Original Article

Diagnostic Value of Urinary Kidney Injury Molecule-1 in Diagnosis of Sepsis Associated Acute Kidney Injury

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ABSTRACT

Background: Sepsis-associated acute kidney injury (SA-AKI) is a common condition found in sepsis. Due to the lack of serum creatinine, this condition possibly makes therapy delayed. Kidney Injury Molecule-1 (KIM-1) is a a type 1 transmembrane protein with immunoglobulin and mucin domains, which is expressed increased in the proximal tubules of the kidney. Elevated urinary KIM-1 levels are an indicator of AKI. However, previous studies have shown varying results.

Objective: This study aims to determine early diagnostic biomarkers for the presence of AKI in sepsis.

Methods: This diagnostic test was conducted at Dr. M. Djamil General Hospital Padang in sepsis patients. The diagnosis of AKI was established based on the 2012 KDIGO criteria.

Results: The study involved 94 sepsis patients; only 22,34% (n=21) of them experienced AKI. Serum creatinine levels at admission and within 48 hours of hospitalization were 0,7 (IQR 0,2-1,6) mg/dl and 0,8 (IQR 0,3-2,2m) mg/dl. A urinary KIM-1 level at admission ≥11,74 ng/mL had a sensitivity of 44,68%, a specificity of 59,57%, a positive predictive value of 52,5%, a negative predictive value of 51,85%, and an accuracy of 52,12% in early diagnosis of AKI in sepsis.

Conclusion: Urinary Klevel has poor diagnostic value in the diagnosis of AKI in sepsis.

Keywords: Sepsis, Kidney injury molecule-1, AKI.

Introduction

Acute kidney injury (AKI) is part of the spectrum of acute kidney disease (AKD) characterized by decreased kidney function and persistent dysfunction associated with functional loss leading to chronic kidney disease (CKD). Acute kidney injury (AKI) is defined as an increase in serum creatinine of ≥ 0.3 mg/dl within 48 hours or an increase in serum creatinine of ≥ 1.5 times the baseline estimated within the

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past week or a decrease in urine output of < 0.5 ml/kg/hour within 6 hours.[1]

The global burden of mortality due to AKI far exceeds the global burden of mortality due to breast cancer, heart failure, or diabetes, with mortality rates remaining high for the past 50 years. Acute kidney injury is a major and significant problem frequently encountered in intensive care units (ICUs). Worldwide, AKI is reported to occur in 20% or even more than 50% of ICU patients. A study by Hoste et al. found that the incidence of AKI in 1,802 ICUs from 33 countries was 57.3%. AKI patients are dominated by sepsis patients, at about 53%.[1–3]

The use of serum creatinine as the basis for AKI diagnosis also has several limitations. Structural kidney injury without a corresponding increase in serum creatinine may occur in conditions such as sepsis due to hemodilution or sarcopenia in geriatric patients, leading to a "failure to rise" in creatinine and delayed treatment. Conversely, conditions without actual kidney injury but accompanied by elevated serum creatinine levels, such as prerenal azotemia, liver cirrhosis, or the early use of diuretics and antihypertensive medications, may result in inappropriate treatment. Therefore, serum creatinine-based diagnosis has low sensitivity and specificity.[4,5]

Kidney injury molecule-1 was first identified by Ichimura et al in 1998. Kidney injury molecule-1 is a type 1 transmembrane protein with immunoglobulin and mucin domains, upregulated in the proximal tubule of the kidney. Normally, this structure is found within cells. When proximal tubule damage occurs, it is released into the extracellular space. This is the basis for KIM-1's use as a diagnostic marker for AKI.[6]

The 28th Acute Disease Quality Initiative (ADQI) consensus recommends the use of additional biomarkers in establishing the diagnosis of AKI in sepsis. The goal is early detection and appropriate management before permanent complications occur. A study by Xie et al. (2021) found that urinary KIM-1 can detect AKI in sepsis patients earlier than several other biomarkers, with urinary KIM-1 increasing within the first 2 hours after kidney injury. Furthermore, a study by Shaker et al. (2023) found that urinary KIM-1 levels were significantly higher in AKI patients with sepsis earlier than serum creatinine. Serum creatinine increased within 24 or even 48 hours after kidney damage in sepsis patients. Another study by Juwono et al. (2024) found that urinary KIM-1 could be a potential marker for early diagnosis of AKI. Urinary Kidney Injury Molecule-1 appears within 6-12 hours after kidney damage, even before serum creatinine increases. Another study conducted by Mohamed et al (2024) also concluded that urinary KIM-1 can detect AKI in sepsis patients earlier than serum creatinine, so that patients can receive faster treatment before it develops into chronic kidney disease.[7–10]

Methods

Design and participants

This study is a diagnostic test using a cross-sectional approach conducted in inpatients of Dr. M. Djamil Central General Hospital, Padang. Samples were collected from October 2025 to February 2026. First, we determined the inclusion and exclusion criteria, then urine and blood tests were performed. In this study, the sample selection was carried out using consecutive sampling. The sample size was determined by using a particular diagnostic formula, and an optimum sample of 94 people was obtained. The subjects taken as samples were subjects who met the inclusion criteria and did not meet the exclusion criteria. The inclusion criteria were sepsis patients with normal serum creatinine levels. Patients with a history of chronic kidney disease (CKD), anuria, lupus nephritis, nephrotic syndrome, nephrolithiasis, polycystic kidney disease, renal cell carcinoma, diabetic nephropathy, and urinary tract infection were excluded from the study.

Testing of Urinary KIM-1 was carried out using the ELISA (Enzyme-linked Immunoassay) method using the YL Biont reagent in the Biomedical Laboratory of the

Medicine Faculty of Andalas University, Padang. An elevated serum creatinine level ≥ 0.3 mg/dl in 48 hours is defined as AKI, and an elevated level <0.3 mg/dl is defined as non-AKI. The optimal cut-off urinary KIM-1 level was calculated by the Youden Index in the ROC. After that, we assessed diagnostic performance by calculating sensitivity, specificity, negative predictive value, positive predictive value, and accuracy using Table 2 x 2.

Results

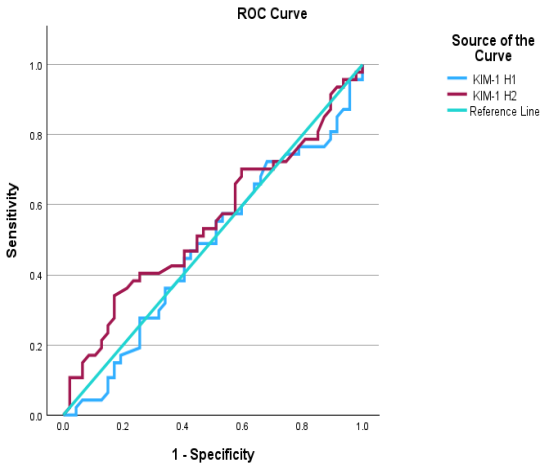
Patient characteristic

This study involved 94 patients with a sepsis diagnosis while admitted. The average age of the sample is 65,5 (IQR 48.8 – 70.0) years. The proportion of the geriatric and nongeriatric subgroups is 67% and 33%, respectively. In this study, female patients with suspected sepsis-associated AKI were more prevalent than males, accounting for 60.6% and 39.4%, respectively. A total of 88.3% of patients were treated in the High Care Unit (HCU), while 11.7% were admitted to the Intensive Care Unit (ICU). The comorbidities identified among sepsis patients included hypertension (67%), diabetes mellitus (33%), chronic heart disease and stroke (36.2%), and malignancy (8.5%).

Median SOFA score at admission is 5. The primary source of infection is pneumonia 89,3%, skin and soft tissue infection (SSTI) 21,3%, and other infection 6,4%. Almost 91.9% were unifocal infections. Laboratory findings demonstrated a median hemoglobin level of 10.3 g/dL (IQR 3.9–16.7 g/dL). The median lactate level was 1.8 mmol/L (IQR 0.5–8.3 mmol/L), while the median albumin level was 2.6 g/dL (IQR 1.3–4.1 g/dL). The median serum creatinine level on the first day of hospitalization was 0.7 mg/dL (IQR 0.2–1.6 mg/dL), increasing to 0.8 mg/dL (IQR 0.3–2.2 mg/dL) on the second day. Median urinary KIM-1 levels on admission were 10.6 ng/mL (IQR 1.2–19.5 ng/mL), while on the second day of hospitalization the median level increased to 11.5 ng/mL (IQR 1.5–19.2 ng/mL).

Diagnostic Value of Urinary KIM-1

First, the optimal cut-off value of urinary KIM-1 level is calculated by the Youden index. A urinary KIM-1 level at admission> 11.74 ng/mL had a sensitivity of 44,68%, specificity of 59,57%, positive predictive value of 52,5%, negative predictive value of 51,85%, and accuracy of 52,12% in early detection of AKI in sepsis. We also calculated the optimal cut-off within 48 hours of hospitalization (H_2). The result is ≥15,41 ng/mL with AUC 0,547 (CI 95%; 0,430-0,665) and Youden Index 0,170. In this study, we found 21 AKI and 19 non-AKI based on KDIGO criteria. The ROC and diagnostic performances from this study can be seen in Picture 1 and the table below.



Picture 1. Receiver Operation Curve (ROC)

Table 1. Characteristics of Respondents

Variable n = 94	Value n = 94
Age (years), median (Min-Max)	65,5 (18–101)
Age group, n (%)	
< 60 years	31 (33)
≥ 60 years	63 (67)
Sex, n (%)	
Male	37 (39,4)
Female	57 (60,6)
Type of care unit, n (%)	
ICU	11 (11,7)
HCU	83 (88,3)
Comorbidities, n (%)	
Diabetes mellitus	31 (33)
Hypertension	63 (67)
Stroke/heart disease[4]	34 (36,2)
Malignancy	8 (8,5)
Number of comorbidities, n (%)	
One comorbidity	58 (61,7)
Multimorbidity	36 (38,2)
SOFA score, median (Min-Max)	5 (3–12)
Source of infection, n (%)	
Pneumonia	84 (89,3)
Skin and soft tissue infection	20 (21,3)
Other infections	6 (6,4)
Focality of infection, n (%)	
Unifocal	74 (73,4)
Multifocal	20 (26,6)

Table 2. Laboratory Parameters

Variable n = 94	Value n = 94
Laboratory parameters, median (Min-Max)	
Hb (g/dL)	10,3 (3,9–16,7)
Lactate (mmol/L)	1,8 (0,5–8,3)
Albumin (g/dL)	2,6 (1,3–4,1)
Creatinine, Day 1 (mg/dL)	0,7 (0,2–1,6)
Creatinine, Day 2 (mg/dL)	0,8 (0,3–2,2)
Urinary KIM-1, Day 1 (ng/mL)	10,6 (1,2–19,5)
Urinary KIM-1, Day 2 (ng/mL)	11,5 (1,5–19,2)

Table 3. Diagnostic Performance of Urinary KIM-1 to Diagnose Sepsis-Associated AKI

Day of Test	KIM-1 (ng/mL)	AKI KDIGO		Sensitivity	Specivicity	NPV	PPV	Acuration
		Yes	No					
at Admission (H_1)	≥11,74	21	9	44,68%	59,57%	52,5%	51,85%	52,12 %
	<11,74	26	28					
48 hours in hospitalization (H_2)	≥15,41	16	8	34,04%	82,9%	66,6%	55,7%	58,51%
	<15,41	31	39					

Discussion

In this study, we reported that urinary KIM-1 has poor diagnostic performance for early detection of AKI in sepsis patients. While serum creatinine was normal at admission, elevated urinary KIM-1 levels of more than 11,74 ng/mL resulted in a sensitivity of 44.68%, specificity of 59.57%, negative predictive value 52,5%, positive predictive value 51,85% and accuracy of 52.12% (AUC 0,478).

A study conducted by Matarneh et al (2025) involving 35 studies covering >6000 critically ill patients evaluated three biomarkers for early detection of AKI, namely: NGAL, KIM-1, and TIMP-2IGFBP7. Kidney injury molecule-1 showed lower overall diagnostic accuracy. However, KIM-1 may offer clinical value in identifying patients with ongoing tubular injury or in risk stratification during the subacute phase. Kidney injury molecule-1 is a transmembrane protein released by injured proximal tubular cells and is usually measured in urine. When compared with NGAL and TIMP-2IGFBP7, KIM-1 reflects more persistent kidney injury. The AUC values in this review ranged from 0.62 to 0.74. The sensitivity and specificity of KIM-1 were more moderate in this study, namely 70-8% and 60-85%, respectively. Several studies have shown its potential to differentiate transient from persistent AKI and to predict long-term renal recovery. Therefore, KIM-1 may be more useful for AKI prognosis and phenotype than for early diagnosis. Several included studies showed that KIM-1 levels remained elevated after 48 hours, supporting its role in detecting ongoing and persistent injury. This is in line with the finding that KIM-1 may be more useful for long-term kidney damage than for early-onset AKI.[11,12]

A study by Puspitasari et al. (2025) found significant differences in urinary KIM-1, IL-18, and IGFBP-7 levels between sepsis patients with and without AKI. The cutoff point for urinary KIM-1 levels in sepsis with and without AKI was 1.666 ng/ml, with a sensitivity of 82.5%, a specificity of 82.2%, and a relative risk (RR) [95% confidence interval (CI)] of 6.866 (95% CI, 3.329–14.165). The cutoff point for urinary IL-18 levels was 3.868 ng/ml, with a sensitivity of 92.50%, a specificity of 91.78%, and an RR of 20.078 (95% CI, 6.593–61.142). The cutoff point for urinary IGFBP-7 levels was ≥0.906 ng/ml with a sensitivity of 75.00%, specificity of 75.34%, and RR of 4.063 (95% CI, 2.206–7.483). This study conducted three sampling sessions: on the first, third, and seventh days. The first day was when the patient was first admitted or diagnosed with sepsis, followed by the third and seventh days. The study sample consisted of 56 individuals, with comorbid diabetes mellitus being the most common, at 23.21%. Differences in population characteristics, including the most common comorbidities and the number of sampling days, could be factors contributing to the differences in study results. In this study, KIM-1 demonstrated a good AUC on the third day of sampling. This suggests that KIM-1 cannot be used in this population, specifically sepsis patients, despite positive results in several previous studies.[13]

According to a study by Zhang and Liu (2025), KIM-1 is normally absent in healthy kidneys, whereas acute kidney injury results in an initial increase in KIM-1 and exhibits anti-inflammatory and protective functions by facilitating the clearance of damaged and apoptotic cells. However, sustained increased KIM-1 expression after AKI is associated with the development of CKD.[14]

A study conducted by Yang et al (2025) stated that urinary KIM-1 can differentiate between transient AKI and persistent AKI. In addition, KIM-1 can also be used to predict long-term kidney damage with an AUC of 0.703, a sensitivity of 78.4%, and a specificity of 60.8%, and KIM-1 levels > 2.37 ng/mg are said to be associated with a poor prognosis. A recent study also stated that in diagnosing AKI, urinary KIM-1 has a sensitivity of 74% and a specificity of 84% with an AUC of 0.622. This study also stated that the sensitivity, specificity, and AUC of urinary KIM-1 in diagnosing contrast-induced AKI (CI-AKI) were 84%, 78%, and 0.88, respectively.[15]

In this study, it was found that the AUC value of urinary KIM-1 in detecting AKI in sepsis patients still showed less than optimal performance. These results indicate that the discriminatory ability of KIM-1 in differentiating AKI and non-AKI patients in this study population is relatively limited. This finding is likely influenced by the heterogeneity of AKI pathophysiology in sepsis. Based on a study by Osterman et al (2018), AKI in sepsis is a complex and heterogeneous condition, involving various mechanisms such as microcirculatory dysfunction, systemic inflammatory response, and cellular metabolic disorders. This condition results in various AKI phenotypes, ranging from hemodynamic disturbances without structural damage to overt tubular injury.[16]

Conclusion

Urinary KIM-1 level tests have poor diagnostic performance for early detection of sepsis-associated AKI.

Limitations of the Study

This study was conducted at a single healthcare center. It also did not evaluate the influence of confounding factors such as comorbidities or compare KIM-1 with other AKI biomarkers.

Declarations

Ethics approval and consent to participate

This study was conducted after obtaining ethical approval from the Health Research Ethics Committee of Dr. M. Djamil Padang General Hospital, Number: DP.04.03/d.XVI.10.1/454/2025.

Competing interests

There are no conflicts of interest in writing this article.

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Author's Contribution

Idea/concept: PAS. Design: PAS. Control/supervision: DP, HH, DV. Data collection/ processing: PAS, DV, NN, FF, DE, AWM. Analysis/interpretation: PAS, DP, HH, DV. Literature review: -. Writing the article: PAS. Critical review: DP, HH, DV, DV, NN, FF, DE, AWM. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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