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ASSOCIATION BETWEEN EARLY URINARY POTASSIUM EXCRETION AND ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS WITH SHOCK: A HOSPITAL-BASED OBSERVATIONAL STUDY

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ABSTRACT

Acute kidney injury (AKI) is a frequent and clinically significant problem in critically ill patients, particularly those presenting with shock, where hemodynamic instability, inflammatory injury, and multi-organ dysfunction contribute to rapid renal impairment. Early recognition of AKI is essential to improving outcomes; however, conventional diagnostic markers such as serum creatinine and urine output rise relatively late in the course of disease, limiting opportunities for timely intervention. The present hospital-based observational study aimed to evaluate whether early urinary potassium excretion specifically urinary potassium concentration and fractional excretion of potassium (FeK) can predict the subsequent development of AKI in critically ill patients with shock admitted to the intensive care unit (ICU). Eighty-five adult patients (18–85 years) admitted to M.S. Ramaiah Hospitals ICU with shock, and catheterized within 24 hours, were prospectively evaluated between May 2023 and December 2024. Patients with pre-existing renal failure, diuretic use within the preceding 24 hours, nephrotoxic exposure, baseline dyskalemia, or anuria at presentation were excluded. Baseline demographics, vital signs, serum and urinary biochemical parameters, daily urine output, creatinine clearance, and severity indices (SOFA and APACHE II) were recorded. AKI diagnosis and staging were performed according to KDIGO criteria. Diagnostic performance of urinary potassium and FeK was assessed using receiver operating characteristic (ROC) analysis. The incidence of AKI in the cohort was 76.5% (n=65), with Stage 1 constituting 56.9% of cases. Septic shock was the predominant etiology (76.4%), and respiratory and urinary infections were the leading septic sources. Patients who developed AKI exhibited significantly higher urinary potassium (49.36 ± 20.15 mEq/L) and FeK (37.13 ± 36.83%) compared to those without AKI ($p < 0.05$). FeK demonstrated excellent diagnostic accuracy with an area under the ROC curve (AUC) of 0.871, sensitivity of 73.85%, and specificity of 85% at an optimal cut-off >10.25%. Urinary potassium alone had moderate predictive ability (AUC 0.691) but high specificity (95%) at a cut-off ≤32.4 mEq/L. AKI was associated with significantly prolonged hospitalization (9.25 vs. 7.30 days, $p = 0.002$), while mortality occurred only in AKI patients (7.7%), though not statistically significant. This study demonstrates that early urinary potassium measurements, particularly FeK, serve as sensitive and practical biomarkers for early identification of AKI in critically ill shock patients. Incorporating these urinary indices into early ICU assessment protocols may facilitate timely recognition of renal deterioration, enabling earlier intervention and improved clinical outcomes.

KEYWORDS: Acute kidney injury, urinary potassium, fractional excretion of potassium, ICU, septic shock, biomarkers.

INTRODUCTION

Acute kidney injury (AKI) is a prevalent and clinically important problem among critically ill individuals, especially those admitted to ICUs with shock. This problem is associated with a sudden drop in renal functioning, resulting in considerable morbidity, mortality, lengthened hospital stay, and health costs of patients with AKI. Research studies have shown that AKI occurs quite often in critically ill patients who face hemodynamic instability, infections, nephrotoxic injury, and inflammatory responses, thus posing a challenging problem for critical care medicine (Bates et al., 2001). The problem of AKI is especially evident in patients with circulatory problems, since their renal perfusion is affected, which causes more rapid development of kidney dysfunction (Behrend & Miller, 1999).

The significance of AKI is not confined to renal injury only. Numerous studies have demonstrated an association of AKI with increased hospital stay duration, increased costs for treatments, increased use of renal replacement therapies, and increased rates of mortality among hospitalized patients (Chertow et al., 2005). In order to increase diagnostic reliability and improve therapeutic strategies, several consensus groups across the globe have developed standardized criteria for AKI and its staging process, stressing the need for early detection and intervention (Bellomo et al., 2004). More so, numerous nephrology sources have described AKI as a multifactorial syndrome characterized by various mechanisms (Clarkson et al., 2007).

There are various clinical disorders that are common among sick individuals and which make them susceptible to AKI. Contrast-induced nephropathy, sepsis, hypovolemia, and circulatory shock are some of the well-known causes of AKI (Eisenberg et al., 1981). Nutritional deficiency and metabolic problems can also contribute to kidney damage and adversely affect the patient's healing process (Fiaccadori et al., 1999). Current treatment guidelines emphasize the importance of detecting and preventing renal injury, and it is imperative to identify the injury prior to permanent functional failure (Fliser et al., 2012). There are several biochemical mechanisms involved in renal functions, and one of the notable mechanisms is the potassium balance, since potassium dysregulation is usually associated with tubular injury and blood flow (Gennari, 2002).

Although major progress has been achieved in critical care nephrology, early diagnosis of AKI still proves to be difficult. Traditional markers of AKI including creatinine and urine output may prove ineffective when it comes to diagnosing renal injury at its very early stage. Creatinine levels may not increase until nephron injury reaches a rather severe level, while urine output can be affected by many other factors, which makes it unreliable as a single indicator of AKI. Therefore, research in the search of new AKI biomarkers has gained popularity. Some of the latest studies have focused on exploring functional and damage biomarkers of AKI and proved the usefulness of early biochemical markers in making diagnoses (Basu et al., 2014).

However, while there are guidelines for diagnosis and management of AKI, they still use traditional methods extensively and do not offer enough information concerning novel biomarkers in urine which might assist in the identification of the onset of kidney damage earlier than current diagnostic practices (Guidelines and Audit Implementation Network, 2014). Also, the effectiveness of therapy trials in patients with acute renal failure is highly inconsistent because treatment is usually initiated after considerable kidney damage has occurred (Hirschberg et al., 1999). Multinational studies further proved the high prevalence of AKI among critically ill patients along with persisting problems associated with early diagnostics and risk stratification (Hoste et al., 2015). Prior prospective studies of hospital-acquired renal insufficiency have revealed the problem with identifying risks before any changes in health state become noticeable (Hou et al., 1983). Also, nephrology societies recognize the necessity of improving methods of predicting the disease beyond existing diagnoses (James et al., 2013). While many different biomarkers have been identified in this regard, the shift from discovery of biomarkers to their clinical application is not completed, especially in poor conditions of healthcare systems in many countries (Kashani et al., 2017). Another interesting but underexploited research area includes measuring urinary potassium excretion and fractional excretion of potassium (FeK). The management of potassium by the nephron is governed by a complicated interaction of various procedures such as hormone regulation, tubular secretion, tubular reabsorption, and glomerular filtration. Studies indicate that renal ischemic and reperfusion injury could induce various physiological changes in the body which would result in a modification in tubular function prior to any changes in renal functional parameters being apparent (Kelly, 2003). Furthermore, various extra-renal regulatory processes are known to affect the progress of renal injury as well as electrolyte balance (Kielar et al., 2002).

The Kidney Disease: Improving Global Outcomes KDIGO guidelines state the significance of detecting early signs of AKI in order to manage patients better (Kellum et al., 2012). Under such circumstances, measurement of urinary potassium and FeK is quite appealing as it would not require much financial investment and would be easy to measure along with having potential of being an indicator of early tubular dysfunction. Some of the earlier studies assessing the effectiveness of various techniques to prevent renal injury have highlighted the significance of early detection of physiological changes before renal insufficiency occurs (Kurnik et al., 1998). There is a lack of information about whether urinary potassium parameters have any value in predicting AKI in patients with shock. Hence, the present investigation was planned in order to assess the relationship of early excretion of urinary potassium with AKI and diagnostic value of urinary potassium concentration and FeK in anticipating AKI in patients in critical condition with shock.

The present study was conducted to investigate:

1. The association between early urinary potassium excretion and subsequent development of AKI.
2. The diagnostic accuracy of urinary potassium and FeK in predicting AKI in critically ill shock patients.

METHODOLOGY

Study Setting and Design

The observational investigation was carried out within the ICU at M.S. Ramaiah Hospitals, Bengaluru, India from May 2023 to December 2024. The study was done to explore any relationship between the early urinary potassium loss and the expansion of AKI in the critically ill peoples with shock.

Study Population

Totally, 85 adult patients who had been admitted to the ICU in the study period participated in the investigation. Patients who met certain criteria for inclusion and exclusion were identified for involvement in the research.

Eligibility Criteria

Inclusion criteria for the individuals were that they should be between 18 and 85 years old; clinically diagnosed to be suffering from shock, have a urinary catheter in situ, and give consent 24 hours after being admitted in ICU. The people would not be included in the study if they had been on diuretics treatment 24 hours before the collection of samples, had renal failure previously, been on renal replacement therapy, had nephrotoxic drug intake before admission, had hyperkalemia and hypokalemia, or anuria at admission.

Data Collection

Baseline demographic characteristics and comorbid conditions were recorded at enrollment. Clinical data regarding the Etiology and types of shock, in addition to vital signs, were obtained. Lab tests included serum electrolyte levels, serum creatinine, urinary sodium, urinary potassium, and urinary creatinine. FeK and FeNa (fractional excretion of sodium) were

also determined. Urinary volume was noted at admission and on the fifth day of admission to the hospital. Further, 24-hour creatinine clearance was done, and severity of illness was measured with the use of SOFA (Sequential Organ Failure Assessment) and APACHE II (Acute Physiology and Chronic Health Evaluation II).

Definition of AKI

AKI was detected and classified using the KDIGO classification system. The detection of AKI was done using decreased urine production and elevated serum creatinine levels throughout the research period.

Follow-Up and Outcome Measures

All patients had been followed to determine the development of and severity of AKI. The outcomes measured were stage of AKI, length of stay in the ICU, and in-hospital mortality.

Statistical Analysis

The mean ± standard deviation was used to report the continuous variables. The diagnostic utility of potassium FeK and serum creatinine in predicting AKI was evaluated using ROC curve analysis. The cut-off values for sensitivity, specificity, and accuracy were calculated by Youden Index. Categorical variables were compared using the Chi-square test. The cutoff point for statistical significance was $p<0.05$.

RESULTS

Baseline Characteristics

A total number of 85 patients suffering from shock were used in the experiment. The average age of the study subjects was 46.38 ± 13.80 years old, and men accounted for 55.3% of the participants. Septic shock was The most prevalent type of shock, making up 76.4% of the cases, where respiratory and urinary tract infections were the leading sources of infections. In terms of co-morbid diseases, type 2 diabetes mellitus (55.3%) and hypertension (47.1%) were the most prevalent forms. The average score of SOFA was 3.73 ± 2.21, and the average APACHE II score was 19.51 ± 9.21, which means that the disease severity is moderate among the investigation participants.

Table 1. Baseline Features (N = 85)

Variable	Value
Age (years), mean ± SD	46.38 ± 13.80
Male sex, n (%)	47 (55.3)
Septic shock, n (%)	65 (76.4)
Type 2 diabetes mellitus, n (%)	47 (55.3)
Hypertension, n (%)	40 (47.1)
SOFA score, mean ± SD	3.73 ± 2.21
APACHE II score, mean ± SD	19.51 ± 9.21

Incidence and Severity of AKI

AKI occurred in 65 out of the total 85 patients admitted, giving an incidence rate of 76.5%. In terms of AKI, stage 1 AKI was predominant in 56.9% of the cases, while stages 2 and 3 followed. Septic shock and respiratory infections were strongly linked to the expansion of AKI, ($p<0.05$). The causative agents of infection play a substantial role in the occurrence of renal dysfunction among critically ill patients (Figure 1).

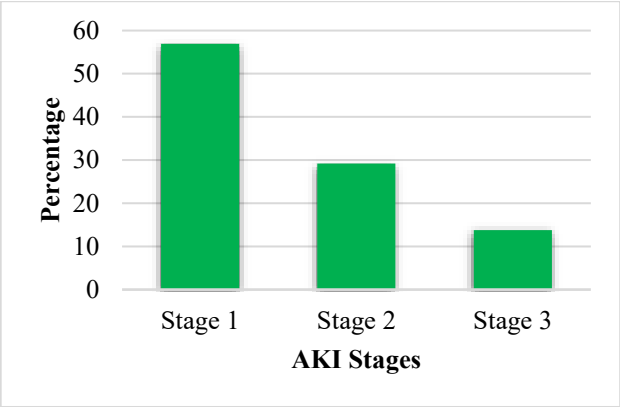

Figure 1. Distribution of AKI Severity According to KDIGO Staging.

AKI stages were distributed among affected individuals as shown in Figure 1. The highest percentage was seen in Stage 1 AKI cases, while Stage 2 and 3 had lower percentages, suggesting that the most common injuries in the sample were mild to moderate.

Urinary and Renal Parameters

In the period of ICU admission, the patient population showed that the mean concentration of potassium in the urine was 42.03 ± 26.33 mEq/L, the mean fraction excretion of potassium (FeK) was 29.98 ± 34.81%, and the mean concentration

of sodium in the urine was 69.11 ± 41.89 mEq/L. There was a substantial variance in the urinary and renal functional variables among patients who developed AKI and those who didn't (Figure 2).

The patients with AKI showed significantly increased urinary potassium excretion (49.36 ± 20.15 vs. 39.77 ± 27.71 mEq/L; $p = 0.01$) and highly increased FeK (37.13 ± 36.83% vs. 6.76 ± 6.83%; $p < 0.001$) when compared to those without AKI. On the other hand, the creatinine clearance was pointedly decreased in AKI individuals (59.14 ± 61.26 vs. 124.22 ± 86.45 mL/min; $p < 0.001$). This shows that the renal dysfunction is more pronounced in the AKI patients. In addition, the urine output recorded at admission and after five days of hospitalization in AKI patients was also significantly decreased ($p < 0.001$). The above results show that changes in the urinary potassium metabolism happen during the very early stage of renal dysfunction.

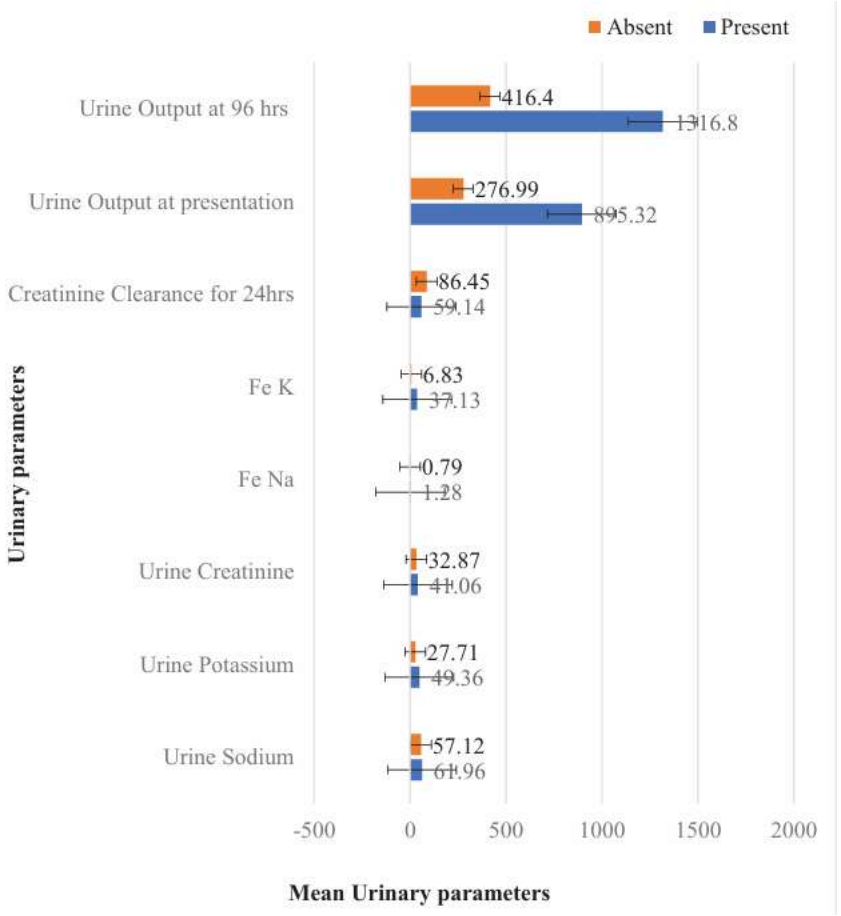

Figure 2. Comparison of Urinary and Renal Parameters Between AKI and Non-AKI Patients

Urinary sodium, potassium, creatinine, FeNa, FeK, creatinine clearance rate, and urine output are compared between patients with and without AKI in Figure 2. Patients with AKI were shown to have reduced urine production and creatinine clearance rates, as well as increased urinary potassium and FeK levels.

Diagnostic Performance of Urinary Potassium and FeK

The predictive value of urine potassium concentration and FeK for AKI was evaluated using receiver operating characteristic (ROC) curve analysis. Both biomarkers demonstrated the ability to distinguish between patients who experienced AKI and those who did not, with FeK exhibiting superior overall diagnostic performance. FeK was also shown to have high diagnostic accuracy, sensitivity and specificity than urinary potassium concentration as seen in Table 2 and therefore could be a helpful method for detecting renal failure early in critically unwell patients experiencing shock.

Table 2. Diagnostic Performance of Urinary Potassium and FeK for Prediction of AKI

Parameter	AUC	Sensitivity (%)	Specificity (%)	Optimal Cut-off
FeK (%)	0.871	73.85	85.00	>10.25%
Urinary potassium (mEq/L)	0.691	55.38	95.00	≤32.4 mEq/L

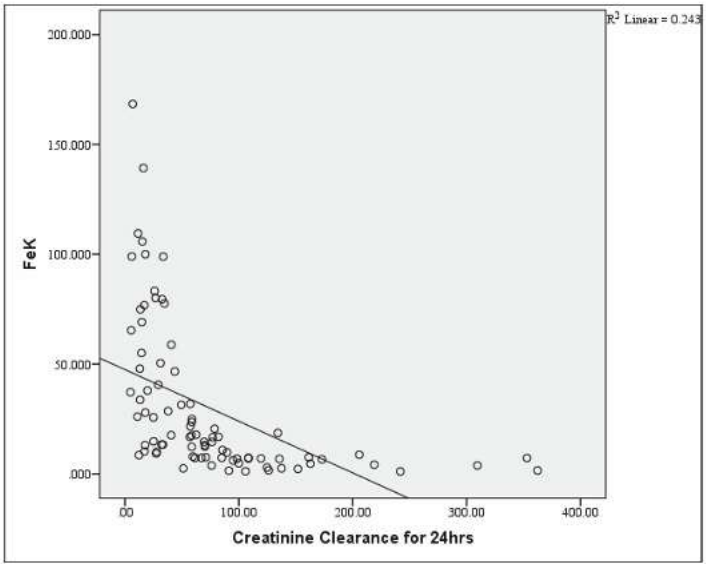

Figure 3. Relationship between FeK and Creatinine Clearance

A negative correlation was found between FeK and creatinine clearance (Figure 3) which means higher FeK values were associated with lower renal function. The data plotted in the scatter plot indicate a negative trend, indicating that high levels of urinary potassium excretion (high FeK values) are associated with lower levels of kidney function. This outcome is consistent with the conclusions of the diagnostic performance results obtained in Table 2 and further validates the usefulness of FeK as a clinically useful intermediate marker for early diagnosis of AKI in patients in critical condition who are in shock.

Clinical Outcomes

Comparison of clinical outcomes was made between the patients that suffered from AKI and those that did not have AKI. Patients suffering from AKI showed significantly longer duration of their stay in hospital in comparison with patients that did not suffer from AKI (9.25 ± 2.39 days vs. 7.30 ± 2.32 days; p = 0.002) due to high morbidity. Only patients with AKI had a death rate of 7.7%; however, this difference was not statistically significant (p = 0.201) (Table 3).

Table 3. Clinical Outcomes According to AKI Status

Outcome	AKI	Non-AKI	p-value
Length of hospital stay (days)	9.25 ± 2.39	7.30 ± 2.32	0.002
Mortality (%)	7.7	0.0	0.201

Discussion

The present investigation aim was to evaluate the value of urinary potassium concentration (UK) and FeK as early markers for AKI in patients in critical condition who are in shock. The prevalence of AKI was high in the study population, highlighting the significant burden of renal dysfunction in patients with critical illnesses. This is in line with earlier studies that have shown that AKI is a common occurrence in intensive care and it is linked to poor clinical outcomes, such as longer hospital stays and higher morbidity (Levy et al., 1996). The relatively high proportion of AKI Stage 1 and 2 in the current study indicates the potential for earlier recognition of renal function abnormalities through systematic biochemical monitoring, thereby preventing the progression of renal function abnormalities to severe renal injury. The current clinical guidelines still highlight the need for early identification and timely intervention of patients at risk of developing AKI (Lewington & Kanagasundaram, 2011; NICE, 2013). One of the key results of this study was that, in predicting AKI, FeK was superior to urinary potassium concentration. The observed diagnostic accuracy of FeK suggests that it may be a potentially early and clinically useful biomarker of renal dysfunction in the extremely sick. This phenomenon may be linked to changes in the renal reabsorption of potassium that happen in renal injury in the early stages. Ischemia-reperfusion injury is another mechanism of AKI that can occur with shock, and causes disruption of tubular transport processes and renal autoregulation before any significant decrease in GFR (Malek & Nematbakhsh, 2015). Thus, alterations in urinary potassium excretion can occur before more conventional renal dysfunction changes. In addition, potassium homeostasis is regulated by several complex mechanisms, including distal tubular secretion, aldosterone activity, and renal perfusion, all of which could be affected by the early phases of AKI (Palmer & Clegg, 2019).

The negative correlation between FeK and creatinine clearance also provides for the biological plausibility of FeK as a method of measuring renal function. As the kidney injury worsens and there is less ability to perfuse the kidney, compensatory changes in tubular electrolyte handling can cause higher levels of potassium to be excreted as the kidneys' filtration capacity diminishes. These data indicate that FeK can offer clinically relevant data both on renal tubular function and renal reserve in the course of the development of AKI.

The results of the current study agree with well-known concepts on the pathophysiology and clinical importance of AKI. Previous studies have highlighted the need for better diagnostic criteria and earlier biomarkers to detect renal injury, prior

to the onset of significant rises in serum creatinine (Mehta & Chertow, 2003; Mehta et al., 2007). Likewise, review papers assessing different AKI classification systems have showed that even mild levels of kidney injury are linked to a significantly higher risk of adverse consequences (Ricci et al., 2008).

The prevalence of AKI in the septic shock population in the present study is consistent with the previous studies in which sepsis has been reported as one of the main causes of acute renal failure in critical ill patients (Schrier & Wang, 2004). Sepsis, part of the systemic inflammatory response, can lead to microvascular dysfunction, inadequate renal perfusion, tubular damage, and thus AKI. Previous research to study post-injury organ dysfunction has also shown that circulatory disturbances and inflammatory mediators play a key role in exacerbation of renal injury (Moore & Moore, 1995).

There have also been several studies confirming the fact that AKI does not only cause damage to the kidneys, but might lead to organ damage at sites distant from the kidneys. Experiments have shown significant interaction of kidney and lungs during acute renal failure, confirming the hypothesis about multiple organ dysfunction in critically ill patients (Rabb et al., 2001; Rabb et al., 2003). Furthermore, experimental data shows that inflammatory signaling pathways associated with ischemia-reperfusion injury can increase the harm done to the kidneys and the body as a whole (Zhang et al., 2004). Connection between deterioration of renal function and disruption in the regulation of electrolytes established in this paper was confirmed in previous studies dealing with the problems of renal injury in high-risk groups of patients (e.g. exposure to contrast media or any other nephrotoxic factor) (Parfrey et al., 1989; Taylor et al., 1998; Wang et al., 2000). Additionally, limitations of serum creatinine, a delayed indicator of kidney injury, have already been studied extensively (Waikar & Bonventre, 2009), making the use of other markers which can identify renal dysfunction earlier necessary. Clinical guidelines suggest the use of modern diagnostic methods as well (Palevsky et al., 2013).

The outcomes of the investigation indicate that measurements of potassium levels in urine, especially FeK, could serve as practical and cost-effective approaches to early detection of AKI among critically ill patients. Since such electrolytes measurements are easily accessible and cheap, FeK might be used as a part of routine ICU evaluation process. Early detection among those who are most susceptible to AKI can help with their close monitoring, optimization of their hemodynamic state, prevention of exposure to any nephrotoxins, and implementation of renoprotection measures.

As is typical of many previous publications, patients with AKI spent more time in the hospital, which shows greater clinical load associated with renal impairment. While individuals with AKI had a higher death rate, the results were not statistically substantial due to the low number of subjects included in the investigation. There are several drawbacks which have to be mentioned. First of all, there are the single-center approach which limits generalizability of the results and the short follow-up period that makes it impossible to evaluate long-term renal outcomes. Besides, excluding those patients taking diuretics can narrow the scope of applicability of the findings.

CONCLUSION

The investigation shows that UK and FeK is useful for the early detection of AKI in shock patients in the critical care setting. Given the high frequency of AKI in this patient population, and the known limitations of using traditional markers like serum creatinine and urine output to diagnose renal dysfunction, it is important that reliable biomarkers be available to detect earlier renal dysfunction. The study's findings indicate that modifications in urinary K handling precede any significant renal dysfunction and thus hold promise for early detection of AKI. The result shows that, of the parameters assessed, FeK has better diagnostic performance and was strongly correlated with renal function decline, which might indicate that this could be used as a sensitive parameter to diagnose early tubular dysfunction and renal perfusion. Moreover, the association of higher FeK value with decreased creatinine clearance observed in the study demonstrates that FeK value is clinically relevant to the deteriorating kidney injury. Urinary potassium concentration was also predictive, but FeK proved to be more precisely and extensively diagnostic and could potentially be a stronger biomarker for risk stratification in critically ill patients.Adopting urinary potassium profiling especially FeK assessment in standard practice on the ICU may improve early detection of AKI and enable prompt clinical action. Recognizing the individuals who is at higher risk for kidney failure early on may allow closer monitoring, optimization of the patient's blood pressure, avoidance of nephrotoxic medications, and initiation of supportive measures designed to save the kidneys. Therefore, these easily accessible and inexpensive urinary markers have promise to enhance patient management and decrease the burden of AKI among patients in critical care. Further multicenter studies with larger patient numbers are needed to confirm the results and to devise standard clinical applications of FeK in the early diagnosis and prognosis of AKI.

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