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Development of Acute Kidney Injury Predictor Score in Intensive Care Unit Patients in Padang, Indonesia

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Abstract

Objective. This study aims to develop and create a specialized acute kidney injury (AKI) predictor score for the intensive care unit (ICU) patients in Padang, Indonesia. **Patients and Methods.** This study was a prospective observational study on 352 ICU patients at three specialized hospitals in Padang City; Dr. M. Djamil General Hospital, Dr. Rasidin General Hospital, and Siti Rahmah Islamic Hospital. Data regarding demographics, clinical characteristics, laboratory results, and outcomes related to AKI were gathered. The factors that predict AKI were identified using multivariate logistic regression analysis to determine independent factors. The predictor scores were created using regression coefficients and then internally confirmed. **Results.** Out of a total of 352 patients, 128 individuals (36.4%) suffered from AKI. Factors that independently predict the occurrence of AKI include age over 60 years old, having a history of chronic kidney disease, having sepsis, need for vasopressors, and having creatinine level 1.3 mg/dL (IQR 1.0-1.8) upon admission to ICU. An area under the curve (AUC) of 0.85 (95% CI 0.80-0.90) indicated the strong performance of the constructed predictor score. **Conclusion.** The constructed AKI predictor score a scale factor of 10, resulting in a range of 0–10 for the AKI predictor score. It demonstrates a good level of accuracy in predicting AKI in ICU patients in Padang. This score can be used by healthcare professionals to quickly identify and categorize individuals based on their risk level, facilitating timely intervention and personalized treatment.

Key Words: Acute Kidney Injury ▪ Creatinine ▪ Hospitals ▪ Intensive Care Units ▪ Sepsis.

Introduction

Acute kidney injury (AKI), also known as acute renal failure, is a medical condition characterized by rapid deterioration in kidney function (1, 2). It is a significant concern in clinical practice due to its significant impact on patient morbidity and mortality. AKI can worsen a critically ill patient's condition, carry a significant risk of complications, longer hospital stays, higher healthcare costs, and mortality (3). In general, the occurrence of AKI in the intensive care units (ICU) varies between 20% and 50% (4). A multinational study reported the occurrence of AKI in ICU patients with rates ranging from 35% to 40% (5). The most severe consequence of AKI is increased mortality, with patients in stage 3 AKI facing the greatest risk of death (6, 7). Timely detection of AKI is crucial for healthcare providers to initiate appropriate treatment, such as optimizing fluid balance, avoiding nephrotoxic medications, and closely monitoring kidney function. Early intervention can effectively prevent or mitigate the severity of AKI, while decreasing the likelihood of complications and mortality (8, 9). Additionally, timely detection allows clinicians to tailor therapy and monitoring for each patient based on their individual risk of AKI, improving ICU resource utilization and care efficiency.

Several AKI diagnostic tools to assist doctors in identifying individuals at increased risk for AKI has been established. The scores utilize a range of clinical and laboratory factors, including

age, comorbidities, administration of nephrotoxic medications, and fluctuations in blood creatinine levels, to determine the likelihood of AKI for individual patients. Three frequently utilized AKI diagnostic tools include RIFLE (Risk, Injury, Failure; and Loss; and End-stage kidney disease) (10), AKIN (Acute Kidney Injury Network) (11), and KDIGO (Kidney Disease: Improving Global Outcomes) (12). The RIFLE score utilizes alterations in serum creatinine levels and urine output to categorize the extent of acute kidney injury (AKI). AKIN score is a revised version of the RIFLE score that offers a more streamlined and user-friendly approach. KDIGO score is the most recent consensus for defining and categorizing AKI, and it provides guidelines for managing it.

While current AKI prediction scores have demonstrated utility in clinical practice, they possess various limitations. A significant constraint is the absence of external verification for particular demographics, such as ICU patients in Indonesia. The scores were derived from data collected from Western populations; hence, they may not entirely align with the features of Indonesian patients. Furthermore, these ratings are limited in their ability to accurately predict AKI in patients with specific circumstances, including chronic kidney disease, multiple organ failure, and those receiving renal replacement therapy. Hence, it is imperative to formulate a more precise and reliable AKI prediction score tailored to the ICU patients in Indonesia.

The objective of this study is to create a specialized AKI predictor score for the ICU patients in Padang, Indonesia. This predictor score is expected to assist doctors in identifying patients who are at a significant risk of developing AKI and enable them to promptly intervene, thereby minimizing the negative effects of AKI on the health outcomes and death rates of ICU patients in Indonesia.

Methods

Study Design and Participants

This study employed a prospective observational research approach. The selection of this design was based on its ability to enable immediate and ongoing monitoring of the progression of AKI in ICU patients, as well as the identification of related risk factors. The study was carried out at three specialized hospitals in Padang City; Dr. M. Djamil General Hospital, Dr. Rasidin General Hospital, and Siti Rahmah Islamic Hospital, which have sufficient intensive care unit (ICU) resources. The three hospitals were chosen based on the criteria of AKI case representation in the ICU and their willingness to participate in the research.

Data collection spanned a duration of one year, commencing in January 2023 and concluding in December 2023. This duration was deemed acceptable to achieve a sufficient and representative sample size. Throughout the study period, all adult patients (>18 years) who received treatment in the ICU at the three hospitals were included. Sample homogeneity and bias were minimized by applying inclusion and exclusion criteria. The inclusion criteria encompass adult patients who are over 18 years old, have been treated in the intensive care unit (ICU) for a minimum of 24 hours, and possess comprehensive data pertaining to the research variables. Patients who have stage 5 chronic kidney disease, a history of kidney transplantation, or a history of kidney replacement therapy (dialysis or hemofiltration) are excluded from the study based on specific criteria. Figure 1 illustrates the study flow and design.

Data Collection

Prospective data collection was conducted using patient medical records. Data collection was conducted by a skilled research team utilizing a structured data form. The data form contains demographic information, including age, gender, and history of comorbidities such as hypertension, diabetes mellitus, heart disease, chronic lung disease, and chronic liver disease. It also includes clinical data, such as the primary diagnosis that led to ICU admission and the use of vasopressors in patients. Vasopressors use is administration of vasopressor drugs to increase blood pressure in emergent hypotensive situations and maintain adequate perfusion when patients being treated in ICU. The

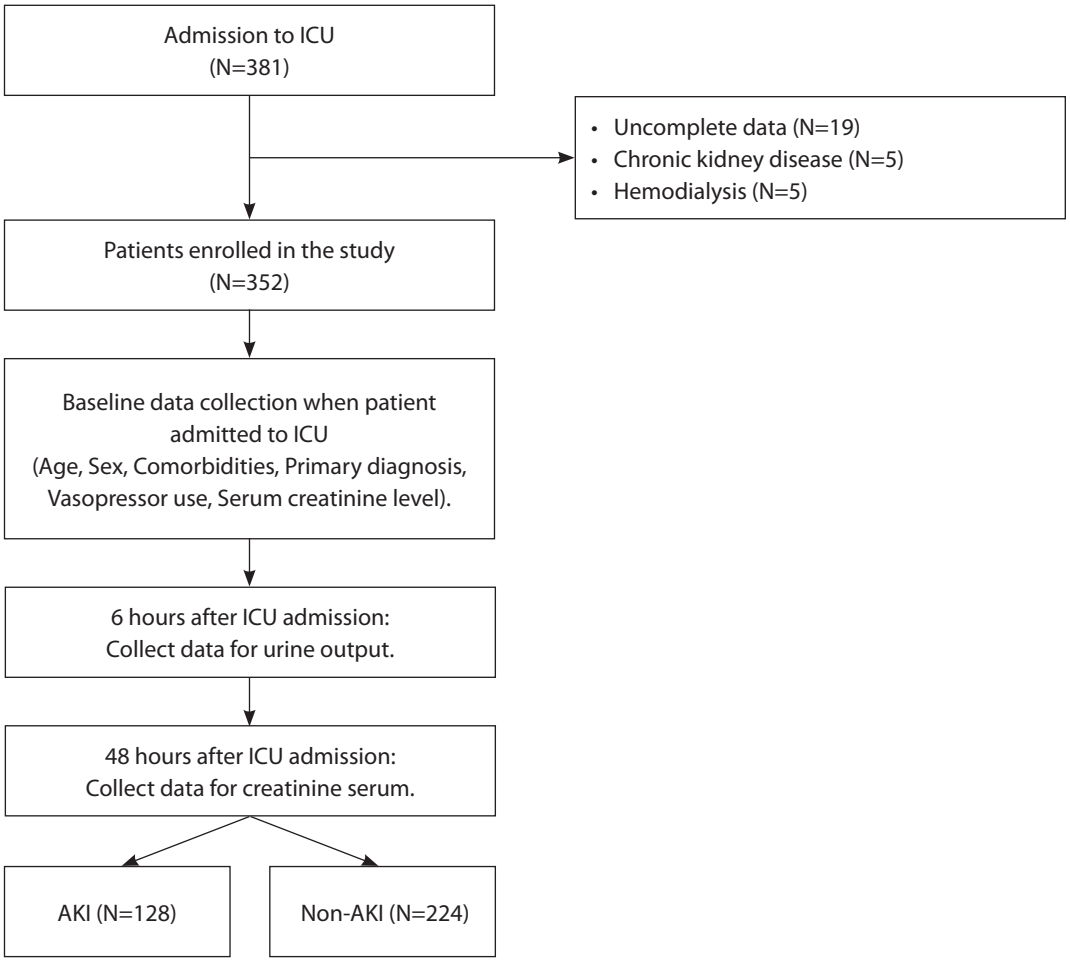

Figure 1. Study flow diagram.

presence of sepsis was determined by Sepsis-3 criteria (suspected infection plus two out of four systemic inflammatory response syndrome (SIRS) criteria; axilla temperature more than 38.3°C or less than 36°C, heart rate more than 90 bpm, respiratory rate more than 20 or $PaCO_2$ less than 32 mmHg, white blood cell count more than 12,000 or less than 4,000). The laboratory data were also evaluated, which includes serum creatinine levels at the intensive care unit (ICU) and during therapy, serum urea levels, serum electrolyte levels (sodium, potassium, chloride), and other important parameters like hemoglobin, leukocyte count, and lactate.

The definition of AKI was established according to the KDIGO criteria, which serves as a globally recognized standard for diagnosing and categorizing AKI. The diagnosis of AKI based on alterations in serum creatinine levels or urine output occurring within a 48-hour timeframe. The KDIGO criteria for AKI in this study was AKI stage 1 which include a rise in serum creatinine of at least 0.3 mg/dL within 48 hours a rise in serum creatinine of at least 1.5 times the baseline value within 7 days, and a urine output of less than 0.5 mL/kg/hour for 6 hours (12).

Ethical Approval

The study has received ethical approval from Health Research Ethics Committee of Faculty of Medicine, Andalas University, Padang, Indonesia

(LB.01.03/5/8/501/2023). The study techniques adhered to the principles outlined in the Declaration of Helsinki and relevant ethical guidelines.

Statistical Analysis

The data were analyzed using the statistical program SPSS version 26 (IBM, Jakarta, Indonesia). The study employed descriptive analysis to provide a detailed description of the demographic and clinical characteristics of the patients, as well as the occurrence rate of AKI. The AKI and non-AKI groups were compared using bivariate analysis, employing either the chi-square test or an independent t test to examine their features. The study employed multivariate logistic regression analysis to determine the factors that independently predict the occurrence of AKI. The regression model included only the variables that showed statistical significance (P<0.05) in the bivariate analysis. Only factors that maintained their significance after accounting for other variables made up the final model. AKI predictor scores were derived using the regression coefficients from the final model. The score for each variable is obtained by multiplying its regression coefficient with the corresponding scale factor. The cumulative score is determined by summing the scores of all predictor factors. The performance of the AKI prediction score was assessed by calculating the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. The AUC is a metric that quantifies the discriminatory power of a prediction model. A value of 0.5 suggests that the model performs no better than random guessing, while a value of 1.0 indicates a flawless prediction model.

Results

Table 1 displays the demographic and clinical characteristics of patients who encountered AKI and those who did not (non-AKI) while receiving care in the intensive care unit (ICU). There was a significant difference in age between the AKI and non-AKI groups, with a p-value of less than 0.001. The median age of AKI patients was 65 years (IQR 55–72), which was higher than the median age of non-AKI patients at 52 years (IQR 40–60). The gender distribution between the two groups did not show any statistically significant difference (P=0.985), suggesting that gender is not a risk factor for AKI in this population. The prevalence of hypertension was significantly greater in AKI patients (64.1%) compared to non-AKI patients (45.5%) (P<0.001). While there was a difference in the incidence rate between the two groups, this difference did not reach statistical significance. There was a notable disparity in the primary diagnosis between the two groups, with a P-value of less than 0.001. AKI patients had a higher prevalence of sepsis (43.0%) compared to non-AKI patients (14.3%). The utilization of vasopressors was significantly higher in AKI patients (53.1%) compared to non-AKI patients (20.1%) (P<0.001). There was a notable disparity in serum creatinine levels upon admission to the intensive care unit (ICU) and in 48 hours between the two groups (P<0.001). Patients with acute kidney injury (AKI) exhibited a higher median serum creatinine concentration of 1.3 mg/dL in comparison to non-AKI patients. Table 1 demonstrates that being over 60 years old, having hypertension, sepsis, using vasopressors, and having a serum creatinine level greater than 1.0 mg/dL at admission to the ICU are significant factors that increase the risk of AKI in ICU patients.

Table 2 displays the results of a multivariate logistic regression analysis that identifies autonomous risk factors for the incidence of AKI in patients in the intensive care unit. The predictors examined in this study were age over 60 years, a previous diagnosis of chronic kidney disease, sepsis, the use of vasopressors, and a serum creatinine level exceeding 1.0 mg/dL upon admission to the intensive care unit. This study included these variables in logistic regression model to develop a predictive score for the likelihood of acute kidney injury in ICU patients.

Patients aged 60 and above had a 3.21-fold greater probability of suffering AKI compared to younger patients (P<0.001). Patients who have previously had chronic kidney disease are at a

Table 1. Demographical and Clinical Characteristics of Patients

Characteristics	AKI (N=128)	Non-AKI (N=224)	P-value
Age (years), median (IQR	65 (55-72)	52 (40-60)	<0.001*
Gender, N (%)			
Male	78 (60.9)	136 (60.7)	0.985†
Female	50 (39.1)	88 (39.3)	
Comorbid disease, N (%)			
Hypertension	82 (64.1)	102 (45.5)	<0.001†
Diabetes mellitus	45 (35.2)	58 (25.9)	0.085†
Heart disease	38 (29.7)	42 (18.8)	0.032†
Chronic lung disease	25 (19.5)	30 (13.4)	0.128†
Chronic liver disease	12 (9.4)	18 (8.0)	0.679†
Main diagnosis, N (%)			
Sepsis	55 (43.0)	32 (14.3)	<0.001†
Heart failure	28 (21.9)	40 (17.9)	0.315†
Pneumonia	20 (15.6)	35 (15.6)	0.999†
Trauma/injury	15 (11.7)	22 (9.8)	0.603†
Others	10 (7.8)	95 (42.4)	<0.001†
Vasopressor use, N (%)	68 (53.1)	45 (20.1)	<0.001†
Serum creatinine levels upon admission to ICU (mg/dL), median (IQR)	1.3 (1.0-1.8)	0.8 (0.6-1.0)	<0.001*
Serum creatinine levels in 48 hours after admission (mg/dL), median (IQR)	2.0 (1.5-2.8)	0.9 (0.7-1.2)	<0.001*
Urine output (mL/kg/hour), median (IQR)	0.3 (0.2-0.4)	0.8 (0.6-1.0)	<0.001*

*Independent t-test; †Chi-square test.

Table 2. Independent Predictors of Acute Kidney Injury (AKI) Determined by a Multivariate Logistic Regression Analysis

Predictors	Regression coefficient	Odds ratio (OR)	95% confidence interval (CI)	P-value*
Age >60 years old	1.17	3.21	1.85 - 5.56	<0.001
History of chronic kidney disease	1.15	2.87	1.54 - 5.34	<0.001
Sepsis	2.43	4.72	2.58 - 8.65	<0.001
Vasopressor use	1.38	3.98	2.25 - 7.04	<0.001
Serum creatinine levels upon admission to ICU >1.0 mg/dL	0.92	2.53	1.42 - 4.51	<0.001

*Multivariate logistic regression analysis.

significantly increased risk, 2.87 times greater, of developing acute kidney injury (P<0.001). Patients diagnosed with sepsis had a risk of having acute kidney injury (AKI) that was 4.72 times greater than that of those without sepsis (P<0.001). Patients who were administered vasopressors had a 3.98-fold increased chance of developing AKI (P<0.001). Patients admitted to the ICU with serum creatinine levels exceeding 1.0 mg/dL had a 2.53-fold increased chance of developing AKI (P<0.001) with median value for AKI group is 1.3 (IQR 1.0-1.8) and non AKI group is 0.8 (IQR 0.6-1.0). All predictors in Table 2 have a P value less than 0.001, indicating that the results are highly statistically significant. Therefore, all these predictors can be deduced as significant independent risk factors for the onset of AKI in patients in the intensive care unit.

This study's multivariate logistic regression analysis yielded the AKI predictor score, which Table 3 displays. The regression coefficient quantifies the extent to which a predictor variable affects the likelihood of AKI, while also taking into account the impact of other predictor factors. In logistic regression analysis, the regression coefficient were computed using a natural logarithm (ln) scale. The regression coefficient was transformed into an OR to facilitate understanding, comparing the likelihood (odds) of AKI between two patient groups with a one unit difference in the predictor variable. For example, the regression coefficient for people over the age of 60 is 1.17. Each additional year of age above 60 raises the likelihood of AKI by a factor of 3.21, after accounting for the impact of other predictor variables. In order to create an AKI predictor score, the regression coefficient of each predictor variable is multiplied by a uniform scale factor. This results in a rounded score that is straightforward to read. The study utilized a scale factor of 10, resulting in a range of 0–10 for the AKI predictor score. The AKI predictor score is determined by summing the scores of all predictor variables. As the total score increases, so does the patient's risk of developing AKI.

Table 3. Acute Kidney Injury Predictor Score

Predictors	Score*
Age > 60 years old	2
History of chronic kidney disease	2
Sepsis	3
Vasopressor use	2
Serum creatinine levels upon admission to ICU >1.0 mg/dL	1

*Range scale from 0-10. Low risk score: 0-3, high risk score: 8-10.

The ROC curve depicted in Figure 2 demonstrates the AKI prediction score's efficacy in distinguishing between patients who develop AKI and those who do not. AUC=0.85 implies that the predictor score has high accuracy in predicting AKI. A model's performance improves when the ROC curve deviates more from the diagonal line, which represents a random prediction model. A 95% confidence interval (CI) of 0.80-0.90 suggests that there is a 95% probability that the actual AUC value in the population falls within that specific range. This demonstrates the reliability of the study's findings and their applicability to a broader population.

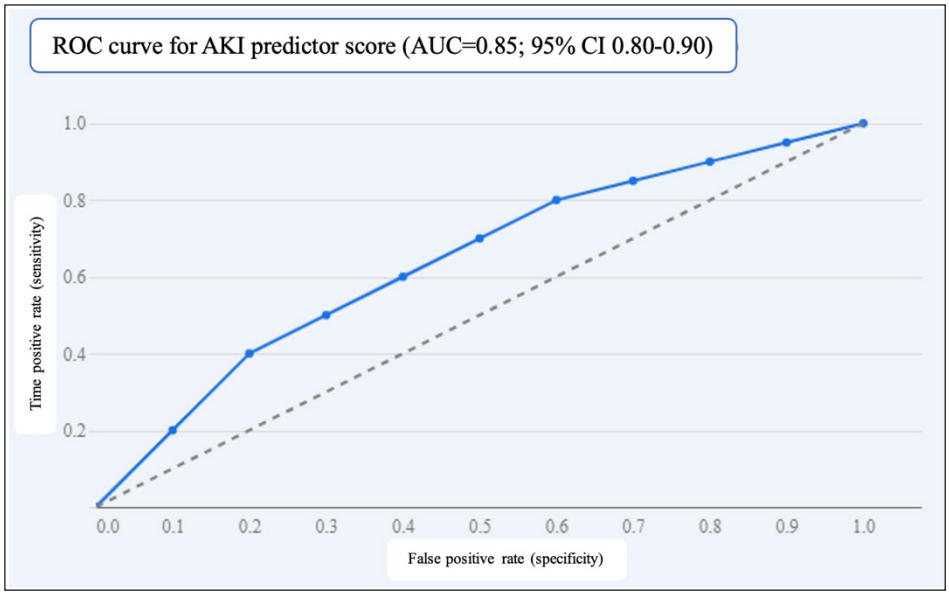

Figure 2. ROC curve for AKI predictor score.

Discussion

This study successfully identified five important independent predictors of acute kidney injury (AKI) development in intensive care unit (ICU) patients in Padang City, Indonesia. Individuals aged over 60 years, those with a history of chronic kidney disease, those with sepsis, those who have used vasopressors, and those with a serum creatinine level exceeding 1.0 mg/dL at admission to the intensive care unit are among the predictors. The findings align with current scientific evidence and enhance our understanding of the etiology of AKI and its therapeutic implications. Aging is an intricate and multifaceted physiological process that impacts different organ systems, including the kidneys. As individuals get older, their kidney function gradually declines (13). This includes a reduction in glomerular filtration rate (GFR), a decrease in kidney mass, and a decrease in the ability to concentrate urine. The decline in kidney function in elderly adults increases their susceptibility to stressors that might induce AKI, such as hypovolemia, infections, and drug-induced nephrotoxicity (14, 15). Furthermore, older adults frequently have comorbidities such as hypertension, diabetes mellitus, and cardiovascular disease, which heighten the risk of AKI. These coexisting medical conditions can hasten the deterioration of kidney function and heighten the vulnerability to sudden kidney damage. People with chronic kidney disease (CKD) have limited renal function, which makes them more likely to have their kidney function decline due to things like low blood volume, infections, and medications that damage the kidneys. Even a slight reduction in GFR can result in medically significant acute kidney injury in individuals with chronic kidney disease (14). Also, people with chronic kidney disease often have problems with their electrolytes, metabolic acidosis, and anemia. These can make the patient's condition worse and increase the risk of complications related to AKI.

Sepsis is a primary contributor to the development of AKI in the ICU (9, 16). Sepsis induces a multifaceted systemic inflammatory reaction that involves the liberation of several inflammatory agents, including cytokines, chemokines, and free radicals (17). The presence of these inflammatory mediators can lead to impaired endothelial cell function, reduced kidney blood flow, and tubule damage, all of which contribute to the development of AKI (18, 19). Also, people with sepsis often have low blood pressure, less blood volume, and are given vasopressor drugs, all of which can make it harder for the kidneys to work and increase the risk of AKI. Vasopressors are administered to elevate blood pressure in individuals experiencing hypotension or shock (20, 21). Nevertheless, the administration of vasopressors can induce renal vasoconstriction, diminish renal blood flow, and initiate renal ischemia. Renal ischemia can cause tubular cell damage and initiate AKI. Furthermore, vasopressors can affect renal endothelial cell function and increase glomerular capillary permeability. This might result in the presence of protein in the urine and worsen damage to the kidneys.

The body eliminates serum creatinine, a byproduct of the breakdown of creatine phosphate in muscle, through the kidneys. Rising levels of serum creatinine are indicative of a decline in the GFR and serve as an early indication of compromised kidney function (22). Patients who have serum creatinine levels greater than 1.0 mg/dL upon admission to the ICU are at a heightened risk of developing AKI due to pre-existing impairment of their kidney function. Numerous causes during care in the ICU, such as hypovolemia, sepsis, and the administration of nephrotoxic medications, can exacerbate the compromised kidney function (22, 23). Compelling evidence of biological plausibility supports the conclusions of this investigation.

Aging leads to a decline in the kidneys' normal functioning, while a previous diagnosis of chronic kidney disease implies past kidney damage (14). Sepsis initiates a widespread inflammatory reaction that can harm the kidneys. The use of vasopressors can cause the kidneys' blood vessels to narrow and blood flow to be reduced, resulting in tissue damage (20). Elevated levels of creatinine in the blood suggest impaired kidney function. The

results of this investigation are consistent with prior studies conducted in various regions around the world. Multiple studies have identified age, previous chronic kidney disease, sepsis, and the use of vasopressors as separate risk factors for AKI among patients in the ICU (24-26). Additional research has also demonstrated that the levels of serum creatinine upon admission to the ICU are a significant indicator of AKI (27).

This work has significant therapeutic implications for the management of patients in the intensive care unit. This study establishes a solid foundation for the creation of prevention and early intervention programs by identifying separate risk factors for AKI. Once generated, the AKI predictor score serves as a valuable tool for identifying patients who are at a higher risk of developing AKI and assessing their individual risk levels. AKI prediction scores can serve as a helpful tool in guiding clinical decision-making in the ICU. We might subject patients with elevated scores to enhanced monitoring, enabling prompt intervention to avert or mitigate the severity of AKI. Possible therapies may involve adjusting fluid volume, refraining from using nephrotoxic medications, and constantly monitoring renal function.

However, our study has limitations. We conducted the study in Padang city, West Sumatra, where the population primarily consists of Malay and Minang ethnicities. While this research makes a significant contribution to the understanding of AKI in Indonesian ICU patients, additional research is still required. The AKI predictor score that has been created must undergo external validation in a larger and more diversified group of patients in the intensive care unit in Indonesia. There is a need for future studies that have specific plans to assess the effects of using AKI predictor scores on patient clinical outcomes, including death, length of hospital stay, and the requirement for renal replacement medication. Novel biomarkers like NGAL, KIM-1, and IL-18 could be used to help predict AKI, but more research needs to be done on this topic. Utilizing both biomarkers and clinical predictor scores can improve AKI prediction precision and provide more targeted therapies (12, 24). Additional investigation could reveal additional risk factors that may lead to AKI in ICU patients, including genetics, environmental variables, and pharmacological interactions.

Conclusion

This study clearly shows that people over 60 who have had chronic kidney disease, sepsis, or used vasopressors in the past, or who had serum creatinine levels above 1.0 mg/dL when they were admitted to the ICU in Padang City, Indonesia, are at a higher risk for acute kidney injury. The newly created AKI predictor score has the potential to enhance ICU patients' treatment by facilitating prompt identification, risk assessment, and early intervention in patients with a high likelihood of developing AKI. Additional research is required to confirm and improve the use of these prediction scores in clinical practice.

What Is Already Known on This Topic:

Several AKI diagnostic tools to assist doctors in identifying individuals at heightened risk for AKI has been established. The scores utilize a range of clinical and laboratory factors, including age, comorbidities, administration of nephrotoxic medications, and fluctuations in blood creatinine levels, to determine the likelihood of AKI for individual patients. These ratings are limited in their ability to accurately predict AKI in patients with specific circumstances, including chronic kidney disease, multiple organ failure, and those receiving renal replacement therapy.

What This Study Adds:

This study establishes a solid foundation for the creation of prevention and early intervention programs by identifying separate risk factors for AKI. Once generated, the AKI predictor score serves as a valuable tool for identifying patients who are at a higher risk of developing AKI and assessing their individual risk levels. AKI prediction scores can serve as a helpful tool in guiding clinical decision-making in the ICU. The newly created AKI predictor score has the potential to enhance ICU patients' treatment by facilitating prompt identification, risk assessment, and early intervention in patients with a high likelihood of developing AKI.

Conflict of Interest: The author declares that she has no conflict of interest.

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