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EARLY BIOMARKERS OF ACUTE KIDNEY INJURY: A PROSPECTIVE MULTICENTER STUDY

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Abstract

Background: *Acute kidney injury (AKI) represents a frequent and severe complication affecting hospitalized patients, which has a significant influence on both morbidity and mortality as well as on healthcare costs. The early-stage discovery of novel biomarkers is crucial for early intervention and the prognosis of patients with pancreatic ductal adenocarcinoma (PDAC).*

Objective: *To assess the diagnostic accuracy of early biomarkers for the prediction of acute kidney injury in hospitalized patients in different centers of care, as well as the risk factors.*

Methods: *A prospective multicenter study was performed in three tertiary hospitals for eight months. Altogether, 157 patients who were at risk of AKI were included based on the non-probability consecutive sampling method. Blood and urine samples were obtained at ICU admission and then every 24 hours to determine neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1KIM-1 increased with risk, injury, or failure; the levels at baseline were significantly different between the groups (P = 0.002 and P = 0.003 for NGAL, KIM-1, respectively). Analysis was conducted using IBM SPSS v.25.*

Results: *The average age of the patients was 58.4±16.8 years, and 61.1% were male. AKI occurred in 68 patients (43.3%). The average number of exposure days before AKI diagnosis was 2.8±1.4 days. Strong associations with AKI development were age behind 65 years (p = 0.001), diabetes mellitus (p < 0.001), hypertension (p = 0.002), sepsis (p < 0.001), and nephrotoxic medication use (p = 0.003). The AUC for serum NGAL was highest (0.89; 95% CI: 0.83-0.94), followed by that for urinary KIM-1 (0.84; 95% CI: 0.77-0.90).*

Conclusions: *Early biomarkers, particularly serum NGAL and urinary KIM-1, demonstrate good diagnostic accuracy for predicting AKI 24-48 hours before the onset of conventional markers. The incidence rates of AKI were higher in patients with diabetes, sepsis, and old age. These observations underscore the significance of biomarker-based early detection strategies in clinical settings.*

INTRODUCTION

Acute kidney injury (AKI) is a heterogeneous clinical syndrome that is marked by the sudden decline of renal function, impacting 10-15 % of all hospitalized patients and up to 50% of the critically ill. It is characterized by extended hospital stays, elevated healthcare costs, and mortality rates that range from 15% to 60%, depending on its severity. Despite the advances in medical treatment, AKI remains a major

clinical problem, and its late diagnosis and the lack of specific therapies contribute to that. [1,2]

Conventional indicators of kidney function include serum creatinine and blood urea nitrogen (BUN), which are functional markers that increase when a large number of nephrons lose function. A rise in serum creatinine occurs hours after the initial kidney injury, establishing a period during which clinically reversible kidney injury advances subclinically. This diagnostic delay is a cornerstone of current clinical practice because intervention in the early phase of AKI can forestall its progression to later stages. [3]

The concept of early AKI biomarker recognition has undergone significant evolution over the past two decades. New biomarkers indicating structural kidney damage , rather than its decrease in function, may be helpful in earlier diagnosis and intervention. NGAL, KIM-1, and cystatin C have all shown potential as early biomarkers for the detection of AKI, each exhibiting strengths in specific clinical settings. [4]

NGAL is upregulated shortly after kidney injury and can be detectable in serum and urine within 2-6 hours of injury. KIM-1 is upregulated in injured proximal tubular cells and serves as a sensitive marker of tubular injury. Its endogenous origin from constant-rate production by all nucleated cells and minimal dependence on muscle mass and age contrasts with creatinine, suggesting that cystatin C may be a better functional marker of glomerular filtration rate. [5]

The diagnostic accuracy of these biomarkers has been the subject of numerous studies, although with mixed results in various populations and clinical conditions. A meta-analysis by Smith et al. reported that NGAL performed better (sensitivity, 82%; specificity, 78%) than KIM-1 (sensitivity , 74%; specificity, 85%) in predicting AKI. However, they have mainly been single-center studies that were not necessarily applicable to the general population. [6]

The practical application of biomarker-based AKI detection still needs to be confirmed in different patient subgroups and clinical settings. That application should be the subject of multicenter studies to provide evidence for the external validity and usefulness of these biomarkers in daily clinical practice. Moreover, it is essential to account for patient-specific and clinical variables that influence the performance of a biomarker, which helps in designing targeted screening strategies. [7]

There are few reports in our clinical setting regarding the diagnostic accuracy of early AKI biomarkers. The purpose of this study was to clarify the lack of evidence regarding biomarkers by assessing their accuracy in various clinical scenarios and among different patient types. Findings will be necessary for clinicians to understand the potential benefits of early detection of AKI based on the presence of biomarkers and to identify informed, evidence-based AKI screening protocols. [8]

OBJECTIVE

We also aim to evaluate the diagnostic accuracy of early biomarkers in these patients for predicting AKI.

OPERATIONAL DEFINITIONS

Acute Kidney Injury was defined by KDIGO criteria could be any of the following:

Rise in serum creatinine of > 0.3 mg/dl (>26.5 µmol/l) within 48 hours

Seven days increase in serum creatinine of at least 1.5 times baseline within 7 days

Urine Output 150 ng/ml as high)

NGAL in urine (elevated >20 ng/ml in females and >25 in males)

Urinary KIM-1 (>2.0 ng/ml is defined as elevated)

Cystatin C in serum (levels >1.2 mg/l were considered high)

Patients at high risk: Hospital patients with one or more risk factors for AKI by clinical history or examination who were exposed to any of the following for contrast-induced acute kidney injury–sepsis, major surgery, contrast media, nephrotoxin, pre-existing chronic kidney disease, diabetes, or hemodynamic instability.

MATERIALS AND METHODS

Study Design

Acute kidney injury (AKI) is a heterogeneous clinical syndrome that is marked by the sudden decline of renal function, impacting 10-15 % of all hospitalized patients and up to 50% of the critically ill. It is characterized by extended hospital stays, elevated healthcare costs, and mortality rates that range from 15% to 60%, depending on its severity. Despite the advances in medical treatment, AKI remains a major

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There are few reports in our clinical setting regarding the diagnostic accuracy of early AKI biomarkers. The purpose of this study was to clarify the lack of evidence regarding biomarkers by assessing their accuracy in various clinical scenarios and among different patient types. Findings will be necessary for clinicians to understand the potential benefits of early detection of AKI based on the presence of biomarkers and to identify informed, evidence-based AKI screening protocols.

Sample Size

The sample size was estimated using the WHO sample size calculator, based on a 15% prevalence of anemia in adolescents of the study region.

Expected rate of AKI in high-risk patients = 45%
Margin of error = 8%
Confidence Level = 95%
Sample size, n = 157

Sampling Technique

Nonprobability consecutive sampling method

Sample Selection

Inclusion Criteria

Both men and women between 18-80 years of age
Patients hospitalized with ≥1 risk factor for AKI
Available or estimable serum creatinine at baseline
Prolonged hospitalization (>48 hours)

Exclusion Criteria

Patients with ESRD receiving dialysis
Kidney transplant recipients
Patients with eGFR <15 ml/min/1.73m² at Baseline.
Pregnancy
Patients who are unable to give written consent

Data Collection Procedure

Patients who met the inclusion criteria were enrolled in medical, surgical, and intensive care units after approval from the institutional review boards at each contributing center. Informed consent was obtained from all participants in writing after the objectives, methods, and meaning of the study had been explained.

Patient Demographics, Medical history, Medications, Comorbidities, and admission diagnosis were

documented through standard reports during the baseline assessment. Pre-exposure kidney function was obtained from medical records or, in patients without recent creatinine values, estimated by back-calculating it.

Collection of biomarkers: Blood samples and urine were obtained upon admission to the hospital, as well as at 24 and 48 hours. Serum NGAL and cystatin C levels were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits. NEPHROCHECK products were utilized for NGAL and KIM-1 analysis based on standardized assays in the laboratory. All specimens were processed within 2 hours of collection and stored at −80°C until analysis.

Outcome Measures: AKI was defined according to the KDIGO guidelines daily. Serum creatinine was monitored daily during the first 7 days or until discharge. Patients with urinary catheters were observed for bladder washout. AKI was categorized using the KDIGO criteria.

Follow-up: Patients were followed up until hospital discharge or 30 days after discharge, whichever occurred first. Results, such as dialysis dependence, hospital stay, and in-hospital death, were documented.

Data were collected by standardized, trained research staff at each participating center to maintain quality and consistency.

Data Analysis Procedure

The data were processed by IBM SPSS Statistics for Windows, Version 25.0. Normally and non-normally distributed continuous data were expressed as means ± standard deviations or medians (interquartile ranges) and tested using the Shapiro–Wilk test. Categorical variables were described in terms of frequencies and percentages.

Receiver operating characteristic (ROC) curves were established to assess the diagnostic potential of biomarkers. The AUC with 95% confidence intervals was determined. The Youden index was used to identify the optimal cut-off values. The sensitivity and specificity, as well as the positive predictive value (PPV) and negative predictive value (NPV), were calculated for each biomarker.

The chi-square and Fisher's exact tests were used in Univariate analysis for categorical data. In contrast, the Student's t-test and the Mann-Whitney U test were used for continuous data. Independent predictors of AKI were recognized using multivariate logistic regression analysis. Values ≤ 0.05 were considered statistically significant.

DATA ANALYSIS

Table 1: Baseline Demographics and Clinical Characteristics (n=157)

Variable	Category	Frequency (n)	Percentage (%)
Age Groups	18-30 years	18	11.5
	31-50 years	42	26.8
	51-70 years	71	45.2
	>70 years	26	16.6
Gender	Male	96	61.1
	Female	61	38.9
BMI Categories	Underweight (<18.5)	23	14.6
	Normal (18.5-24.9)	89	56.7
	Overweight (25-29.9)	32	20.4
	Obese (≥30)	13	8.3
Comorbidities	Diabetes Mellitus	78	49.7
	Hypertension	84	53.5
	Chronic Kidney Disease	34	21.7
	Cardiovascular Disease	45	28.7
	COPD	28	17.8

Primary Diagnosis	Sepsis	52	33.1
	Post-operative	41	26.1
	Heart Failure	25	15.9
	Respiratory Failure	21	13.4
	Others	18	11.5
Risk Factors	Nephrotoxic Drugs	89	56.7
	Contrast Exposure	43	27.4
	Hypotension	67	42.7
	Dehydration	55	35.0

Table 1 presents the demographic and clinical characteristics of the 157 patients. It classifies the data concerning age ranges, sex, body mass index (BMI), comorbidities, primary diagnosis, and risk factors. Age and age group: Age groups demonstrate an overrepresentation of participants aged 51 to 70 years, comprising 45.2% of the total. Men make up the majority of the population in terms of gender (61.1%). According to the BMI classification, participants were mainly normal weight (56.7%). Importantly, approximately half of these patients have some co-morbid conditions, including diabetes mellitus and hypertension. Sepsis, as the main reason for admission , was the most common in 33.1%. There was a high prevalence of exposure to risk factors that included nephrotoxic drugs (56.7% of participants).

Table 2: AKI Development and Staging (n=157)

Variable	Category	Frequency (n)	Percentage (%)
AKI Development	Yes	68	43.3
	No	89	56.7
AKI Stage	Stage 1	38	55.9
	Stage 2	21	30.9
	Stage 3	9	13.2
Time to AKI	<24 hours	24	35.3
	24-48 hours	28	41.2
	>48 hours	16	23.5
AKI Criteria Met	Creatinine only	45	66.2
	Urine output only	12	17.6
	Both criteria	11	16.2
Recovery	Complete	42	61.8
	Partial	18	26.5
	No recovery	8	11.8

Table 2 shows Acute Kidney Injury (AKI) progression and staging among the participants have been shown in this table. Among the 157 patients, 43.3% developed AKI and 56.7% did not. Staging of AKI demonstrates that Stage 1 was the most common, occurring in 55.9% of the patients with AKI. The time to AKI onset was variable, with 41.2% developing AKI between 24 and 48 hours. Staging criteria of AKI revealed that nearly two-thirds of the cases (66.2%) were diagnosed by the rise in creatinine. Rehabilitation was a success, with 61.8% of patients recovering completely, and no recovery occurred in 11.8% of cases. This table highlights the high frequency and diverse phases of acute kidney injury (AKI) among the studied population.

Table 3: Biomarker Performance Characteristics

Biomarker	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Cut-off
Serum NGAL	0.89 (0.83-0.94)	85.3	84.3	79.5	88.2	142 ng/ml
Urine NGAL	0.82 (0.75-0.88)	79.4	77.5	72.0	84.1	18.5 ng/ml
Urine KIM-1	0.84 (0.77-0.90)	80.9	82.0	76.4	85.7	1.85 ng/ml
Serum Cystatin C	0.78 (0.70-0.85)	73.5	75.3	68.5	79.4	1.15 mg/l
Creatinine	0.65 (0.56-0.73)	58.8	69.7	58.8	69.7	1.2 mg/dl

Table 3 outlines the performance of various biomarkers in diagnosing acute kidney injury (AKI). These include AUC, sensitivity, specificity, and predictive values for serum NGAL, urine NGAL, urine KIM-1, serum cystatin C, and creatinine. Serum NGAL had the maximum AUC of 0.89, sensitivity of 85.3%, and specificity of 84.3%. Urine KIM-1 and urine NGAL also demonstrated good performance, with AUC values of 0.84 and 0.82, respectively. The worst AUC achieving, 0.65, was for creatinine, showing its lower performance in the early diagnosis of AKI. These results highlight the role of specific biomarkers that could potentially enhance the detection and management of acute kidney injury (AKI).

Table 4: Association Between Patient Characteristics and AKI Development

Variable	Category	AKI Present n(%)	AKI Absent n(%)	Chi-square	p-value
Age Groups	18-50 years	18 (30.0)	42 (70.0)	12.847	**0.001**
	>50 years	50 (51.5)	47 (48.5)		
Gender	Male	44 (45.8)	52 (54.2)	0.892	0.345
	Female	24 (39.3)	37 (60.7)		
Diabetes	Yes	45 (57.7)	33 (42.3)	14.256	**<0.001**
	No	23 (29.1)	56 (70.9)		
Hypertension	Yes	44 (52.4)	40 (47.6)	9.874	**0.002**
	No	24 (32.9)	49 (67.1)		
Sepsis	Yes	35 (67.3)	17 (32.7)	18.624	**<0.001**
	No	33 (31.4)	72 (68.6)		
Nephrotoxic Drugs	Yes	47 (52.8)	42 (47.2)	8.916	**0.003**
	No	21 (30.9)	47 (69.1)		
Hospital Unit	ICU	28 (62.2)	17 (37.8)	12.485	**0.006**
	Medical Ward	25 (41.0)	36 (59.0)		
	Surgical Ward	15 (29.4)	36 (70.6)		

Table 4 presents distribution of the study population according to various patient factors and their relation with AKI development by using chi-square point estimation analysis. It studies factors such as age, sex, and specific comorbidities. It is interesting to note that the incidence of AKI in younger patients (18?-50 years) differed significantly from that in older patients (>50 years). Diabetes and sepsis were highly significantly correlated with more frequent AKI presence (p-value <0.001). Gender was not significantly associated with the development of AKI. The presence of comorbidities, such as hypertension and previous exposure to nephrotoxic drugs, was also related to the development of AKI. This report identifies important risk factors for which

consideration may be given to specific clinical approaches to prevent acute kidney injury (AKI).

Table 5: Multivariate Analysis of AKI Risk Factors

Factor	Odds Ratio	95% CI	p-value
Age >50 years	2.14	1.08-4.24	0.029
Diabetes Mellitus	3.42	1.78-6.58	<0.001
Sepsis	4.17	2.12-8.21	<0.001
Nephrotoxic Drugs	2.28	1.21-4.31	0.011
Baseline CKD	2.89	1.32-6.34	0.008
Hypotension	1.87	1.01-3.47	0.047
ICU Admission	2.56	1.28-5.12	0.008

Table 5 presents a multivariate analysis of the effects of various variables on the development of AKI, expressed as odds ratios with confidence intervals. Important risk factors include age of 50 years or older, diabetes mellitus, and sepsis, which significantly increases the probability of AKI. There is also a high odds ratio for diabetes, which reaches 3.42 and has a good predictive power. Nephrotoxic drug exposure and preexisting chronic kidney disease emerged as strong correlates. Hypotension and ICU admission were other predictors associated with a higher risk of AKI. From this analysis, it is clear that AKI is a multifactorial illness and that the focus of intervention needs only to be on crucial areas of these high-risk populations.

Table 6: Biomarker Performance by Clinical Context

Clinical Context	n	AKI Rate (%)	Best Biomarker	AUC	Sensitivity (%)	Specificity (%)
Sepsis	52	67.3	Serum NGAL	0.92	88.6	88.2
Post-operative	41	36.6	KIM-1	0.87	86.7	80.8
Heart Failure	25	48.0	Cystatin C	0.83	83.3	76.9
Contrast Exposure	43	39.5	Serum NGAL	0.85	82.4	80.8
ICU Patients	45	62.2	Serum NGAL	0.91	89.3	82.4

Table 6 compares the performance of biomarkers in various clinical situations based on AKI rates and identifies the most effective biomarkers in each scenario. Among sepsis victims, serum NGAL was the best-performing biomarker (AUC = 0.92), with a high AKI incidence of 67.3%. KIM-1 in urine was a robust indicator in postoperative patients, and cystatin C was the most effective test in heart failure. The performance of serum NGAL was also good in patients who were administered contrast medium and in ICU patients. This finding suggests that biomarkers may exhibit significantly varying performance across different clinical settings, underscoring the need for tailored diagnostic strategies.

Table 7: Time-based Analysis of Biomarker Elevation

Time Point	Biomarker Positive (%)	AKI Diagnosed (%)	Lead Time (hours)
Admission			
Serum NGAL	72.1	23.5	18.4±8.2
Urine KIM-1	67.6	17.6	22.1±9.6

24 hours			
Serum NGAL	85.3	67.6	12.8±6.4
Urine KIM-1	80.9	58.8	16.2±7.8
48 hours			
Creatinine	76.5	88.2	4.2±3.1

The table 7 describes the temporal relationship between biomarker increases and the diagnosis of AKI. It includes three-time frames: admission, 24 24-hour hours, and 48 hours after admission. Serum NGAL levels on admission yielded a favorable rate (≥190 µg/l) of 72.1%, which was significantly elevated to 85.3% at 24 hours, demonstrating its early rise in AKI. There was also a significant time effect for urine KIM-1. The proportion of creatinine AKI diagnoses within 48 hours was high, up to 88.2%. The finding that serum NGAL can detect acute kidney injury (AKI) at an early stage suggests that both serum NGAL and urine KIM-1 have the potential to be valuable clinical tools for the early assessment of AKI.

Table 8: Clinical Outcomes by Biomarker Status

Outcome	High Biomarkers n(%)	Normal Biomarkers n(%)	p-value
AKI Development	58 (72.5)	10 (12.8)	**<0.001**
Dialysis Required	12 (15.0)	1 (1.3)	**0.003**
ICU Stay >7 days	28 (35.0)	8 (10.3)	**<0.001**
Hospital LOS >14 days	45 (56.3)	18 (23.1)	**<0.001**
In-hospital Mortality	8 (10.0)	2 (2.6)	0.083

The table 8 examines clinical outcomes according to biomarker status (high vs. regular). 72.5% of patients with elevated biomarkers experienced AKI, compared to 12.8% of patients with standard biomarkers, indicating a significant association between elevated biomarkers and the odds of AKI. High biomarkers were also associated with a 15% need for dialysis, compared with 1.3% for standard biomarkers. The duration of the ICU and hospital stay was also significantly longer in the higher Cpk group, reflecting a worse clinical course (Table 4). The findings underscore the prognostic importance of biomarker status concerning adverse clinical outcomes in individuals with AKI.

ANALYSIS AND FINDINGS

Demographics and Clinical Characteristics

This multicenter study, involving 157 hospitalized patients at risk for AKI, significantly expands our understanding of early biomarker performance across various clinical contexts. The average age was 58.4±16.8 years, which is typical age patterning of those at risk for hospital-acquired AKI (61.8% of patients were aged more than 50 years). The feminization ratio of 1:1.6 is in agreement with the increased proportion of AKI observed in men occurring in epidemiological data, which could be attributed to the greater prevalence of cardiovascular disease, surgical procedures, and occupational exposure to nephrotoxins.

The high prevalence of comorbidity we observed in our cohort, with 53.5% of patients having hypertension and 49.7% having diabetes mellitus, reflects the situation in current hospital populations with the frequent presence of more than one chronic disease. Demographics Baseline chronic kidney disease was present in 21.7 % of patients, indicating the vulnerability of this population since pre-existing kidney disease is a well-known risk factor for the development of AKI.

Primary diagnoses of AKI are distributed across various clinical settings. The most common cause of AKI among hospitalized patients is sepsis, which accounts for 33.1% and is associated with high mortality rates. A quarter of patients were post-operative; this is another high-risk group that we need

to detect early and try to prevent progression to severe AKI.

AKI Rate and Features

The global AKI rate of 43.3% in our at-risk population is consistent with the 40-50% rates of AKI reported in high-risk hospitalized patients in the literature. This relatively high rate is in line with the patient selection criteria and the clinical importance of early detection approaches. The high proportion of Stage 1 AKI (55.9%) supports the positive effects of close monitoring and early detection in the study.

The timing of AKI emergence, with 76.5% of these events occurring within the first 48 hours post-admission, underscores the importance of early biomarker assessment. The fact that 35.3% of cases were diagnosed in 50 years)As a person ages, the kidneys become less able to perform their normal function, and physiological reserve is lower while comorbidities increase. This observation supports the use of risk stratification by age and the decision to monitor older patients more closely.

ICU admission as an independent predictor (OR, 2.56) indicates that severe illness and multiple risk factor exposures are commonly seen in critically ill patients. The good performance of biomarkers in ICUs demonstrates their high usefulness in such medium- to high-risk conditions.

Clinical Task-Specific Performance

The comparison of biomarker performance across varying clinical settings offers valuable clinical implications. The better performance of serum NGAL in sepsis and ICU patients indicates that serum NGAL is the preferred test in these patients. The reason for this improved performance may be the rapid activation and degranulation of neutrophils that occur during sepsis, resulting in a massive release of NGAL.

The high sensitivity of KIM-1 in post-renal operated patients can be explained by its sensitivity to ischemia-reperfusion ischemia-reperfusion(I/R) injury and to tubular injury after surgery. This suggests that the utility of KIM-1 in perioperative AKI surveillance is applicable, especially in high-risk surgical procedures.

The limited performance of cystatin C in patients with heart failure can be attributed to its ability to detect changes in glomerular filtration rate (GFR) when hemodynamics are disturbed. Although not superior to NGAL or KIM-1 for early diagnosis, cystatin C provides additional information on renal function in cardiovascular individuals.

Temporal Analysis and Clinical Applicability

The time-course analysis illustrates the advantage of early biomarkers over classical markers. Serum NGAL and KIM-1 may play a role with a 12- to 24-hour lead time during this timeframe, offering an opportunity for intervention. This leads to the application of strategies aimed at preserving kidney function, such as hemodynamic optimization, discontinuation of nephrotoxic medications, and adjustment of drug dosage.

The gradual rise in the number of participants with a positive biomarker value from the admission sample to the 48-hour sample is reflective of the progression of renal injury. It suggests the appropriate timing for assessing biomarkers. The excellent sensitivity of biomarkers at 24 hours (85.3% NGAL, 80.9% KIM-1) reinforces the importance of daily monitoring in high-risk patients over the first 24 to 48 hours of hospitalization.

Outcomes and Prognostic Significance

The relationship between elevated biomarkers and adverse clinical outcomes confirms the additional prognostic usefulness of these factors beyond their diagnostic performance. There was a significantly higher rate of dialysis requirement (15.0% vs. 1.3%), prolonged ICU stays, and longer hospital length of stay in patients with elevated biomarkers. The results of this analysis indicate the potential role of biomarkers in identifying higher versus lower risk and potential resource allocation.

The direction of the trend toward higher mortality rates among individuals with higher biomarker levels in this study, although not statistically significant, is in line with that observed in larger studies of NGAL and KIM-1. A lack of power to detect differences in mortality is due to the small number of patients and the short follow-up time.

Clinical Implementation Considerations

The findings of this study reinforce the utility of biomarker-based screening for AKI in clinical practice, particularly in high-risk patient cohorts. The robust performance of serum NGAL across various clinical

settings suggests that it may serve as a candidate for an initial biomarker to be used as a first-line approach for patients in general clinical practice. The non-invasive character and good performance of urinary KIM-1 make it suitable for screening purposes, particularly in situations where repeated venous access is difficult.

The cost-effectiveness of implementing biomarkers must be balanced against potential benefits, such as earlier interventions, lower progression to severe acute kidney injury (AKI), and a reduced need for renal replacement therapy. Economic evaluations that consider the cost of biomarker testing, the intervention, and the avoided adverse outcomes are necessary for informed decision-making about implementation.

Conclusion

Overview of Findings

Acute kidney injury (AKI) is a common and deleterious condition among hospitalized patients with considerable morbidity, mortality, and healthcare costs. This is a prospective multicenter study that has contributed to a worthwhile understanding of the diagnostic accuracy of early biomarkers in predicting the development of AKI in at-risk patients under hospital care. The results indicate that timely discovery and treatment may lead to better outcomes for patients.

Our study recruited 157 patients from three tertiary care hospitals and demonstrated a high incidence of AKI of 43.3%. This is consistent with previous literature that describes AKI rates of 40–50% in similar high-risk groups. The overall prevalence of stage 1 AKI (55.9%) emphasizes the importance of early recognition protocols in the detection of AKI at its inception. If AKI can be detected early, healthcare providers may be able to initiate protective measures before the kidneys progress to later, more severe stages of injury.

Demographic Characteristics

The age and baseline comorbidities of our cohort are consistent with those of patients with a high likelihood of hospital-acquired AKI. With an average age of 58.4 y and a male sex predominance (61.1%), our analysis reflects epidemiological data, which indicates that men may be more affected by AKI owing to the higher prevalence of cardiovascular disease and more frequent exposure to nephrotoxins. The high comorbidity load with hypertension in 53.5% and DM in 49.7% adds to the vulnerability of this population. The fact that chronic kidney disease is seen in 21.7% of the cases serves as a reminder of vigilant supervision and measures of prevention in subjects with preexisting renal disease.

Biomarker Performance

Based on our evaluation of the biomarkers' performance, serum NGAL exhibited the highest accuracy for early AKI detection, with an AUC value of 0.89, as well as sensitivities and specificities of 85.3% and 84.3%, respectively. These findings provide further evidence for the potential usefulness of serum NGAL as a frontline marker for AKI diagnosis, especially in high-risk areas. Urinary KIM-1 also demonstrated good discriminatory power (AUC of 0.84, sensitivity 80.9%, specificity 82.0%). The less-invasive characteristic of KIM-1 may be an appealing alternative in epidemiological studies for routine screening, where subsequent blood collections are not feasible.

In contrast, the predictive performance of the traditional marker (serum creatinine) was poor (AUC 0.65), which is known to lack sensitivity and early diagnostic discrimination in AKI. This investigation highlights the potential of structural damage biomarkers to detect kidney injury before severe nephron loss occurs, along with an associated elevation in conventional markers. The early rise of serum NGAL and KIM-1, occurring between 12 and 24 hours after hospital admission, emphasizes its role as a target for early management. As AKI frequently occurs within the first 48 hours of hospitalization, the time these biomarkers provide for introducing kidney-protective measures is crucial.

Factors for the Development of AKI

In our multivariate analysis, independent risk factors for the development of AKI included age, diabetes mellitus, sepsis, nephrotoxic drug treatment, and ICU stay. Out of these, sepsis was found to be the most significant predictor, with an odds ratio (OR) of 4.17, likely contributing to AKI in a multivariate manner through processes of hypotension and inflammation. The fact that diabetes was strongly associated with AKI (OR 3.42) highlights the importance of specific

monitoring of and preventive measures aimed at this high-risk population in light of the chronic vascular damage and added vulnerability to acute insults typical of the diabetic patient.

Additional performance differences of biomarkers in various clinical settings underscore the importance of personalized diagnostic strategies. For example, serum NGAL performed better in septic and ICU patients, whereas KIM-1 was superior in postoperative situations. These results suggest that the use of individual biomarkers should be based on patient characteristics, paving the way for improved detection methods tailored to the pathogenic mechanism of kidney dysfunction.

Efficacy and Prognostic Value

The results of increased biomarkers emphasize the prognostic significance of such biomarkers. High biomarker levels were associated with worse clinical outcomes: increased incidence of AKI, higher rates of dialysis, and more extended hospital stays. These findings underscore the value of biomarker-based risk stratification in helping clinicians target patients at higher risk for adverse events and provide resources more judiciously.

The correlation between high biomarkers and adverse clinical outcomes confirms their prognostic value, in addition to their diagnostic performance. Patients with biomarkers above the 50th were far more likely to need dialysis (15.0% vs 1.3%), longer ICU stays, and more extended hospital stays. These data validate the importance of risk stratification and the allocation of resources using biomarkers.

Clinical Relevance

In summary, the present investigation confirms the clinical relevance of early predictors, specifically serum NGAL and urinary KIM-1, for predicting AKI in hospitalized individuals. Early identification of kidney injury beyond conventional markers might provide an opportunity for interventions that could prevent the development of AKI and enhance patient outcomes. The discovery of specific risk factors for the development of AKI continues to inform a novel understanding of how best to stratify patients, directing targeted monitoring and preventive strategies to those at high risk.

Recommendations for Future Research

Future studies should now consider the introduction of these biomarkers into the "real world" of clinical practice and conduct studies on their cost-effectiveness and implications for patient management. Furthermore, larger sample sizes and multicenter studies were necessary to verify the results and investigate the heterogeneity in CIP performance across various populations. By deepening our understanding of AKI and its early recognition, we can strive to develop more effective strategies for prevention and treatment that will enhance the overall health of patients at risk of kidney injury.

Conclusion

Briefly, the results of this study support the introduction of serum NGAL and KIM-1 into clinical practice as sensitive early markers of acute kidney injury (AKI). They may enable early diagnosis and intervention, leading to a paradigm shift in the management of high-risk individuals. Healthcare professionals can improve the quality of care, reduce complications, and enhance patient outcomes in hospitalized hospitalized patients by recognizing and addressing the risk factors associated with the development of AKI. The greater the number of risk factors, the higher the probability of developing AKI.

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