Research Article

Acute Kidney Injury in Malaysian Intensive Care Setting: Incidences, Risk Factors, and Outcome

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Abstract

Introduction: Acute kidney injury (AKI) is common in the intensive care unit (ICU) with a high risk of morbidity and mortality. The high incidence of AKI in our population may be attributed to sepsis. We investigated the incidence, risk factors, and outcome of AKI in four tertiary Malaysian ICUs. We also evaluated its association with sepsis. **Materials and Methods:** This retrospective cohort study extracted de-identified data from the Malaysian Registry of Intensive Care in four Malaysian tertiary ICUs between January 2010 and December 2014. The study was registered under the NMRR and approved by the ethics committee. AKI was defined as twice the baseline creatinine or urine output <0.5 ml/kg/h for 12 h. **Results:** Of 26,663 patients, 24.2% had AKI within 24 h of admission. Patients with AKI were older and had higher severity of illness compared to those without AKI. AKI patients had a longer duration of mechanical ventilation, length of ICU, and hospital stay. Age, Simplified Acute Physiological II Score, and the presence of sepsis and preexisting hypertension, chronic cardiovascular disease independently associated with AKI. About 32.3% had sepsis. Patients with both AKI and sepsis had the highest risk of mortality (relative risk 3.43 [3.34–3.53]). **Conclusions:** AKI is common in our ICU, with higher morbidity and mortality. Independent risk factors of AKI include age, the severity of illness, sepsis and preexisting hypertension, and chronic cardiovascular disease. AKI independently contributes to mortality. The presence of AKI and sepsis increased the risk of mortality by three times.

Keywords: Acute kidney injury, epidemiology, intensive care unit, mortality, risk factors

Introduction

Acute kidney injury (AKI) is common in patients admitted to the intensive care unit (ICU), occurring in 30%–60% of patients.[1-3] AKI is an independent risk factor for mortality,[4,5] leading to a new understanding that patients may die due to AKI, not only with AKI.[6] The high incidence of AKI in our population may be attributed to sepsis. About 60% of patients with severe sepsis had AKI. Septic AKI was associated with higher severity and mortality.[7-9] AKI was associated with increasing length of ICU stay, mechanical ventilation, and mortality.[10,11]

Most epidemiology researches on AKI were conducted in Western populations setting. To the best of our knowledge, there was only a small single-center study on the epidemiology of AKI in Malaysia.[2] The Malaysian Registry of Intensive Care (MRIC),[9] is an annual ICU audit performed in all Malaysian ICUs. This registry serves as an excellent avenue to explore the incidence of septic AKI in our local ICU. This will provide an important epidemiological data for the future design of AKI study. We aimed to evaluate the incidence, risk factors, and outcome of AKI in four tertiary hospitals from the MRIC data. These hospitals represent four areas, i.e., North, South, West, and East of Peninsular Malaysia.

Materials and Methods

This retrospective cohort study extracted de-identified data from the MRIC for patients admitted to four tertiary hospitals. All complete data of patients older than 18-year-old were included in the analysis. The study was registered under the

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NMRR (NMRR-14-1938-23183) and approved by the ethics committee.

AKI was defined as twice the baseline creatinine or urine output of <0.5 ml/kg/h for 12 h.[9] Sepsis is defined as documented infection with two out of four systemic inflammatory response syndrome (SIRS) criteria and/or clinical suspicion of infection.[9] Patients were grouped into sepsis and no sepsis. Patients were further subgrouped to sepsis with AKI (sepsis-AKI), sepsis with No AKI (sepsis-No AKI), no sepsis with AKI (No sepsis-AKI), and no sepsis with No AKI (No sepsis-No AKI). Other data that were collected includes age, sex, height, weight, ethnicity, clinical or surgical admission, and primary admission diagnosis, comorbid diseases, duration of ICU and hospital stay, mechanical ventilation and its length, mortality, and dialysis. The baseline Simplified Acute Physiological II (SAPS II) and Sequential Organ Failure Assessment scores were used to assess the severity of illness in each patient.

Statistical analysis

Results are presented as mean ± standard deviation for normally distributed variables or median (inter-quartile range) for nonnormally distributed variables. Comparison of variables between the two groups was analyzed using the independent *t*-test for normally distributed variables or the Mann–Whitney test for nonnormally distributed variables. Categorical variables were compared with Chi-square test for independent variables, or McNemar test for paired variables. Multivariate logistic regression analysis was used to analyze the independent risk factors for AKI and death. Odds ratio (OR) from the logistic regression described the strength of association of each variable with the outcome. OR were presented with 95% confidence intervals.

Results

A total of 26,663 ICU admissions were analyzed. Of these, 6443 (24.2%) had AKI within 24 h of admission. 8609 (32.3%) had sepsis, of those with AKI, 4129 (64.1%) had sepsis, and those without AKI, 4319 (22.4%) had sepsis. Figure 1 shows the patients flow when grouped into the presence of AKI and sepsis.

Demographic, clinical characteristics, and outcomes

Patients with AKI were older and had higher severity of illness compared to those without AKI [$P < 0.0001$, Table 1]. Sepsis was more common in patients with AKI (64.1% vs. 22.2%, $P < 0.0001$). Hypertension, diabetes mellitus, chronic renal failure, chronic cardiovascular disease, and immunosuppression were more common in patients with AKI. Patients' outcome is shown in Table 2. A total of 4966 (18.6%) of patients received dialysis, and 7059 (26.5%) died. A higher percentage of patients with AKI died compared to those without AKI. Of those who survived, AKI patients had a longer duration of mechanical ventilation, length of ICU, and hospital stay ($P < 0.0001$).

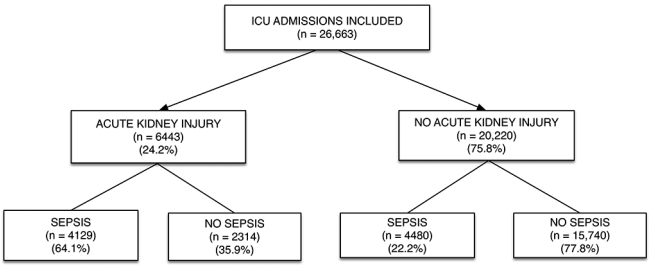

Figure 1: Classification of patients according to the presence of sepsis and acute kidney injury

Independent risk factors of acute kidney injury

Risk factors that were associated with AKI on univariate analysis include older age, higher severity of illness, medical category admission, sepsis, preexisting hypertension, diabetes mellitus, chronic renal failure, chronic cardiovascular disease, and immunosuppression. Of these, age, SAPS II score, and the presence of sepsis and preexisting hypertension, and chronic cardiovascular disease were independently associated with AKI [Table 3].

Acute kidney injury and sepsis

Sepsis occurs in 32% of patients, of this 64% of patients with AKI had sepsis, compared to 22% with No AKI had sepsis. Table 4 shows the percentage of patients who died stratified based on the presence of sepsis and AKI. About 54% of patients with sepsis and AKI died, compared to 33% with sepsis and No AKI, and 35% with No sepsis and AKI. Patients with both AKI and sepsis were at least three times more likely to die compared to those without sepsis or AKI (relative risk of 3.43 [3.34–3.53]).

Acute kidney injury in contributing to mortality

Twenty-seven percent of patients died, more in patients with AKI compared to those without AKI (48% vs. 20%, $P < 0.0001$). After adjusting for other co-variates that contributed to mortality, namely age, severity of illness and the presence of sepsis, AKI independently increased the risk for death [Table 3].

Discussion

In this large study of ICU audit involving four tertiary hospitals, AKI defined as doubling of serum creatinine or AKIN Stage 2 or urine output of <0.5 ml/kg/h occurred in 24.2% of ICU admissions. These patients had higher death and dialysis, and in those who survived, AKI patients had longer ICU and hospital stay. Independent risk factors for AKI include age, the severity of illness, the presence of sepsis and preexisting hypertension, and chronic cardiovascular disease. AKI independently contributes to mortality. Patients who have both AKI and sepsis had three times the risk of mortality compared to those without AKI or sepsis.

Our previous prospective study[2] showed a higher incidence of AKI defined by the creatinine criteria of the KDIGO guideline, of 46% in our ICU population, of which 30% were of AKI Stage 2 and 3. In this current large study investigating the existing audit, AKI was defined as doubling of baseline

Table 1: Demographic and clinical characteristics

Variables	All patients (*n*=26,663)	AKI (*n*=6443)	No AKI (*n*=20,220)	*P*
Age (years)	49±17	54±16	47±18	<0.0001
Ethnicity				
Malay	14,120 (53.0)	3388 (52.6)	10,732 (53.1)	<0.0001
Chinese	5963 (22.4)	1582 (24.6)	4381 (21.7)	
Indian	3645 (13.7)	832 (12.9)	2813 (13.9)	
Others	2910 (10.9)	640 (9.9)	2270 (11.2)	
Gender (male)	16,099 (60.4)	4102 (63.7)	11,997 (59.4)	<0.0001
SOFA score	6.9±4.2	10.5±3.8	5.7±3.7	<0.0001
SAPS II score	38±18	53±17	33±16	<0.0001
Sepsis	8609 (32.3)	4129 (64.1)	4480 (22.2)	<0.0001
Admission category				
Medical	16,461 (61.8)	4792 (74.5)	11,669 (57.8)	<0.0001
Surgical	10,165 (38.2)	1636 (25.4)	8529 (42.2)	
Comorbid diseases				
Hypertension	10,524 (39.5)	3366 (52.3)	7158 (35.4)	<0.0001
Diabetes mellitus	8717 (32.7)	2896 (45.2)	5821 (28.8)	<0.0001
Chronic cardiovascular disease	3198 (12.0)	1001 (15.5)	2197 (10.9)	<0.0001
Chronic renal failure	3359 (12.6)	1282 (19.9)	2077 (10.3)	<0.0001
Chronic lung disease	1609 (6.0)	365 (5.7)	1244 (6.2)	0.15
Chronic liver disease	181 (0.7)	41 (0.6)	140 (0.7)	0.63
Immunosuppression/HIV	449 (1.7)	163 (2.5)	286 (1.4)	<0.0001
Cancer	312 (1.2)	78 (1.2)	234 (1.2)	0.73

Data expressed as mean±SD, *n* (%), or median (lower quartile-upper quartile). AKI: Doubling of serum creatinine during ICU admission. SOFA: Sequential Organ Failure Assessment; SAPS II: Simplified Acute Physiology Score II; AKI: Acute kidney injury; ICU: Intensive care unit; SD: Standard deviation

Table 2: Patients' outcomes

Variables	All patients (*n*=26,663)	AKI (*n*=6443)	No AKI (*n*=20,220)	*P*
Dialysis	4966 (18.6)	2944 (45.7)	2022 (10.0)	<0.0001
Death	7059 (26.5)	3068 (47.6)	3991 (19.7)	<0.0001
MV	18,845 (70.7)	5063 (78.6)	13,782 (68.2)	<0.0001
In survivors (*n*=820) (h)				
Duration of MV	47 (23-109)	76 (38-76)	42 (22-95)	<0.0001
Length of stay ICU	63 (32-131)	113 (59-207)	55 (28-113)	<0.0001
Length of stay hospital	278 (163-525)	385 (229-709)	259 (153-483)	<0.0001

Data expressed as mean±SD, *n* (%), or median (lower quartile-upper quartile). Comparison of variables between the two groups was analysed using the independent *t*-test for normally distributed variables or the Mann-Whitney test for nonnormally distributed variables. Categorical variables were compared with Chi-square test. MV: Mechanical ventilation; AKI: Acute kidney injury; ICU: Intensive care unit; SD: Standard deviation

creatinine, i.e., Stage 2 AKI or urine output of <0.5 ml/kg/h. We reported an almost similar percentage of AKI Stage 2 in this large multicenter study involving four tertiary ICUs. This audit missed those with a smaller increase in plasma creatinine defined as KDIGO Stage 1, hence explained its lower incidence compared to the other studies.

Patients with AKI had a higher percentage of death and need of dialysis. In those who survived, they had longer duration of mechanical ventilation, ICU and hospital stay. This was similar to other studies which showed an association of AKI with increasing length of ICU stay, mechanical ventilation, and mortality.[10,11] We showed that the independent risk factors for AKI include age, the severity of illness, sepsis and preexisting hypertension, and chronic cardiovascular disease. An observational meta-analyses study showed the 13 risk factors for AKI, which includes older age, diabetes, hypertension, higher baseline creatinine, heart failure, sepsis/SIRS, use of nephrotoxic drugs, higher severity of disease scores, use of vasopressors/inotropes, high-risk surgery, emergency surgery, use of IABP, and longer time in cardiopulmonary bypass pump.[12] Other risk factors involved include hypovolemia, the presence of sepsis, and chronic renal disease.[13,14]

Sepsis is the leading cause of ICU admission in our country. The 2015 MRIC reported that sepsis is the second leading cause of ICU admission in Malaysian ICU, with severe sepsis occurring in 17.5% of patients.[9] Over 5 years of this audit, we showed that sepsis occurs in 32% of patients. More patients with AKI had sepsis compared to those without AKI. In our previous study, we showed that sepsis occurred in 50%–55% of patients.[2,15,16] A similar high incidence of AKI was shown

Table 3: Multivariable logistic regression analysis for diagnosis of acute kidney injury and prediction of death

Variables	OR (95% CI)	*P*
Diagnosis of AKI		
Age	0.99 (0.97-1.00)	0.04
SAPS II score	1.05 (1.04-1.06)	<0.0001
Medical category	1.29 (1.19-1.38)	<0.0001
Sepsis (yes or no)	3.66 (3.42-3.93)	<0.0001
Hypertension (yes or no)	1.36 (1.25-1.49)	<0.0001
Chronic cardiovascular disease (yes or no)	1.14 (1.03-1.26)	0.01
Prediction of death		
Age	0.99 (0.99-1.00)	0.03
SAPS II score	1.07 (1.06-1.08)	<0.0001
Sepsis (yes or no)	1.64 (1.53-1.76)	<0.0001
AKI (yes or no)	1.15 (1.06-1.25)	<0.0001

SAPS II: Simplified Acute Physiological Score II; AKI: Acute kidney injury; OR: Odds ratio; CI: Confidence interval

Table 4: Mortality and relative risk in acute kidney injury and sepsis

	n (%)		RR (95% CI)	
	No-AKI	AKI	No-AKI	AKI
No sepsis	2497 (15.9)	820 (35.4)	1 (referent)	2.23 (2.17-2.13)
Sepsis	1494 (33.3)	2248 (54.4)	2.10 (2.06-2.14)	3.43 (3.34-3.53)

McNemar test, *P*<0.0001. RR: RR of mortality in relation to the referent group of no-AKI and no sepsis. *n* (%): Number (percentage) of mortality in each group; AKI: Acute kidney injury; CI: Confidence interval; RR: Relative risk

to occur in a study involving 107 sepsis patients.[17] Sepsis is the main contributing factor for AKI, with almost half of AKI cases related to sepsis or septic shock.[4,18]

We showed that patients with sepsis and AKI were at least three times more likely to die compared to those without AKI or sepsis. This is similar to other studies which showed higher severity and mortality in patients with septic AKI.[7,8] After adjusting for age, the severity of illness and the presence of sepsis, AKI independently predicted death. Other studies similarly showed a high risk of death in those with AKI, with mortality exceeding 50%.[4,19-21] About 20%–40% of hospitalized patients with AKI died, higher in patients with greater AKI severity.[22,23]

Study strength and limitations

The strength of the study is that it involves a large number of patients admitted over 5 years in four large tertiary centers in our country. This may be representative of our ICU population in Malaysia. However, this study is limited by several factors. First, the retrospective nature of the study limits the definition of AKI to Stage 2 and greater. This audit fails to capture those with a smaller increase in plasma creatinine which were shown to be associated with higher mortality and morbidity. Second, baseline creatinine of prehospitalization records was not available, first creatinine measured in the hospital was used as baseline creatinine. Hence, this may miss patients who had AKI on hospital admission. Finally, urine output of <0.5 ml/kg/h was used to define AKI. We have previously showed that this definition is too liberal and may overestimate the incidence of AKI.[2,24]

Conclusions

AKI is common in our ICU, with higher morbidity and mortality. Risk factors of AKI include age, the severity of illness, the presence of sepsis and preexisting hypertension, and chronic cardiovascular disease. AKI independently contributes to mortality. Patients who have both AKI and sepsis had three times the risk of mortality compared to those without AKI or sepsis.

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Conflicts of interest

There are no conflicts of interest.

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