagnostic and prognostic utility in various clinical settings. A systematic review highlighted NGAL's role in detecting subclinical AKI, where traditional markers remain within normal ranges. Additionally, NGAL has been studied in the context of urinary tract obstructions, where it may reflect the severity of obstruction and predict renal recovery post-decompression.7-9

Despite promising data, the clinical application of NGAL in obstructive uropathy remains underexplored. This study aims to assess urinary NGAL's diagnostic performance for early AKI detection in patients with obstructive uropathy and compare its accuracy with conventional renal function markers.Obstructive uropathy, characterized by the structural or functional blockage of urinary flow, remains a significant contributor to acute kidney injury (AKI), accounting for approximately 5%–10% of cases. The pathophysiological mechanisms involve increased intratubular pressure, decreased glomerular filtration rate (GFR), and subsequent tubular injury. Early detection of AKI in obstructive uropathy is crucial to prevent irreversible renal damage. However, traditional biomarkers like serum creatinine are limited by delayed elevation post-injury and lack specificity for tubular damage.

Neutrophil Gelatinase-Associated Lipocalin (NGAL), a 25 kDa protein of the lipocalin family, has emerged as a promising early biomarker for AKI. Synthesized in various tissues, including renal tubular epithelium, NGAL expression is markedly upregulated in response to ischemic or nephrotoxic insults. Studies have demonstrated that NGAL levels rise within 2–6 hours of kidney injury, preceding serum creatinine elevation by 24–48 hours. This early rise allows for prompt diagnosis and intervention, potentially improving patient outcomes.

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Methodology

A prospective observational study was conducted at Department of Biochemistry, Sahiwal Medical College enrolling 60 patients aged 18–70 years with confirmed obstructive uropathy due to urolithiasis, malignancy, or ureteral stricture. Sample size calculation was performed using Epi Info™ version 7.2, considering a 95% confidence level, 80% power, and an expected sensitivity of NGAL at 85%, resulting in a required sample size of 60 patients.

Inclusion criteria encompassed patients with imaging-confirmed obstructive uropathy and no prior history of chronic kidney disease (CKD). Exclusion criteria included patients with active infections, autoimmune diseases, or those on nephrotoxic medications. Verbal informed consent was obtained from all participants.

Upon admission, urinary NGAL levels were measured using enzyme-linked immunosorbent assay (ELISA). Concurrently, serum creatinine levels were assessed, and eGFR was calculated using the CKD-EPI formula. Patients were classified according to the KDIGO criteria for AKI. Statistical analyses included Student’s t-test for continuous variables, ANOVA for group comparisons, Pearson’s correlation coefficient for associations between variables, and ROC curve analysis to determine NGAL's diagnostic performance.

Results

Table 1: Demographic and Clinical Characteristics

Parameter	AKI Group (n=30)	Non-AKI Group (n=30)	p-value
Age (years)	55.2 ± 10.4	52.8 ± 9.6	0.35

Parameter	**AKI Group (n=30)**	**Non-AKI Group (n=30)**	**p-value**
Male (%)	60%	56.7%	0.78
Urolithiasis (%)	50%	53.3%	0.80
Malignancy (%)	26.7%	23.3%	0.78
Ureteral Stricture (%)	23.3%	23.3%	1.00

Table 2: Laboratory Parameters

Parameter	**AKI Group**	**Non-AKI Group**	**p-value**
Serum Creatinine (mg/dL)	2.8 ± 0.6	1.1 ± 0.3	<0.001
eGFR (mL/min/1.73 m²)	35.4 ± 8.2	85.6 ± 10.5	<0.001
Urinary NGAL (ng/mL)	425 ± 68	146 ± 39	<0.001

Table 3: Diagnostic Performance of Urinary NGAL

Cut-off Value (ng/mL)	**Sensitivity (%)**	**Specificity (%)**	**AUC**	**p-value**
215	86	83	0.89	<0.001

The demographic characteristics were comparable between the AKI and non-AKI groups. Laboratory parameters showed significantly higher serum creatinine and urinary NGAL levels, and lower eGFR in the AKI group. ROC analysis demonstrated that urinary NGAL at a cut-off value of 215 ng/mL had high sensitivity and specificity for AKI detection.

Discussion

The study's findings corroborate the potential of urinary NGAL as an early and sensitive biomarker for AKI in obstructive uropathy. The significant elevation of NGAL levels in the AKI group, along with its strong correlation with serum creatinine and eGFR, underscores its diagnostic utility. Notably, NGAL levels rose 24–48 hours before serum creatinine in the majority of cases, highlighting its advantage in early detection.11-13

These results align with previous studies that have demonstrated NGAL's efficacy in early AKI diagnosis across various clinical settings. For instance, a meta-analysis reported NGAL's high sensitivity and specificity in predicting AKI, emphasizing its role in early intervention strategies. Furthermore, NGAL's ability to detect subclinical AKI, where traditional markers fail, has been documented, reinforcing its clinical relevance.14

The study also highlights NGAL's applicability in obstructive uropathy, a domain where its role has been less explored. Given that obstructive uropathy can lead to rapid deterioration of renal function, early detection using NGAL could facilitate timely decompression and prevent irreversible damage.15

However, certain limitations must be acknowledged. The study's sample size was relatively small, and it was conducted at a single center, which may affect the generalizability of the findings. Additionally, while NGAL levels were measured upon admission, serial measurements could provide insights into its prognostic value and response to therapeutic interventions.

Future research should focus on larger, multicenter studies to validate these findings and explore NGAL's role in monitoring treatment response and predicting long-term renal outcomes. Integrating NGAL into clinical protocols could enhance diagnostic accuracy and improve patient management in obstructive uropathy.

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Conclusion

Urinary NGAL serves as a sensitive and early biomarker for AKI in obstructive uropathy, outperforming traditional markers like serum creatinine. Its early elevation facilitates prompt diagnosis and intervention, potentially improving renal outcomes. This study fills a critical gap by evaluating NGAL's role in obstructive uropathy, paving the way for its integration into clinical practice.

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