Predictors of acute kidney injury and mortality in an Intensive Care Unit

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Abstract

Introduction and Objectives: To compare clinical characteristics and outcomes of patients with and without acute kidney injury (AKI), to evaluate the incidence and mortality of AKI and predictors of AKI and death in patients hospitalized in an Intensive Care Unit (ICU). **Methods:** A retrospective study analyzed 152 patients admitted to a single ICU. We assessed age, gender, reason for hospitalization, risk factors for ARF, laboratory data, the need for renal therapy substitutive and mortality. Acute Physiology and Chronic Health Evaluation (APACHE II), Sequential Organ Failure Assessment (SOFA) and RIFLE were recorded on the day of ICU admission. We determined the incidence of AKI, mortality and the independent predictors of AKI and death using logistic regression model. **Results:** Mean age was 57.1 ± 20 years, ranging between 19 to 88 years, and 60.1% were male. Non-dialysis dependent AKI occurred in 81 patients (53.2%) while the ARF requiring dialysis occurred in 19 patients (12.4%). The overall mortality rate in the ICU was 35.9%, whereas the mortality rate in patients with non-dialysis dependent AKI was 43.2% and the IRA with dialysis of 84.2%. In multivariate analysis, invasive mechanical ventilation, elevated creatinine and urea at admission were independent risk factors for AKI, whereas clinical diagnosis, invasive mechanical ventilation, increased lactate and urea and hypernatremia were independent risk factors for ICU mortality. **Conclusion:** The incidence and mortality of AKI in ICU were high in this study, despite the advances that have been emerging in their management.

Keywords: acute kidney injury; dialysis; intensive care units.

Introduction

Acute kidney injury (AKI) has been the topic of several studies in nephrology due to the severe renal and systemic complications associated with it.[1] Although care has been improved, AKI is seen in as many as 15% of hospitalized individuals and in about 40% of the patients referred to intensive care.[2,3] Eighty percent of the intensive care unit (ICU) patients with AKI die, and 13% of the survivors require dialysis.[4] These rates have remained virtually unchanged despite the optimization of care,[4] as a consequence of difficult and late diagnosis of AKI, advanced patient age, presence of multiple comorbidities, and patients undergoing a greater number of invasive procedures.[5]

AKI is a syndrome characterized by an abrupt deterioration of renal function followed by a sharp decrease in the patient's glomerular filtration rate, which may result in the accumulation of nitrogenous metabolites and water-electrolyte imbalances, which produce a wide array of clinical manifestations in patients. In an attempt to standardize the various published diagnostic criteria, Mehta *et al.*[6] have defined AKI as an acute increase in the absolute level of serum creatinine of more than 0.3 mg/dl or a decrease in urine output to less than 0.5 ml/kg/hour for more than six hours.

The etiology of AKI is multifactorial, and kidney function deterioration may

fall into three major categories: prerenal, intrinsic renal, and postrenal. This categorization offers a simplified perspective on the underlying pathogenic mechanisms related to AKI. Patients in the first category are usually hypovolemic, and many of their organs - kidneys included - suffer with hypoperfusion mainly due to sepsis, other systemic inflammatory conditions, surgery, or trauma.[7] If the underlying disease and hypoperfusion are not resolved, prolonged exposure to prerenal azotemia leads to ischemic cell injury and acute tubular necrosis, the main cause of intrinsic AKI. Postrenal AKI sets in as a consequence of urinary tract obstruction.[8-10] Among all causal factors, septic shock is the one most commonly associated with the onset of AKI.[10]

The risk factors for AKI in ICU patients described in the literature include old age, previous renal disease, sepsis, obesity, hypovolemia, surgery, history of hypertension, and cardiovascular disease, to name a few.[11]

The risk factors associated with death reported in the literature on critically ill patients with AKI include old age, prolonged hospitalization, high scores on the Acute Physiology and Chronic Health Evaluation (APACHE II) scale, presence of comorbidities, oliguria, hypovolemia, metabolic acidosis, sepsis, multiple trauma, in addition to the use of vasoactive drugs and invasive mechanical ventilation.[12]

This paper aimed to assess the incidence, mortality rates, and the risk factors and factors associated with the death of patients with AKI seen in an intensive care unit.

Method

The Research Ethics Committee at Assis Gurgacz College approved this retrospective study. The data of interest were collected by one of the authors from the medical records of the patients admitted to an intensive care unit between August 2012 and June 2013 (n = 152); the data reflect the patients' statuses while they were in the ICU.

The following data were collected: age, gender, reason for hospitalization in the ICU based on the clinical or surgical diagnosis on admission, comorbidities such as hypertension, *diabetes mellitus*, congestive heart failure, chronic kidney failure, respiratory disease and smoking, surgical procedures offered before ICU admission, prescribed medication, workup, urine volume within the first 24 hours of admission, need for dialysis or surgery during hospitalization, mechanical ventilation, presence of infection/sepsis and primary site (when known), and death.

Patients with increases in creatinine levels greater than 0.3 mg/dL or increases greater than 50% from baseline levels, and/or oliguria regardless of adequate fluid replacement were diagnosed with AKI. Patients were also analyzed for need for renal replacement therapy (hemodialysis or peritoneal dialysis) during the ICU stay. Hypokalemia and hyperkalemia were diagnosed when plasma potassium levels were under 3.5 mEq/L and above 5.5 mEq/L, respectively. Patients were considered to have hyponatremia and hypernatremia when sodium levels were under 135 mEq/L and above 145 mEq/L, respectively. Acidosis was defined for plasma pH levels under 7.35. The RIFLE, APACHE II, SOFA and Glasgow Coma Scale (GCS) scores were used to assess patients on admission.

The data sets were compiled on Microsoft Excel and analyzed using descriptive statistics (interquartile range; absolute and percent frequencies). The incidences of AKI, patients with AKI requiring dialysis, and death were calculated. The chi-square test, Student's *t*-test, the Mann-Whitney U test, and Fisher's exact test were used as needed. Bivariate and multivariate logistic regressions were used to analyze death rates and occurrence of AKI as a function of risk factors on ICU admission. Variables with $p < 0.20$ in bivariate analysis were included in multivariate analysis; stepwise variable selection was used from this point on.

Results

The patients had a mean age of 57.1 ± 20 years (19 to 88 years) and 92 (60.1%) were males. The mean length of ICU stay was 12 ± 11.8 days (two to 50 days). Clinical causes ranked atop all other reasons for hospitalization (110 patients; 72.3%). Mechanical ventilation within 24 hours of admission was offered to 60.8% of patients. Forty-two

patients (27.6%) had undergone surgery prior to ICU and 31 (20.7%) were operated while at the ICU.

The mean APACHE II and SOFA scores on admission were 18.9 ± 8.3 and 4.5 ± 2.9, respectively. Forty-four individuals (28.7%) had sepsis. The RIFLE scale scores on admission revealed that 26 patients were in the Risk, 28 in the Injury, and 46 in the Failure group. Eighty-one patients (53.2%) had AKI. Nineteen of them (12.5%) required renal replacement therapy (RRT). The overall mortality of ICU patients was 35.9%; the death rate among non-dialysis patients with AKI was 43.2%; and 84.2% of the dialysis patients with AKI died.

Table 1 shows patient clinical data according to presence and absence of AKI. Patients with AKI were older and diagnosed more often with clinical conditions on admission and sepsis during their ICU stay; prevalence of systemic hypertension was also higher in this group of subjects. Patients with AKI required invasive mechanical ventilation (IMV) more often. On admission, the APACHE II and SOFA scores were higher and the GCS scores were lower. Death rates were higher among patients with AKI. Table 2 presents patient workup data according to presence and absence of AKI. Patients with AKI had elevated creatinine, urea, and lactate levels, but reduced levels of bicarbonate; subsequently, more individuals in this group had metabolic acidosis. Potassium disorders were statistically more frequent in the group with AKI ($p < 0.05$).

Table 3 shows patient clinical data according need for dialysis. Dialysis patients with AKI were more frequently affected by comorbidities, sepsis, and oliguria. They also required more mechanical ventilation, and had high APACHE II and SOFA and low GCS scores. They stayed for longer in the ICU and death was more prevalent among them.

The workup data on admission in accordance with need for dialysis is shown in Table 4. Creatinine, urea, and potassium levels were statistically higher and bicarbonate was statistically lower in the dialysis group ($p < 0.05$).

Table 1 Clinical data of patients admitted to the intensive care unit according to occurrence of AKI

Variable	With AKI (n = 100)	Without AKI (n = 52)	*p* value
Male	63 (63.0%)	31 (59.6%)	0.684*
Median age (P25-P75)	64.5 (48.0-76.75)	52.0 (33.25-63.00)	0.001†
Diagnosis			
Clinical	78 (78%)	32 (61.5%)	0.031*
Surgical	22 (22%)	20 (38.5%)	
Comorbidities			
With comorbidities	79 (79%)	32 (61.5%)	0.021*
Without comorbidities	21 (21%)	20 (38.5%)	
Systemic Hypertension	60 (60%)	17 (32.7%)	0.001*
DM	26 (26%)	7 (13.5%)	0.075*
Median GCS (P25-P75)	10.00 (6.00-14.75)	13.50 (9.25-15.00)	0.004†
IMV on admission	72 (72.0%)	22 (42.3%)	< 0.001*
Vasoactive drugs on admission	10 (10%)	5 (9.6%)	0.940*
Aminoglycosides	8 (8.0%)	5 (9.6%)	0.765‡
Sepsis on admission	32 (32%)	12 (23.1%)	0.250 *
Urine output < 400 mL	4 (4%)	0 (0.0%)	0.300‡
Median APACHE II (P25-P75)	21.00 (15.00-7.75)	15.00 (9.00-18.00)	< 0.001†
Median SOFA (P25-P75)	5 (4-7)	2 (1-4)	< 0.001†
Median time on ICU in days (P25-P75)	8.50 (4-16)	7 (3-23.75)	0.243†
Death	52 (52%)	3 (5.8%)	< 0.001*

* Chi-square test; † Mann-Whitney U test; ‡ Fisher's exact test.

Table 5 presents the multivariate analysis of AKI risk factors as a function of patient variables on admission. Higher creatinine and urea levels on admission and need for invasive mechanical ventilation during ICU stay were independent risk factors for AKI.

Table 6 shows the multivariate analysis of patient death risk factors on admission. Higher frequency of clinical diagnoses, increased need for IMV, high

Table 2 Workup data of patient admitted to intensive care unit according to occurrence of AKI

Workup on admission (Mean ± SD)	With AKI (n = 100)	Without AKI (n = 52)	*p* value
Median creatinine (mg/dL) (P25-P75)	1.68 (1.06-2.93)	0.82 (0.63-0.99)	< 0.001*
Median urea (mg/dL) (P25-P75)	67.15 (38.6-111.05)	30 (21.88-42.15)	< 0.001*
Hyponatremia (mEq/L)	36 (36%)	22 (42.3%)	0.448†
Hypernatremia (mEq/L)	6 (6%)	1 (1.9%)	0.423‡
Hypokalemia (mEq/L)	11 (11%)	12 (23.1%)	0.049†
Hyperkalemia (mEq/L)	17 (17%)	2 (3.8%)	0.020†
Lactate (mmol/L)			
Median (P25-P75)	1.6 (1-2.8)	1.3 (0.9-1.8)	0.023*
Bicarbonate (mEq/L)			
Median (P25-P75)	20.95 (17-25)	24.75 (20.9-27.45)	0.001*
Acidosis on admission (%)	54 (54%)	16 (30.8%)	0.006†

DM: *Diabetes mellitus*; GCS: Glasgow coma scale; IMV: Invasive mechanical ventilation; Acute Physiology and Chronic Health Evaluation: APACHE II; Sequential Organ Failure Assessment: SOFA; P25: 25th percentile; P75: 75th percentile; * Mann-Whitney U test; † Chi-square test, ‡ Fishers exact test.

levels of urea and lactate, and hypernatremia were independent risk factors for ICU mortality.

Discussion

This retrospective study included individuals admitted within a ten-month period to an intensive care unit for the purposes of assessing the incidence, death rates, and clinical characteristics of patients with AKI on admission, and the risk factors related to AKI and death.

Approximately 40% of the patients treated in intensive care settings suffer with AKI.[13] A higher incidence was observed in this study, as 66% of our patients were diagnosed with AKI. It should be noted that the group of patients treated in this unit is highly diverse. The studied population included less severe patients, with GCS scores in the 13-15 range and low APACHE II and SOFA scores, along with a large portion of individuals with severe, complex involvement and low GCS and high APACHE II and SOFA scores requiring invasive mechanical ventilation and prescription of vasoactive drugs. This reflects the heterogeneity of the group of patients included in our study.

Although patients with AKI are predominantly males,[14] our study failed to statistically reflect such preponderance.

The mean age of the patient population seen in adult intensive care units has increased.[13] In our study, patients with AKI were about 10 years older on average than patients without AKI, revealing a statistically significant difference ($p < 0,05$). Clinical conditions were the main cause of hospitalization in the study population.

A retrospective cohort study carried out in 2008 by Peres *et al.*[15] in the same region, but in another ICU, reported an incidence of dialysis patients with AKI of 7.1%, against the 12.5% observed in our study. One possible reason for the difference in incidence is the higher mean age seen in our study (58 *vs.* 48 years). In a study similar to ours, Carmo *et al.*[16] reported an incidence of 9.5% in a population with a mean age of 53 years, further supporting this observation. Incidences among non-dialysis subjects with AKI have been reported to surpass 67% in critical patients.[17,18] In our study, the incidence of non-dialysis AKI patients was 53%.

Higher creatinine and urea levels on admission, along with need for invasive mechanical ventilation during ICU hospitalization, were independent risk factors for AKI. More specifically, the risk factors for dialysis AKI patients were presence of morbidity, need for mechanical ventilation, sepsis during hospitalization, low GCS score, high APACHE II and SOFA scores, and longer ICU stay. Workup on admission revealed higher creatinine, urea, and potassium levels and lower bicarbonate levels.

Table 3 Clinical data of patients admitted to intensive care unit with AKI according to need for dialysis

Variable	Dialysis patients (n = 19)	Non-dialysis patients (n = 133)	*p* value
Gender			0.528*
Male	13 (68.4%)	81 (60.9%)	
Age in years			0.560†
Median (P25-P75)	66 (51-71)	60 (43-71.5)	
Diagnosis			0.493*
Clinical	15 (78.9%)	95 (71.4%)	
Surgical	4 (21.1%)	38 (28.6%)	
Comorbidities			0.085*
With comorbidities	17 (89.5%)	94 (70.7%)	
Without comorbidities	2 (10.5%)	39 (29.3%)	
Hypertension	13 (68.4%)	64 (48.1%)	0.098*
DM	8 (42.1%)	25 (18.8%)	0.021*
GCS			0.006†
Median (P25-P75)	6 (6-13)	13 (6-15)	
IMV on admission	19 (100%)	75 (56.4%)	< 0.001*
Vasoactive drugs on admission	1 (5.3%)	14 (10.5%)	0.695‡
Aminoglycosides	0 (0%)	13 (9.8%)	0.373‡
Sepsis on admission	10 (52.6%)	34 (25.6%)	0.015*
Urine output < 400 mL	3 (15.8%)	1 (0.8%)	0.006‡
APACHE II			< 0.001†
Median (P25-P75)	28 (22-33)	17 (12.5-23.5)	
SOFA			< 0.001†
Median (P25-P75)	7 (6-10)	4 (2-6)	
Median time on ICU (P25-P75)	13 (6-23)	8 (4-13.5)	0.035†
Death	16 (84.2%)	39 (29.3%)	< 0.001*

DM: *Diabetes mellitus*; GCS: Glasgow coma scale; IMV: Invasive mechanical ventilation; Acute Physiology and Chronic Health Evaluation: APACHE II; Sequential Organ Failure Assessment: SOFA; P25: 25th percentile; P75: 75th percentile; * Mann-Whitney U test; † Chi-square test, ‡ Fishers exact test.

Table 4 Workup data of patients admitted to intensive care unit with AKI according to need for dialysis

Workup on admission (Mean ± SD)	Dialysis patients (n = 19)	Non-dialysis patients (n = 133)	*p* value
Median creatinine (mg/dL) (P25-P75)	2.85 (1.77-4.05)	1.04 (0.80-1.75)	< 0.001*
Median urea (mg/dL) (P25-P75)	84.3 (56.6-153)	42.7 (28-72.75)	< 0.001*
Hyponatremia (mEq/L)	8 (42.1%)	50 (37.6%)	0.705†
Hypernatremia (mEq/L)	2 (10.5%)	5 (3.8%)	0.212‡
Hypokalemia (mEq/L)	1 (5.3%)	22 (16.5%)	0.310‡
Hyperkalemia (mEq/L)	8 (42.1%)	11 (8.3%)	< 0.001‡
Lactate (mmol/L)			0.334*
Median (P25-P75)	2.5 (0.8-3.4)	1.5 (1.0-2.2)	
Bicarbonate (mEq/L)			0.006*
Median (P25-P75)	19.5 (14-22.8)	22.9 (18.8-26.1)	
Acidosis on admission (%)	16 (84.2%)	54 (40.6%)	< 0.001†

P25: 25th percentile; P75: 75th percentile; * Mann-Whitney U test; † Chi-square test; ‡ Fisher's exact test.

Table 5 Logistic regression for AKI in patients admitted to intensive care unit as a function of risk factors

Variable	Complete model				Forward selection model			
	OR	95% CI	*p* value		OR	95% CI	*p* value	
Gender (Male/Female)	0.40	0.10	1.65	0.208				
Age (years)	1.03	0.99	1.08	0.162				
Diagnosis (Clinical/ Surgical)	1.17	0.24	5.61	0.848				
Comorbidities (Yes/No)	0.26	0.04	1.66	0.154				
Glasgow	0.92	0.70	1.21	0.562				
IMV on admission (Yes/No)	4.46	0.75	26.48	0.100	4.48	1.47	13.70	0.008
Vasoactive drugs on admission (Yes/No)	0.65	0.06	7.49	0.727				
Aminoglycosides (Yes/No)	1.29	0.11	15.52	0.842				
Sepsis on admission (Yes/No)	0.36	0.07	1.80	0.216				
Urine output < 400 mL (Yes/No)	2936.00	0.00	.	0.999				
APACHE II	0.97	0.85	1.10	0.590				
SOFA	1.00	0.70	1.43	0.987				
Creatinine on admission (mg/dl)	96.08	6.83	1351.70	0.001	67.65	8.91	513.39	< 0.001
Urea on admission (mg/ dl)	1.05	1.02	1.09	0.002	1.05	1.02	1.07	0.001
Hyponatremia on admission (mEq/L) (Yes/No)	0.43	0.11	1.64	0.216				
Hypernatremia on admission (mEq/L) (Yes/No)	4.17	0.00	50593627	0.864				
Hypokalemia on admission (mEq/L) (Yes/No)	0.32	0.05	2.01	0.225				
Hyperkalemia on admission (mEq/L) (Yes/ No)	0.98	0.03	31.14	0.990				
Lactate on admission (mmol/L)	1.12	0.65	1.96	0.682				
Bicarbonate (mEq/L) on admission	0.98	0.87	1.11	0.769				
Acidosis on admission (Yes/No)	1.43	0.38	5.38	0.595				

IMV: Invasive mechanical ventilation; Acute Physiology and Chronic Health Evaluation: APACHE II; Sequential Organ Failure Assessment: SOFA.

Despite therapeutic and diagnostic advances, the mortality of AKI patients has remained high in recent decades. Death rates of dialysis patients with severe AKI and multiple organ failure may reach 80%.[19,20] Similarly to data published in the literature, in this study approximately 80% of the patients with AKI requiring dialysis died. The association between need for dialysis and higher death rates in this group of individuals has been described for quite some time.[21]

The independent risk factors for death found in this study were: clinical diagnosis, high levels

Table 6 Logistic regression for death as a function of risk factors in the intensive care unit for 152 patients admitted to intensive care unit

Variable	Complete model				Stepwise selection model			
	OR	95% CI		*p* value	OR	95% CI		*p* value
Gender (Male/Female)	0.533	0.201	1.416	0.207				
Age (years)	1.000	0.969	1.033	0.984				
Diagnosis (Clinical/ Surgical)	3.710	1.041	13.216	0.043				
Comorbidities (Yes/No)	1.028	0.270	3.914	0.968				
Glasgow	1.143	0.951	1.374	0.155				
IMV on admission (Yes/No)	11.117	2.740	45.103	0.001	10.176	3.546	29.197	< 0.001
Vasoactive drugs on admission (Yes/No)	1.098	0.202	5.957	0.913				
Aminoglycosides (Yes/No)	0.705	0.121	4.122	0.698				
Sepsis on admission (Yes/No)	0.451	0.146	1.391	0.166				
Urine output < 400 mL (Yes/No)	90.613	0.104	79032.469	0.192				
APACHE II	1.026	0.940	1.120	0.571				
SOFA	1.146	0.915	1.434	0.236				
Creatinine on admission (mg/dl)	0.764	0.566	1.030	0.077				
Urea on admission (mg/dl)	1.017	1.004	1.031	0.010	1.011	1.002	1.019	0.011
Hyponatremia on admission (mEq/L) (Yes/No)	0.885	0.331	2.367	0.808				
Hypernatremia on admission (mEq/L) (Yes/No)	20.472	1.291	324.672	0.032	16.278	1.202	220.522	0.036
Hypokalemia on admission (mEq/L) (Yes/No)	0.316	0.072	1.376	0.125				
Hyperkalemia on admission (mEq/L) (Yes/No)	0.461	0.089	2.379	0.355				
Lactate on admission (mmol/L)	1.597	1.111	2.295	0.011	1.440	1.097	1.892	0.009
Bicarbonate (mEq/L) on admission	1.032	0.945	1.128	0.480				
Acidosis on admission (Yes/No)	1.271	0.451	3.579	0.650				

IMV: Invasive mechanical ventilation; Acute Physiology and Chronic Health Evaluation: APACHE II; Sequential Organ Failure Assessment: SOFA.

of creatinine, urea, sodium, and lactate on admission, and need for invasive mechanical ventilation. Oliguria often occurs in ICU patients with AKI and is seen as a more sensitive marker than increases in serum creatinine.[22] Although it has been recognized as an early predictor of higher death rates in critically ill patients, oliguria was not a predictor of death in our study. Peres *et al.*[15] described oliguria as an independent risk factor for death.

The risk factors for death of critically ill patients with AKI recognized in the literature include: older age, prolonged hospitalization, high APACHE II scores, comorbidities, oliguria, high lactate, hypovolemia, metabolic acidosis, sepsis, multiple trauma, vasoactive drugs, and need for invasive mechanical ventilation.

In our study, clinical diagnosis, high levels of urea, sodium and lactate on admission, and need for IMV predicted increased mortality. We tried to use admission criteria already implemented in our unit to predict AKI and mortality.

Samimagham *et al.*[23] studied 235 ICU patients and used admission criteria to predict AKI. In the group that developed AKI, the authors observed that older age, high potassium levels, and high APACHE II scores on admission were independent predictors of AKI in the ICU. Peres *et al.*[15] also described AKI patients as being older and having higher potassium levels and APACHE II scores on admission, but failed to find these as independent risk factors in multivariate analysis. The latter findings were similar to the results reported in our study, in which older age and higher APACHE II scores and potassium levels did not yield statistically significant differences in multivariate analysis.

The main limitations of this study were the reduced size of our patient population and the fact that this was a retrospective study. However, the standardized procedures for data collection in the ICU provide for good reliability. This study has opened our institution for the possibility of organizing future research efforts.

Conclusion

The high incidence of AKI and mortality in ICU patients pose a significant public health challenge. Further studies are required to uncover innovative therapeutic strategies to prevent the occurrence of AKI in ICU patients and reduce death rates.

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