KARBALA JOURNAL OF MEDICINE

Research Article

Estimation of KIM-1 in Patients with Chronic Kidney Disease

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Article information:

Received: 15-07-2025
Accepted: 17-08-2025
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https://doi.org/10.70863/karbalajm.v18i2.4926

Abstract

Background: Chronic kidney disease (CKD) is a progressive condition with a high morbidity and mortality rate, frequently associated with hypertension and diabetes. Early detection is critical to management. Kidney Injury Molecule-1 (KIM-1) has emerged as a potential biomarker for proximal tubular injury, with higher diagnostic value than conventional markers.

Methods: A case-control study involving 90 people aged 30-70 years was conducted. It included 60 CKD patients (30 on dialysis and 30 pre-dialysis) and 30 age- and gender-matched healthy controls. Venous blood samples were collected to measure serum KIM-1 levels using an ELISA assay, as well as serum creatinine and the estimated glomerular filtration rate (eGFR).

Results: Serum KIM-1 levels were not significantly elevated in pre-dialysis CKD patients compared to healthy controls (AUC = 0.489, $p = 0.897$), indicating poor diagnostic performance in early CKD. However, levels were significantly higher in dialysis patients ($p = 0.001$). KIM-1 correlated positively with serum creatinine and negatively with eGFR ($p < 0.001$), with an AUC of 0.75 and sensitivities of 79%. Levels increased progressively across CKD stages. Smokers showed elevated KIM-1, while no significant differences were observed by age, gender, or comorbidities.

Conclusions: Elevated KIM-1 levels in advanced CKD suggest that the protein may serve as a disease progression marker. However, its limited sensitivity in the early stages suggests that more research is required to determine its full diagnostic utility.

Keywords: KIM-1; chronic kidney disease; Dialysis; Pre-dialysis; Biomarker; Renal Function.

Introduction

Chronic kidney disease (CKD) is a worldwide public health concern characterized by a progressive and irreversible decline in renal function. It is associated with higher morbidity, mortality, and economic burden, especially when it progresses to end-stage renal disease (ESRD), which necessitates dialysis or transplantation [1-2]. CKD is a major public health issue that impairs people's quality of life and contributes to the rising burden of cardiovascular disease and healthcare costs [3]. A significant impact on the clinical and economic well-being of populations around the globe has also been recorded. CKD is defined as structural or functional abnormalities of the kidney that have existed for more than three months and are commonly accompanied by a decreased estimated glomerular filtration rate (eGFR) and/or increased albuminuria [4]. The disease is divided into five stages based on eGFR levels, which range from renal damage without functional decline (stage 1) to complete renal failure requiring dialysis (stage 5) [5]. CKD prevalence rises with age, with higher rates observed in people over 60 years old [6]. Middle Eastern and Arab populations often develop CKD at a younger age than Western populations, owing to the high prevalence of diabetes, hypertension, and obesity [7-8]. Despite its growing impact, there are insufficient regional epidemiological data to determine its true burden [9]. CKD, like the cardiovascular disease continuum, progresses through a pathological sequence caused by modifiable risk factors such as diabetes mellitus (DM), hypertension, obesity, and chronic exposure to nephrotoxic agents [10]. These conditions cause both glomerular and tubular damage, eventually leading to end-stage renal disease (ESRD). Many patients, particularly the elderly, are thought to have accelerated CKD progression

due to modifiable metabolic and vascular risk factors such as hypertension, type 2 diabetes, and cardiovascular disease. These factors frequently act together, either directly or via intermediate renal insults, to cause chronic nephron loss [11].

Kidney injury molecule-1 (KIM-1) is a type I membrane glycoprotein expressed at low levels in healthy kidneys but significantly upregulated in proximal tubular epithelial cells following ischemic or toxic injury [12]. It has emerged as a promising biomarker for acute kidney injury (AKI) and has recently gained attention in the context of chronic kidney disease (CKD). Its presence in urine or serum is thought to reflect ongoing tubular damage and may offer diagnostic and prognostic value in patients with chronic kidney failure [13-14]. KIM-1 is a type I membrane glycoprotein that is underexpressed in healthy kidneys but significantly upregulated in proximal tubular epithelial cells after ischemic or toxic injury [12]. It has emerged as a promising biomarker for acute kidney injury (AKI) and has recently received attention in the context of chronic kidney disease (CKD). Its presence in urine or serum is thought to indicate ongoing tubular damage and may provide diagnostic and prognostic information in patients with chronic kidney failure [13-14]. In proximal tubular epithelial cells, the transmembrane glycoprotein KIM-1 is significantly upregulated after ischemic, toxic, or inflammatory insults. Its expression contributes to both maladaptive repair and injury response by facilitating the phagocytosis of apoptotic debris by epithelial cells and modifying immune signaling [16]. Mechanistically, KIM-1 expression is tightly controlled and highly localized within the damaged proximal tubules, regardless of systemic factors like muscle mass, fat distribution, or hormonal status. KIM-1 is a direct reaction to epithelial cell injury and dedifferentiation rather than a byproduct of general metabolism, in contrast to serum creatinine, which is influenced by muscle mass (and thus impacted by age, sex, and BMI) [18-19].

The purpose of this study was to assess serum KIM-1 levels in patients with CKD at various stages and determine its potential utility as a non-invasive biomarker for distinguishing CKD patients from healthy individuals. Furthermore, the study intends to investigate the relationship between KIM-1 levels and clinical variables such as kidney function indicators and comorbidities like smoking. Understanding the diagnostic significance of KIM-1 in CKD may improve current monitoring strategies and aid in the detection of kidney damage. The study aims to answer the following questions: the role of KIM-1 in the diagnosis, prognosis, and risk assessment of chronic kidney disease (CKD)?

Materials and Methods

Study Design and Patients

This case-control study was conducted between November 2024 and March 2025 at Imam Al-Hussein Medical City Hospital in Karbala, Iraq. A total of 90 participants aged 30–70 years were recruited. The study population included three groups. The first group (dialysis CKD) involved 30 patients with confirmed end-stage renal disease undergoing regular hemodialysis. The second group (pre-dialysis stages CKD) include 30 patients in CKD stages 2–4 not on dialysis. The third group (controls) individuals 30 age- and sex-matched apparently healthy individuals with no history of renal disease.

Inclusion criteria: Iraqi males and female patients with chronic kidney disease diagnosed by specialized physician according to kidney disease improving global outcomes Diagnostic criteria involved the clinical medical and history examination.

Exclusion criteria: Patients who had suffering acute kidney injury, cardiovascular diseases, COVID-19, recent cardiac or kidney surgery, or renal cancer were excluded from current in this study.

Data collection and clinical evaluation

Demographic data, smoking status, comorbidities (diabetes, hypertension), medication use, and family history of CKD were collected via structured questionnaires. Physical examinations included height, weight, and blood pressure (systolic and diastolic). Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) and categorized according to WHO guidelines.

Sample collection and storage

Venous blood samples (5 mL) were collected using gel tubes. After clotting, the samples were centrifuged at 3000 rpm for 20 minutes. The separated serum was aliquoted into three 1.5 mL Eppendorf tubes and stored at −20°C until analysis. One aliquot was designated for biomarker assessment (KIM-1), and others for routine kidney function and electrolyte testing and 25-OH Vitamin D and PTH.

Biomarker and biochemical analyses

KIM-1 level were determined using human-specific sandwich ELISA kits (BT LAB, China), following the manufacturer's protocols. Absorbance was measured at 450 nm, and concentrations were calculated from standard curves. Creatinine was measured by kinetic alkaline picrate method (Jaffe

reaction) using Architect c4000 autoanalyzer (Abbott, USA). eGFR was calculated using the CKD-EPI equation. Urea was determined enzymatically via urease and GLDH reactions. Sodium was measured via sodium-dependent β-galactosidase method and potassium via pyruvate kinase-lactate dehydrogenase coupled assay. Calcium was determined colorimetrically using Arsenazo-III dye. 25-OH Vitamin D and parathyroid hormone (PTH) were quantified using CMIA (Chemiluminescent Microparticle Immunoassay) on the Architect i1000SR system (Abbott, USA).

Ethical Approval

An ethical certificate was obtained from the relevant committees at the University of Karbala, at document No. 24-31 on 29 June 2025. All research participants were informed and allowed to give their consent before sample collection. By document number 2690 on 22 October 2024, a local college and hospital ethics committee reviewed and approved the protocol, subject information, and consent form.

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM, USA). Categorical variables were presented as numbers and percentages, while continuous data were expressed as median (interquartile range). Normality was assessed via the Shapiro-Wilk test. Between-group comparisons were performed using the Mann-Whitney U test or Kruskal-Wallis test, depending on the number of groups. Spearman's rank correlation coefficient was used to assess relationships between continuous variables. Logistic regression was applied to evaluate associations with CKD status. ROC curve analysis was conducted to determine diagnostic performance. A p-value < 0.05 was considered statistically significant.

Results

The current study investigated serum KIM-1 levels and their relationship to various clinical and biochemical parameters in CKD patients and healthy controls. As shown in Table 1, no statistically significant difference was observed in serum KIM-1 levels between the overall CKD group and healthy controls ($p = 0.066$). Serum KIM-1 levels were significantly higher in the dialysis group than in pre-dialysis patients and healthy controls ($p = 0.001$). However, no significant differences were found between the pre-dialysis and control groups. KIM-1 levels were also significantly higher in smokers than in nonsmokers in the CKD population ($p = 0.011$) as shown in Table 1. However, there were no significant differences by gender, age, or BMI category. There were no significant relationships with comorbid conditions like diabetes or hypertension. Furthermore, KIM-1 showed a positive correlation with serum creatinine. But a negative correlation with urea and eGFR, indicating a link with deteriorating renal function. There were no significant correlations between KIM-1 and serum sodium, potassium, calcium, vitamin D3, or parathyroid hormone as shown in Table 2. Logistic regression analysis yielded a borderline odds ratio of 1.625 (95% CI: 0.948-27.2) for KIM-1 in predicting CKD status, with a p-value of 0.058 as shown in Table 3.

Data are presented as median (IQR). Kruskal-Wallis and Mann–Whitney U tests were used to assess group differences. Spearman's rank correlation was used to evaluate associations between KIM-1 and continuous variables. Statistical significance was considered at $p \leq 0.05$; r: Spearman correlation coefficient; +: positive correlation; N: number of participants; Min: minimum; Max: maximum.

Table 4 shows the results of ROC analysis, which evaluated KIM-1's diagnostic performance across CKD stages. As shown in Figure 1, KIM-1 had low discriminatory power in pre-dialysis patients compared to controls (AUC = 0.489, $p = 0.897$). Figure 2 demonstrates that in the dialysis group, KIM-1 showed fair diagnostic accuracy (AUC = 0.751, $p = 0.001$), with a cut-off value of 0.48 ng/mL yielding 79% sensitivity and 67% specificity. Figure 3 shows similar discrimination between pre-dialysis and dialysis patients (AUC = 0.743, $p = 0.001$).

Discussion

Kidney Injury Molecule-1 (KIM-1) is a sensitive, stage-dependent biomarker of renal tubular injury in chronic kidney disease (CKD), and this study supports its clinical and biological significance. In current study, KIM-1 demonstrated limited utility in distinguishing between healthy individuals and pre-dialysis CKD patients, with an AUC of 0.489 and low sensitivity and specificity. These findings indicate that, whereas KIM-1 may be increased in the presence of renal damage, its discriminatory value in the early stages of CKD is limited. The inability of KIM-1 to reliably differentiate early CKD stages from healthy states may stem from its expression being more reflective of tubular injury rather than overall kidney function decline. Since early CKD may involve minimal or heterogeneous tubular damage, KIM-1 levels may not consistently rise until later stages or during acute episodes. Although KIM-1 levels rise in response to tubular injury, new research suggests that KIM-1 alone may

be insufficiently sensitive for early-stage CKD identification. Combining KIM-1 with additional tubular stress indicators can improve diagnosis accuracy [26-27].

Table 1: Serum KIM-1 levels and their clinical and biochemical associations across CKD groups

Biomarker	**Control n=30**		**Patients n=60**		**p-value**
	Median (min-max)	**IQR**	**Median (min-max)**	**IQR**	
KIM-1 (ng/mL)	0.46 (0.29-1.58)	0.13	0.51 (0.17-1.91)	0.33	0.066

	Control n=30		Pre-dialysis stages n=30		On dialysis n=30		p-value
KIM-1 (ng/mL)	0.462 (0.29-1.58)	0.31	0.446 (0.17-1.45)	0.190	0.689 (0.22-1.91)	0.900	0.001

Smoking Status					
	Yes n=28		**No n=37**		**p-value**
KIM-1	**0.633 (0.39-1.59)**	**0.43**	**0.444 (0.26-1.91)**	**0.36**	**0.011**

Table 2: Correlation of serum KIM-1 with clinical and biochemical parameters

Parameter	Correlation (r)	p-value
eGFR (mL/min/1.73 m²)	–0.439	0.001
Creatinine (mg/dL)	0.375	<0.001
Urea (mg/dL)	0.100	0.355
Sodium (Na) mmol/L	–0.110	0.307
Potassium (K) mmol/L	0.071	0.510
Calcium (Ca) mg/dL	–0.110	0.309
Vitamin D3 (ng/mL)	–0.168	0.118
PTH (pg/mL)	0.161	0.227

Table 3: Odds ratio for serum KIM-1 in CKD patients

Marker	Odds Ratio	95% CI (Lower–Upper)	p-value
KIM-1	1.625	0.948 – 27.207	0.058

OR: Odds Ratio, CI; Confidence Interval

Table 4: Diagnostic performance of serum KIM-1 based on ROC analysis across CKD stages

Groups	AUC	P-value	Cut-off (ng/L)	Sensitivity	Specificity
Control vs. Pre-dialysis	0.489	0.897	0.45	0.52	0.44
Control vs. Dialysis	0.751	0.001	0.48	0.79	0.67
Pre-dialysis vs. Dialysis	0.743	0.001	0.48	0.79	0.57

ROC: Receiver operating characteristic; significant at $p \leq 0.05$; AUC; Area under curve,

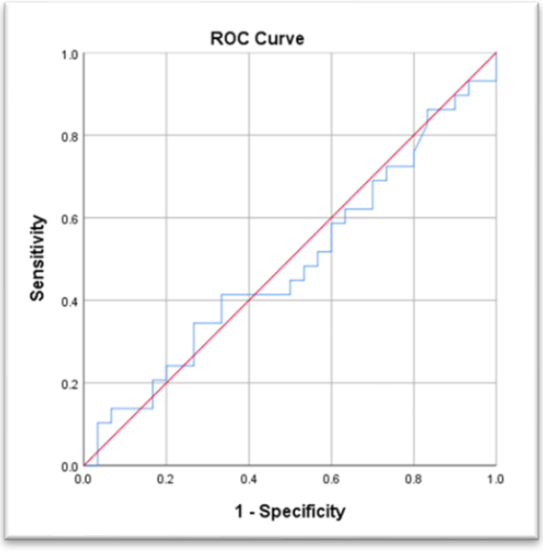

Figure 1: Receiver Operating Characteristic (ROC) of KIM--1 in pre-dialysis CKD patients compared to control group.

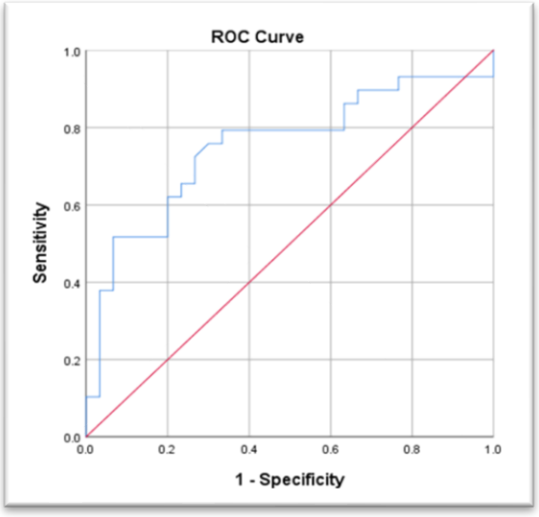

Figure 2: Receiver Operating Characteristic (ROC) of KIM-1 for on-dialysis CKD patients compared to control group

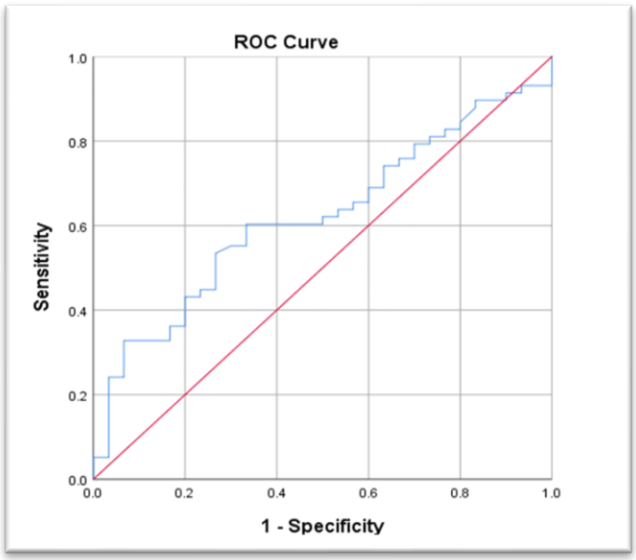

Figure 3: Receiver Operating Characteristic (ROC) Analysis of KIM-1 for pre-dialysis and on-dialysis CKD patients' group

The current investigation found a statistically significant variation in KIM-1 concentrations among dialysis patients compared to pre-dialysis phases and the control group. Although the total difference in KIM-1 serum levels between CKD patients and controls was not statistically significant, a definite upward trend was seen. Importantly, KIM-1 levels were significantly greater in dialysis patients than in pre-dialysis stages and control groups, implying that KIM-1 may be a marker of severe tubular injury in end-stage renal disease (ESRD). Recent research has revealed the potential of serum KIM-1 (sKIM-1) as a predictive biomarker in chronic renal disease. The Boston Kidney Biopsy Cohort and the CRIC Study found that increased plasma KIM-1 levels were independently linked with tubulointerstitial inflammation, fibrosis, and mesangial expansion. Furthermore, greater sKIM-1 concentrations predicted a considerably higher probability of development to end-stage kidney disease (ESKD), even after accounting for baseline renal function [28]. Serum KIM-1 concentrations rose dramatically as CKD progressed, with dialysis patients having the highest values. This trend is consistent with the biomarker's involvement in detecting continuous tubular stress and interstitial inflammation. The significant increase in dialysis patients confirms prior research associating chronic tubular injury to prolonged KIM-1 expression [16, 21]. The study's most clinically useful conclusion is that there was no significant relationship between serum KIM-1 levels and typical demographic factors like age, gender, or body mass index (BMI). This biological specificity reduces the possibility of false elevation or suppression brought on by non-renal systemic factors, improving the reliability of KIM-1 as a biomarker of renal injury. This demographic independence has been confirmed by numerous large-scale biomarker studies. KIM-1 levels were not significantly associated with age or gender in both diabetic and non-diabetic populations, indicating that it is stable across clinical subgroups [18]. Although studies in pediatric and elderly CKD cohorts have reported consistent KIM-1elevation, the current study included participants aged 30–70, limiting direct comparison. [20-21]. This property is especially useful in precision nephrology, where traditional markers frequently underperform in patients with unusual body composition (e.g., elderly, cachectic, or obese). In such cases, serum creatinine levels may appear deceptively low despite significant renal impairment. KIM-1 levels reflect localized renal pathology rather than whole-body physiology, giving it an advantage in diagnostic accuracy and inter-patient comparability. As a result, the lack of demographic correlation in our study further validates KIM-1 as a biologically precise and demographically neutral marker, suitable for use across diverse CKD populations and potentially useful in individualized risk stratification and monitoring. Surprisingly, the ROC analysis showed poor diagnostic performance in distinguishing pre-dialysis stage patients from healthy controls. This limitation may be due to the heterogeneous pathology of early CKD, in which mild or intermittent injury may not reach the threshold for significant KIM-1 elevation. Furthermore, because KIM-1 reflects active epithelial damage rather than glomerular dysfunction, its expression may remain low in early-stage patients with primarily glomerular involvement and little tubulointerstitial change [22].

Additionally, our research revealed that smokers' KIM-1 levels were significantly higher than those of non-smokers. Through the production of reactive oxygen species (ROS), microvascular ischemia, and low-grade inflammation, smoking is a known cause of oxidative stress and endothelial dysfunction, all of which can have a direct effect on renal tubular cells [23]. This suggests that KIM-1 could serve as a sentinel biomarker in detecting environmentally or behaviorally induced subclinical renal injury. Both a positive association with serum creatinine and a moderate inverse correlation between KIM-1 and eGFR support the biomarker's usefulness in reflecting ongoing tubular damage concurrent with declining filtration function. A more pathophysiologically direct indicator of nephron stress is that KIM-1 is highly specific to

tubular epithelial cells and reflects localized injury processes, in contrast to creatinine, which increases late in CKD and is influenced by non-renal factors like age and muscle mass [24]. There was no significant correlation found between KIM-1 levels and parathyroid hormone (PTH), vitamin D3, urea, or electrolytes (Na, K, Ca). This demonstrates that KIM-1 is largely unaffected by the systemic metabolic disturbances that define the later stages of CKD-mineral and bone disease (CKD-MBD) and supports its tubular epithelial specificity. Such independence enhances its diagnostic precision in complex metabolic profiles [25].

Conclusions

The current study underscores the growing importance of kidney injury molecule-1 (KIM-1) as a promising biomarker for detecting and monitoring tubular epithelial damage in chronic kidney disease (CKD). KIM-1 levels are significantly higher in dialysis patients than in pre-dialysis patients and healthy controls, suggesting a link between progressive renal deterioration and advanced tubular injury. Although KIM-1 did not demonstrate a statistically significant distinction between early-stage CKD and controls, its upward trend across CKD stages suggests it is more useful in reflecting disease severity than in early detection. Importantly, KIM-1 levels were not affected by demographic factors such as age, sex, and body mass index, confirming its role as an independent and objective indicator of kidney injury. The significant associations found with smoking support its sensitivity to subclinical nephrotoxic exposures, an important feature for risk stratification in at-risk populations. Although it has not been associated with systemic markers of mineral imbalance, such as calcium, vitamin D3, and parathyroid hormone, KIM-1's specificity for proximal tubule injury makes it an effective tool for identifying the location and nature of kidney disease. Based on these findings, KIM-1 has significant potential as part of a biomarker panel to improve clinical decision-making in the management of chronic kidney disease (CKD). Its integration with traditional kidney function indices may provide a more accurate understanding of disease progression, especially in patients at risk of rapid deterioration. Future prospective studies are needed to validate its prognostic value, longitudinal dynamics, and therapeutic implications in both early and late stages of CKD.

Funding: There is no funding for this research.

Conflict of interest: The authors state that there is no conflict of interest.

Author contributions: Conceptualization, A.M.M.; Methodology, A.M.M. and H.A.H.; Formal analysis and investigation, M.A.M; Writing, F.N.H; Resource, F.N.H; Supervision, M.A.M.

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