Acute kidney injury incidence and acute renal replacement modality in intensive care unit patients in Indonesia: A result from Southeast Asia-Acute Kidney Injury Study

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Abstract

Background : Currently, there is limited data of large databases of acute kidney injury (AKI) epidemiology from Southeast Asia, especially in Indonesia, the biggest countries in. Therefore, we aimed to provide demographic data of intensive care unit (ICU) patients with AKI and the utilization of renal replacement therapy (RRT) in Indonesia.

Methods : We collected demographic and clinical data from 952 ICU patients. Patients were classified into AKI and non-AKI. AKI was classified according to the Kidney Disease Improving Global Outcome (KDIGO) criteria in three stages. We then assess the Acute Physiology and Chronic Health Evaluation (APACHE) II score of AKI and non-AKI patients. RRT modalities were listed down by the number of procedures conducted.

Results : Overall incidence of AKI was 43%, distributed among three stages: 18.5 % stage 1, 33% stage 2, 48.5 % stage 3. Patients developing AKI need mechanical ventilation more often in comparison with non-AKI. Patients with AKI have an average APACHE score of 16.5, while non-AKI patients have an average score of 9.9. Among AKI patients, 24.6% requires RRT. The most common RRT modalities were intermittent hemodialysis (69.4%), followed by slow low efficiency dialysis (22.1%), continuous renal replacement therapy (4.2%), and peritoneal dialysis (1.1%).

Conclusions: This study showed that AKI is a common problem in Indonesian ICU with containing a high mortality rate. We strongly believe that identification the risk factor of AKI will provide the opportunity to develop the predictability score for AKI prevention and finally improve AKI outcome.

Background

Acute kidney injury (AKI) is a common problem and often associated with high morbidity and mortality worldwide. The International Society of Nephrology (ISN) truly emphasizes the importance of preventing mortality of untreated AKI in low resource regions by 2025. This notion is emphasized towards poor countries with poor medical access and resources in Africa, Latin America, and Asia.⁽¹⁾ Acute kidney injury occurring in the intensive care unit (ICU) patients complicates and further worsen their clinical condition. Recently, the incidence of AKI varies between 6–70% among patients treated in the ICU and 57% of ICU patients tend to develop AKI.⁽²⁾

On average, 5% of ICU patients with severe AKI require renal replacement therapy (AKI-RRT).⁽³⁾ AKI in ICU patients presents with diverse forms of clinical outcomes such as prolonged ICU stay by 3.5 days, reduced health-related quality of life, a requirement of mechanical ventilation, and detrimental clinical consequences (acid-base disorders, hypervolemia, hyperkalemia, uremia, immune system depression). These variables are highly associated with the current mortality rates of AKI patients ranging from 40–60%.^(4, 5) These findings suggested that ICU patients are highly susceptible to AKI and most of the time portends poor prognosis.

This study aimed to fill in the gap of the minimal amount of AKI epidemiology data in Indonesia. Moreover, we intended to explore the risk factors of AKI and evaluate the incidence of acute RRT-treated in ICU.

Methods

Patient and data collection

This study was a prospective observational study in ICU of the Gatot Soebroto Indonesia Central Army Hospital. We collected ICU database for adult patients from January 2017 until December 2018, and further staged the severity of the disease (stage I - III). We enrolled patients aged > 15 years. Patients with end-stage renal disease (ESRD) on chronic dialysis were excluded (Fig. 1). For patients with multiple admissions, we collected data from only the first admission. The study protocol was reviewed by the institutional review boards (IRB No. B/2212/VIII/2019) and the need for informed consent was waived.

Demographic and clinical data from all patients were collected, such as admission date, gender, age, body mass index (BMI), primary diagnosis at ICU admission, history of comorbid conditions, AKI stages, RRT modes and mechanical ventilation during ICU stay. Severity of the patient's was determined with the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scoring system. RRT modes was recorded accordingly per technique, the main-4 techniques are acute peritoneal dialysis (PD), intermittent hemodialysis (IHD), sustained low efficiency dialysis (SLED), and continuous renal replacement therapy (CRRT). We recorded the amount of each technique used most or as an initiation mode throughout the period of January 2017-December 2018 for each patient.

Definition And Classification Of Acute Kidney Injury

Definition of AKI was determined based on the worst of either creatinine or urine output criteria during hospital stay. Urine output was hourly measured during ICU stay. The cutoffs for AKI were based on the KDIGO criteria as meeting one of the following criteria: an increase serum creatinine of ≥ 0.3 mg/dL (≥ 26.4 μ mol/L) or an increase in creatinine $\geq 50\%$ (1.5 fold from baseline) in a 48-hour time frame, or reduction in urine output with documented oliguria of ≤ 0.5 mL/kg per hour for ≥ 6 hours. Patients were divided into three groups according to the KDIGO criteria: stage 1–3.⁽⁶⁾ When a patient's condition met the aforementioned criteria, the patient was classified as stage 1 AKI. In the case of more severe derangement, i.e., a decrease in GFR $\geq 50\%$ or an increase in creatinine $\geq 100\%$ (2 fold from baseline) in a 48-hour time frame, or a reduction in urine output with documented oliguria of ≤ 0.5 mL/kg per hour for ≤ 12 hours, stage 2 AKI was defined. Stage 3 AKI was defined as follows: a decrease in GFR $\leq 75\%$ or an increase in creatinine $\geq 200\%$ (3 fold from baseline) in a 48-hour time frame, or a reduction in urine output with documented oliguria of ≤ 0.3 mL/kg per hour for ≥ 24 hours or anuria for ≥ 12 hours. Serum creatinine ≥ 4.0 mg/dL with acute increase of ≥ 0.5 mg/dL was also defined as stage 3 AKI.⁽⁷⁾

Statistical analysis

Categorical data were presented as counts and percentages. Continuous data were presented as mean and standard deviation (SD) if normally distributed or median with interquartile range if non-normally distributed. Kaplan-Meier survival curves were also generated for each AKI class. The Chi-square test of independence was used to compare the proportions of different types of patients between patients by AKI status, whereas as ANOVA was used to compare continuous patient characteristics by AKI status.

Results

Flow chart of the study can be seen in Fig. 1. Among all study participants (N = 952), 87 were excluded because 1 patient is admitted with no creatinine data and 86 patients are admitted due to ESRD. From 865 patients, almost half of the patients (43%) suffer from AKI. In terms of staging, 48.5% patients suffered from stage III AKI, far higher than the number of patients with AKI stage I, 18.5%, and AKI stage II, 33%.

Among all ICU patients diagnosed with AKI, the average age of those patients was 58 ($\pm$ 15) years old and 64.6% were male. Patients primary diagnosis upon ICU admission were most likely due to surgical-related disease, 23.5% (N = 87), cardiovascular disease, 19.2% (N = 71), and neurologic disease, 15.9% (N = 59). Metabolic problems such as hypertension 39.4% (N = 147) and diabetes mellitus 38.9% (N = 145) happened to be the most common comorbid conditions in AKI patients. Table 1 showed statistically significant difference between AKI patients and non-AKI patients in need of mechanical ventilation, when 49.6% of AKI patients (N = 185) need mechanical ventilation, and only 17.3% in non-AKI patients (N = 85). The severity scoring (APACHE II) was significantly higher in AKI patients (17.1) compared to non-AKI patients (11.2). Non-renal SOFA score was also found to be significantly higher in AKI patients compared to non-AKI patients (5.0 vs 3.0, $p < 0.001$). (Fig. 2)

Table 1
Patients characteristics stratifies by AKI status (N = 865)

Characteristics	Non-AKI (N = 492)	AKI (n = 373)	All (N = 865)	P-value
Age, years, mean (sd)	55 (15)	58 (15)	57 (15)	0.008
Male gender, n (%)	297 (60.4)	219 (58.7)	516 (59.7)	0.62
Reimbursement	(N = 486)	(N = 362)	(N = 848)	0.45 ¹
- Government officer	261 (53.7)	190 (52.5)	451 (53.2)	
- Private health insurance	0 (0.0)	2 (0.6)	2 (0.2)	
- Social security system	211 (43.4)	159 (43.9)	370 (43.6)	
- Cash/self-pay	14 (2.9)	10 (2.8)	24 (2.8)	
- Unknown	0 (0.0)	1 (0.3)	1 (0.1)	
BMI, n (%)				< 0.001
- Underweight	14 (2.8)	16 (4.3)	30 (3.5)	
- Normal	421 (85.6)	287 (76.9)	708 (81.8)	
- Overweight	54 (11.0)	56 (15.0)	110 (12.7)	
- Obese	3 (0.6)	14 (3.8)	17 (2.0)	
Primary diagnosis, n (%)	(N = 491)	(N = 370)	(N = 861)	< 0.001
- Cardiovascular diseases	106 (21.6)	71 (19.2)	177 (20.6)	
- Endocrine Diseases	11 (2.2)	18 (4.9)	29 (3.4)	
- Gastrointestinal Diseases	13 (2.6)	18 (4.9)	31 (3.6)	
- Hematologic Diseases	1 (0.2)	1 (0.3)	2 (0.2)	
- Infectious Diseases	14 (2.9)	36 (9.7)	50 (5.8)	
- Neurologic Diseases	42 (8.6)	59 (15.9)	101 (11.7)	
- Oncologic Diseases	13 (2.6)	12 (3.2)	25 (2.9)	

BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation II, SOFA: sequential organ failure assessment.

†All these parameters came from the first day of ICU admission.

*P value from Fisher's exact test instead of chi-square

Characteristics	Non-AKI (N = 492)	AKI (n = 373)	All (N = 865)	P-value
- Renal Diseases	9 (1.8)	29 (7.8)	38 (4.4)	
- Respiratory Diseases	17 (3.5)	36 (9.7)	53 (6.2)	
- Rheumatologic Diseases	0 (0.0)	3 (0.8)	3 (0.3)	
- Surgical related diseases	265(54.0)	87(23.5)	352(40.9)	
Comorbidity, n (%)				
HT	210 (42.7)	147 (39.4)	357 (41.3)	0.33
DM	114 (23.2)	145 (38.9)	259 (29.9)	< 0.001
CKD	3 (0.6)	43 (11.5)	46 (5.3)	< 0.001 [†]
Cerebrovascular	4 (0.8)	11 (2.9)	15 (1.7)	0.017
Malignancy	24 (4.9)	18 (4.8)	42 (4.9)	0.97
CAD	52 (10.6)	19 (5.1)	71 (8.2)	0.004
APACHE-II score, mean (sd)	9.9 (4.4)	16.5 (7.3)	12.7 (6.7)	< 0.001
Non-renal SOFA score, mean (sd)	3.0 (1.6)	5.0 (2.5)	3.9 (2.3)	< 0.001
Vasopressors, n (%)	4 (0.8)	41 (11.0)	45 (5.2)	< 0.001
Mechanical ventilation, n (%)	85 (17.3)	185 (49.6)	270 (31.2)	< 0.001
BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation II, SOFA: sequential organ failure assessment.				
†All these parameters came from the first day of ICU admission.				
*P value from Fisher's exact test instead of chi-square				

Table 2 further elaborates the risk factors for developing AKI. it shows that patients who developed AKI during ICU stay are 4.53 times more likely to be admitted to the ICU with renal disease as their primary diagnosis, and has 1.14 times more likely to have higher APACHE II compare to those without AKI.

Table 2
Risk factors for AKI development using logistic regression analysis.

• Characteristics	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age, 10-year increment	1.11 (1.02, 1.22)	0.019	0.90 (0.80, 1.02)	0.11
Male gender, n (%)	0.93 (0.70, 1.22)	0.598		
Reimbursement, N = 834				
- Government officer	0.98 (0.74, 1.29)	0.869		
- Social security system	Reference			
- Private health insurance /Cash/self-pay	1.18 (0.53, 2.61)	0.690		
BMI				
- Underweight	1.60 (0.76, 3.36)	0.217	1.18 (0.48, 2.91)	0.73
- Normal	Reference		Reference	
- Overweight / obese	1.67 (1.14, 2.47)	0.009	1.55 (0.97, 2.49)	0.07
Primary diagnosis**, N = 846				
- Cardiovascular diseases	0.90 (0.64, 1.26)	0.528		
- Endocrine Diseases	2.31 (1.08, 4.95)	0.032	0.97 (0.38, 2.49)	0.95
- Gastrointestinal Diseases	1.94 (0.94, 4.02)	0.073	1.20 (0.49, 2.99)	0.69
- Hematologic Diseases	1.37 (0.09, 21.99)	0.824		
- Infectious Diseases	3.81 (2.02, 7.17)	< 0.001	1.15 (0.51, 2.57)	0.74

†All these parameters came from the first day of ICU admission

‡exclude 15 patients who had AKI as the primary diagnosis for ICU admission

BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation I, SOFA: sequential organ failure assessment. NA: not included in the multivariable model even if *P < 0.20 because it didn't have enough data

• Characteristics	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
- Neurologic Diseases	2.06 (1.35, 3.15)	0.001	0.97 (0.53, 1.77)	0.92
- Oncologic Diseases	1.27 (0.57, 2.83)	0.552		
- Renal Diseases	3.87 (1.61, 9.31)	0.003	4.53 (1.67, 12.33)	0.003
- Respiratory Diseases	2.92 (1.61, 5.32)	< 0.001	1.53 (0.72, 3.25)	0.27
- Surgical related diseases	0.27 (0.20, 0.37)	< 0.001	0.60 (0.39, 0.93)	0.021
Comorbidity***				
HT	0.88 (0.66, 1.16)	0.348		
DM	2.05 (1.52, 2.77)	< 0.001	1.08 (0.73, 1.61)	0.71
Cerebrovascular	3.83 (1.21, 12.13)	0.022	1.55 (0.39, 6.17)	0.53
Malignancy	1.02 (0.55, 1.91)	0.946		
CAD	0.47 (0.27, 0.81)	0.006	0.50 (0.26, 0.98)	0.042
APACHE-II score	1.21 (1.17, 1.25)	< 0.001	1.14(1.09, 1.20)	< 0.001
Non-renal SOFA score	1.62 (1.49, 1.76)	< 0.001	1.14 (1.00,1.31)	0.050
Vasopressors	13.08 (4.61, 37.17)	< 0.001	2.99 (0.93, 9.62)	0.067
Mechanical ventilation	4.76 (3.49, 6.51)	< 0.001	1.29 (0.80, 2.08)	0.30
†All these parameters came from the first day of ICU admission				
‡exclude 15 patients who had AKI as the primary diagnosis for ICU admission				
BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation I, SOFA: sequential organ failure assessment. NA: not included in the multivariable model even if *P < 0.20 because it didn't have enough data				

Among those patients who received RRT support, IHD is the most common procedure used as the initial mode of RRT in ICU (66 procedures, 71.7%), followed by SLED (21 procedures, 22.8%), then CRRT (4

procedures, 4.34%) and acute PD (1 procedure, 1.08%). (Table 3)

Table 3
Mode of RRT (initiation mode if there were many most used modes with same duration)

Mode of RRT	N (%)
IHD	66 (71.7)
CRRT	4 (4.34)
PD	1 (1.08)
SLED	21 (22,8)
IHD: intermittent hemodialysis, CRRT: continuous renal replacement therapy, PD: peritoneal dialysis, SLED; sustained low efficiency dialysis	

Table 4 summarized the severity in AKI patients. The number of patients who were grouped into severe AKI reached 48.5% of the populations with AKI (N = 181). Based on multivariate analysis using logistic regression, patients who developed severe AKI are 2.47 times more likely to be male, 9.47 times more likely to have CKD and 3.43 times more likely to have malignancy as their comorbidities. They also more likely to have higher APACHE II score (OR: 1.07; 95% CI: 1.01–1.13), compare to less severe AKI patients. Patients with severe AKI were also 5.41 times more likely to require vasopressors during their ICU stay.

Table 4

Patients characteristics and risk factors for severity of AKI using logistic regression (N = 226)

Characteristics	Severity of AKI, n (%)					
	Non-severe (N = 192)	Severe (N = 181)	Unadjusted OR (95% CI)	P- value	Adjusted OR (95% CI)	P- value
Age, 10-year increment [†]	59 (14)	57 (15)	0.93 (0.81, 1.07)	0.284		
Male gender, n (%)	98 (51.0)	121 (66.9)	1.93 (1.27, 2.94)	0.002	2.47 (1.48, 4.12)	0.001
Reimbursement, N = 361						
- Government officer	96 (51.3)	94 (54.0)	1.04 (0.68, 1.59)	0.85		
- Social security system	82 (43.9)	77 (44.3)	Reference			
- Private health insurance/Cash/self-pay	9 (4.8)	3 (1.7)	0.35 (0.09, 1.36)	0.13		
BMI						
- Underweight	6 (3.1)	10 (5.5)	2.32 (0.82, 6.56)	0.11	2.26 (0.7, 7.32)	0.18
- Normal	167 (87.0)	120 (66.3)	Reference		Reference	
- Overweight / obese	19 (9.9)	51 (28.2)	3.74 (2.10, 6.65)	< 0.001	2.26 (0.7, 7.32)	0.18
Primary diagnosis, N = 370						
- Cardiovascular diseases	40 (21.1)	31 (17.2)	0.78 (0.46, 1.31)	0.35		
- Endocrine Diseases	12 (6.3)	6 (3.3)	0.51 (0.19, 1.39)	0.19	0.41(0.12, 1.44)	0.16
†Value in cell is mean (sd) instead of n (%)						
‡All these parameters came from the first day of ICU admission						
BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation II, SOFA: sequential organ failure assessment						
NA: not included in the multivariable model even if P < 0.20 because it didn't have enough data						

Characteristics	Severity of AKI, n (%)					
	Non-severe (N = 192)	Severe (N = 181)	Unadjusted OR (95% CI)	P- value	Adjusted OR (95% CI)	P- value
- Gastrointestinal Diseases	11 (5.8)	7 (3.9)	0.65 (0.25, 1.74)	0.40		
- Hematologic Diseases	0 (0.0)	1 (0.6)	NA			
- Infectious Diseases	13 (6.8)	23 (12.8)	2.00 (0.98, 4.07)	0.058	1.24 (0.51, 2.97)	0.64
- Neurologic Diseases	27 (14.2)	32 (17.8)	1.31 (0.75, 2.28)	0.35		
- Oncologic Diseases	6 (3.2)	6 (3.3)	1.06 (0.33, 3.34)	0.92		
- Renal Diseases	8 (4.2)	21 (11.7)	3.00 (1.30, 6.97)	0.010	1.5 (0.5, 4.56)	0.47
- Respiratory Diseases	16 (8.4)	20 (11.1)	1.36 (0.68, 2.71)	0.38		
- Rheumatologic Diseases	1 (0.5)	2 (1.1)	2.12 (0.19, 23.62)	0.54		
- Surgical related diseases	56 (29.5)	31 (17.2)	0.50 (0.30, 0.82)	0.006	0.8 (0.43, 1.49)	0.48
Comorbidity						
HT	70 (36.5)	77 (42.5)	1.29 (0.85, 1.96)	0.23		
DM	63 (32.8)	82 (45.3)	1.70 (1.11, 2.58)	0.014	1.15 (0.65, 2.02)	0.63
CKD	4 (2.1)	39 (21.5)	12.91 (4.51, 36.96)	< 0.001	9.47 (3.1, 28.91)	< 0.001

†Value in cell is mean (sd) instead of n (%)

‡All these parameters came from the first day of ICU admission

BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation II, SOFA: sequential organ failure assessment

NA: not included in the multivariable model even if P < 0.20 because it didn't have enough data

Characteristics	Severity of AKI, n (%)					
	Non-severe (N = 192)	Severe (N = 181)	Unadjusted OR (95% CI)	P- value	Adjusted OR (95% CI)	P- value
Cerebrovascular	8 (4.2)	3 (1.7)	0.39 (0.10, 1.48)	0.17		
Malignancy	6 (3.1)	12 (6.6)	2.20 (0.81, 5.99)	0.12	3.43 (1.11, 10.57)	0.032
CAD	10 (5.2)	9 (5.0)	0.95 (0.38, 2.40)	0.92		
APACHE-II score [†]	14.8 (6.9)	18.3 (7.3)	1.07 (1.04, 1.10)	< 0.001	1.07 (1.01, 1.13)	0.018
Non-renal SOFA score [‡]	4.6 (2.4)	5.5 (2.6)	1.14 (1.05, 1.24)	0.002	0.92 (0.78, 1.08)	0.29
Vasopressors	5 (2.6)	36 (19.9)	9.29 (3.55, 24.26)	< 0.001	5.41 (1.8, 16.29)	0.003
Mechanical ventilation	83 (43.2)	102 (56.4)	1.70 (1.13, 2.55)	0.012	1.31 (0.69, 2.49)	0.41
†Value in cell is mean (sd) instead of n (%)						
‡All these parameters came from the first day of ICU admission						
BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation II, SOFA: sequential organ failure assessment						
NA: not included in the multivariable model even if P < 0.20 because it didn't have enough data						

Kaplan-Meier analysis were performed for survival analysis. It was tabulated for the duration of 60 days in hospital, and 28 days in ICU. In Fig. 3(a), the curve estimates overall survival from AKI on the basis of AKI staging in the hospital. Higher AKI stages associated with a significant increase in overall hospital mortality. Figure 3(b) shows that AKI patients have higher hospital mortality than non-AKI patients. Median survival of hospital mortality for AKI patients is laid between 10 to 15 days and median survival for non-AKI patients laid in 30 days (p value < 0.001). Kaplan-Meier curve for AKI patients in ICU is steeper than the curve for non-AKI patients, this means AKI patients have higher ICU mortality compared to non-AKI patients. Median survival for AKI patients laid below 7 days, while non-AKI patients survival rate is longer and laid between 14 to 21 days (p < 0.001)

Discussion

Multiple studies have proven the detrimental impact of AKI on ICU patients, unfortunately their etiology and mechanism remain unclear. In ICU, a variety of conditions related to their reasons of admission such as infection, trauma, and other problems could prompt the induction of AKI or worsen any pre-existing condition of AKI.⁽¹⁾ Therefore, this stressed out the important to study epidemiology of each countries, especially in the countries, like Indonesia, where resources were limited and might have different risk factors for the AKI development. AKI has been reported to occur in 20–50% of patients in ICUs around the world.⁽⁸⁾ In Indonesia, at Central Army Hospital of Gatot Soebroto, almost half of ICU patients, 43% suffered from AKI. Thus, indicating that AKI is also a common problem in Indonesian ICU (Fig. 1). This high incidence of AKI may reflect the problem of public health issues and socioeconomic factors affect the epidemiology of AKI in low resource settings.⁽⁹⁾

Among 373 patients in ICU suffered from AKI, 181 patients (48.5%) belong to stage III of the KDIGO criteria for AKI. Early diagnosis for AKI in ICU patients proved to be challenging, no wonder the number of patients with severe AKI in our center is high and might require extensive studies. Contrary to the results of most published studies, our center has higher proportion of AKI stage III compare to AKI stage I or II (Fig. 1). Recently, a published study in Australia reported that 37.1% patients on ICU who developed AKI, categorized as follows: AKI stage I 18.1%; stage II 10.1%; and stage III 8.9%.⁽¹⁰⁾ Meanwhile, our data correspond to the data from less developed area. Recently, Srisawat et al reported the data from Thai ICU and showed the incidence of AKI stage 3 (28.9%) was the most common followed by stage 2 (16.4%) and stage 1 (7.5%).⁽¹¹⁾ The investigators showed that most of AKI patients have reached AKI stage 3 at the time of ICU admission and might reflect the delayed ICU admission and delayed AKI recognition as the main explanation.

In our center, based on multivariate analysis using logistic regression, the significant factors contribute toward the severity of AKI were male, patients with CKD and malignancy, higher APACHE II score, and vasopressor usage (Table 4).

The mean of patients age with AKI in our center is 58 years old ($\pm$ 15 years old), and one published study in Malaysia which showed similar result of AKI severity, with more proportion of AKI Stage 3 (56%) compare to AKI stage 1 (18%) and AKI stage 2 (25%), has similar mean of AKI patients' age with our center, 53 years old ($\pm$ 16 years old).⁽¹²⁾ But, there is no explanation on the association between age and AKI severity. Age might contribute as a risk factor of AKI occurrence in different races and countries. The causes not only because the kidney undergoes age dependent structural and functional alterations over time but also because of the comorbidities that accumulate with age.⁽¹³⁾ One experimental study using rats showed that aged rats exhibited reduced antioxidant potential and increased oxidative stress after ischemia-reperfusion, compare to young rats.⁽¹⁴⁾ This study showed that the total plasma antioxidant potential (AOP) of aged rats was lower than that of young rats regardless of whether they underwent ischemia-reperfusion. In addition, renal tissue 8-OHdG levels, which contributes to the destruction of

kidney were increased in aged rats after reperfusion injury. Elderly patients have an increased risk for non-recovery of renal function after acute ischemia and a heightened susceptibility to AKI.⁽¹⁵⁾

The two most comorbidities of AKI in our study was hypertension and diabetes mellitus, with the number of patients admitted with those conditions were 147 and 145 patients respectively. This study is comparable to previous study in 2013 showed that diabetes was associated with a 2.8 fold increased risk of developing AKI.⁽¹⁶⁾ The mechanism by which diabetes increases the severity of AKI has not yet been well established, but a great deal of research supports the connection between obesity, inflammation, and insulin resistance.⁽¹⁷⁾ Inflammatory cytokines such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) are produced by adipocytes and have been shown to cause insulin resistance.⁽¹⁸⁾

History of hypertension in patients also contributed to the increased risk of AKI incidences (OR, 1.13; 95% CI, 1.02–1.05). Hypertension is commonly found in patients with AKI and vice versa due to several mechanism with inter-related complications, such as balance disorders of vascular active substances, renin-angiotensin system activation, changes in inflammatory factors, and increases in active oxygen species.⁽¹⁹⁾ Inflammation causes changes in endothelial function and further increasing the arterial stiffness, oxidative stress and increased circulating angiotensin II levels caused by inflammation will also reduce the availability of nitric oxide (NO) and worsen the vascular damage. Thus, the combination of hypertension, increased angiotensin II levels and oxidative stress initiates events will also lead to the damage of the renal system.⁽²⁰⁾

In this study, 9.47 times more likely to have CKD as their comorbidities. In recent years, studies in different regions have found that CKD is a strong risk factor for the development of AKI, mainly in septic patients. Currently, CKD is found in 30% of patients who develop AKI in the intensive care unit (ICU).⁽²¹⁾ It is noteworthy that CKD was the variable with the highest percentage of association, which makes it a strong predictor for the development of AKI in critically ill patients.

This study confirmed that almost a half population (49.6%) of patients with AKI needed mechanical ventilation, while less than a fifth (17.3%) among non-AKI patients required the use of mechanical ventilation. Compared with ventilated non-AKI patients, ventilated AKI patients had a higher APACHE and three days SOFA score. This study result might support current view that AKI in ICU is a prominent risk factor contributes to the worsening of patients' health conditions, more specifically in low-risk AKI-RRT patients.⁽²²⁾ Based on the study conducted by Vieira, et al shows that renal dysfunction has serious consequence in the duration of mechanical ventilation and weaning from mechanical ventilation. The median duration of mechanical ventilation use in AKI patients was 3 days longer than non-AKI patients (10 vs 7 days).⁽²³⁾ The underlying mechanism that may contribute to the use of mechanical ventilation in AKI patients because patients experienced severe acute respiratory insufficiency, which will increase the intrathoracic pressure to reach acceptable gas exchange to compensate these changes. This will eventually result in renal dysfunction such as renal tubular apoptosis.⁽²²⁾

There are 92 patients (24.6%) AKI patients required RRT(AKI-RRT), this result might validate the importance of RRT in ICU settings, despite certain challenges such as availability of modalities and understaffing of nephrologist.⁽²⁴⁾ It is important to remember that AKI is a case with a staggering amount of mortality rates, especially for critically ill patients in ICU setting.⁽²⁵⁾

At our center, like most hospitals in developing country, IHD is the most commonly used method (66 procedures, 71.7%). On the other hand, a study using online questionnaire responded by members of European Society of Intensive Care Medicine from 50 countries, showed that half of the intensivists, preferred the use of CRRT compare to IHD. The reasons for preferring CRRT were the perception of better hemodynamic stability, better therapeutic effect resulting from cytokine removal and easier fluid balance control.⁽²⁶⁾

A cohort study done by Mandelbaum, et al. to measure the outcome of critically ill patients with AKI shown that the rate of hospital mortality and ICU mortality are both worse in patients with AKI at any given stage compared to in-hospital mortality rate in non-AKI patients, shown as follow: rate of mortality in non-AKI patients were 6.25%, AKI stage I 13.87%, AKI stage II 16.42%, and AKI stage III 33.76%. The ICU mortality rate is also higher in AKI patients as follow non-AKI 4.54%, AKI stage I 10.06%, AKI stage II 13.15%, and AKI stage III 30.48%.⁽²⁷⁾ A significant survival differences is shown by Kaplan-Meier survival curves according to the presence of AKI, where the curve for AKI patients survival is steeper compare to non-AKI patients. This represents worse survival rate in patients with AKI compare to non-AKI.⁽²⁸⁾ With previous published studies clearly emphasized the worse outcome in AKI patients compare to non-AKI patients, we are certain that it is important to prevent AKI from happening or to manage AKI at earlier stage. This will be beneficial to decrease the healthcare burden and bring betterment towards patients' overall survival rate.

We believe that identification the risk factor of AKI will provide the opportunity to develop the predictability score for AKI prevention and finally improve AKI outcome. Another key strength was the availability of data to permit the detailed analysis of risk factors of AKI between mild (AKI stage 1/2) and severe AKI (AKI stage 3), something that has received little attention. Another strength was that our AKI criteria were from KDIGO which employs both the information from creatinine and urine output data. This research will be a reference research for other studies of AKI patients in ICU in other hospitals, especially in Indonesia. However, this reference will improve the completeness of epidemiological data and risk factors for AKI patients in Indonesia.

Our study did have limitation. We collected data only in ICU patients in Gatot Soebroto Hospital. So our patient sample may not truly represent the incidence of AKI in all hospitalized ICU patients in all over Indonesia.

Conclusion

In Indonesia, like other developing countries, many ICU patients are at risk of developing AKI. The incidence of AKI in our center alone exceeds almost half of the patients (43%) with 48.5% belong to stage III.

Declarations

Ethics approval and consent to participate

The study protocol was reviewed by the institutional review boards (IRB No. B/2212/VIII/2019) and the need for informed consent was waived.

Consent for publication

Not applicable

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Authors' contributions

Conceived and design the study: J, NS. Enrolled the patients and conducted the study: J, MH, VA, AJ, LH, VK, NS. Analyzed the data: J, NS. Wrote the paper: J, NS. All authors read and approved the final manuscript.

Competing interests

Authors declare that they have no competing interests.

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Figures

Figure 1. Study flow chart

Figure 1

Study flow chart ICU, Intensive Care Unit; ESRD, End Stage Renal Disease; AKI, Acute Kidney Injury

Figure 2. Forest plot of risk factors of AKI, no AKI vs stage 1 or stage 2, no AKI vs AKI stage 3

Figure 2

Forest plot of risk factors of AKI, No-AKI vs stage-1/stage-2, No-AKI vs AKI stage-3 CAD, Cardiovascular Disease; APACHE II, Acute Physiologic and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment

Figure 3. Kaplan-Meier survival curves for each AKI stage on hospital mortality, N=855 (excluded 10 event time missing).

Figure 3

Kaplan-Meier survival curves for each AKI stage on hospital mortality