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Original Article

Impact of Acute Kidney Injury on In-Hospital Outcomes Amongst Critically Ill Patients

Huma Gul, Abdul Rehman Arshad, Haider Ali Khan, Muhammad Mubasher Ijaz

Combined Military Hospital Peshawar

Abstract

Objective: Present research was conducted study to determine frequency of acute kidney injury in intensive care unit and its impact on duration of stay and mortality.

Methods: Patients aged ≥12 years having normal serum creatinine on admission were consecutively enrolled. Exclusion criteria included chronic kidney disease, unwilling patients and those developing acute kidney injury outside intensive care unit. Urine output and serum creatinine were monitored daily to detect acute kidney injury using KDIGO criteria. Duration of in hospital stay and intensive care unit, need for mechanical ventilation and in-hospital mortality were compared amongst patients with and without acute kidney injury.

Results: 163 patients aged 53.67±21.69 years were enrolled of which 27 (16.56%) developed acute kidney injury, 13 (7.98%) required hemodialysis, 26 (15.95%) required mechanical ventilation and 37(22.70%) died. Patients with acute kidney injury stay longer in intensive care unit as compared to those not developing it (median 5 vs 2 days, p=0.013). Same was the case with total stay in hospital (median 11 vs 8 days, p=0.044). Acute kidney injury did not influence need for mechanical ventilation (14.81% vs 16.18%, p=1.000) or mortality (29.63% vs 21.32%, p=0.347).

Conclusion: Patients with Acute kidney injury stayed longer in intensive care unit but it does not affect mortality or need for mechanical ventilation.

Keywords: critical care, hospitalization, intensive care unit, outcome assessment, renal dialysis, renal replacement therapy

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Corresponding Author: Dr. Huma Gul **Email:** humagulaly@gmail.com

Introduction

Despite aggressive efforts to timely recognize and prevent acute kidney injury (AKI), its incidence is progressively increasing. It is estimated that 13 million people are affected every year, a vast majority of whom are from developing countries.[1] Pakistan is facing the same problem, with an escalating trend in the incidence and prevalence of renal diseases. This has placed a significant burden on the overall healthcare budget in terms of resources utilized during the acute phase, and the potential long-term outcomes including the development of chronic kidney disease with long term requirement of renal replacement therapy.[2]

AKI is commonly seen in intensive care unit (ICU) settings and could be associated with a need for more prolonged indoor care as well as an increased short- and long- term mortality risk. It is generally seen with the first 72 hours of ICU transfer, but some patients could have an element of preexisting renal dysfunction beforehand.[3] It is particularly important to identify the exact time of onset of AKI, since the clinical features and outcomes vary amongst patients with AKI developing before transfer to ICU as compared to those developing this in the succeeding days.[4] Unfortunately, we still do not have an ideal marker that could pick up AKI very early, may be in the subclinical stage.[5] This hampers our efforts to initiate adequate treatment well in time to avoid further progression of renal injury.

It has been estimated that more than 50% patients develop some degree of AKI in the ICUs.[6] AKI resulting from a wide range of predisposing factors may present with different incidences and prognoses. Hence there is difficulty in generalizing results from different studies. We do not have adequate statistics on this subject from

local setups. It is well known that the outcomes in our setups could be different from those in the Western world because of resource limitations.[7] This study was therefore planned to determine the true extent of the problem in our hospital. The results would help create an awareness on this topic and thus help in implementing strategies to reduce the incidence of AKI in ICU, thereby preventing the associated complications.

Methods

This observational study was conducted at the intensive care unit of Combined Military Hospital Peshawar from October 2021 to January 2022. Ethical Review Committee for Medical and Biomedical Research of Combined Military Hospital Peshawar had already given approval before the start of data collection (Letter number 00205/21). For sample size calculation, Epitools sample size calculator for two means with unequal sample size and unequal variances was used. A minimum sample size of 58 patients (including 23 with AKI and 35 without AKI) was calculated assuming that the expected frequency of AKI would be around 40% and the length of hospital stay amongst patient developing AKI would be 6.7± 3.8 days, and amongst those not developing AKI would be 4.1±3.1 days, using statistics from a study carried out in Sudan recently.[8] All patients or their next of kins provided consent for participation in this study, depending on capacity of the patients. We consecutively enrolled patients aged 12 years or more, who had normal renal excretory functions at the time of admission to ICU, but later developed AKI during stay in ICU. Exclusion criteria included development of AKI in community or the hospital, but outside ICU; chronic kidney disease or end-stage renal failure; unwillingness to participate in this study.

Urine output monitoring and assessment of renal functions through blood testing (serum urea, creatinine, sodium and potassium) was routinely done on daily basis for all patients as part of the ICU protocol. These were reviewed every day to pick up cases of acute kidney injury using Kidney Disease Improving Global Outcomes (KDIGO) criteria. Severity was also gauged using the same definition. We also noted down the baseline demographic data as well as the comorbidities. The primary outcomes of interest were the total duration of stay in hospital, duration of stay in ICU, need for mechanical ventilation and in-hospital mortality. This relevant information was thus also noted down for all cases.

Data was analysed using the Statistical Package for Social Sciences version 24. Normality of data was checked using Shapiro- Wilk test. Most data had non-parametric distribution and was thus defined as median and inter quartile ranges. Data with normal distribution was described as mean± standard deviation. Comparison of outcomes amongst patients with and without AKI was made using independent samples Mann-Whitney U test for medians, independent samples t-test for means and Chi Square test/ Fischer's Exact test for proportions. Statistical significance was set at $p \leq 0.05$ for all tests of comparison. Survival analysis as a function of the duration of ICU stay was done for patients with and without AKI using Kaplan-Meier plots and Generalized Wilcoxon test.

Results

We studied 163 patients aged 53.67±21.69 years. Their essential characteristics are listed in Table 1. Durations of stay in hospital and intensive care unit (median and inter quartile ranges) were 9 (4-16) and 2 (1-6) days respectively. AKI developed in 27 (16.56%) cases, out of which 13 (7.98%) required haemodialysis. Most of these patients (19; 70.37%) had stage 3 AKI, whereas stage 2 and stage 1 AKI were seen in 2 (7.41) and 6 (22.22%) patients respectively. During stay in hospital, 37(22.70%) patients died. Mechanical ventilation was required in 26(15.95%) patients. As shown in Table 2, patients with AKI had longer duration of stay in hospital

Table 1: *Comparison of Characteristics Amongst Patients with and without AKI*

	Characteristic	AKI (n=27)	No AKI (n= 136)	*p*
Age (years)		55.48± 20.17	53.32± 22.04	0.619
Gender	Male	12 (44.44%)	83 (61.03%)	0.110
	Female	15 (55.56%)	53 (38.97%)	
Comorbidities	Diabetes Mellitus	10 (37.04%)	54 (39.71%)	0.795
	Hypertension	14 (51.85%)	55 (40.44%)	0.273
	Ischemic heart disease	12 (44.44%)	23 (16.91%)	0.001
	Stroke	2 (7.41%)	8 (5.88%)	0.763
	Obstructive airway disease	0 (0.00%)	5 (3.68%)	0.312
	Chronic liver disease	0 (0.00%)	7 (5.15%)	0.228
Specialty	Internal Medicine	16 (59.26%)	58 (42.65%)	0.293
	General Surgery	6 (22.22%)	29 (21.32%)	
	Neurosurgery	0 (0.00%)	22 (16.18%)	
	Orthopaedics	2 (7.41%)	10 (7.35%)	
	Gynaecology	3 (11.11%)	15 (11.03%)	
	ENT	0 (0.00%)	2 (1.47%)	
Direct admission to ICU	Yes	6 (22.22%)	50 (36.76%)	0.146
	No	21 (77.78%)	86 (63.24%)	
Baseline serum creatinine (µmol/l)		92.75± 16.57	86.47± 15.51	0.077
Maximum serum creatinine (µmol/l)		612 (183-700)	98.11 (88.39-109.25)	<0.001

AKI= acute kidney injury; ICU= intensive care unit

and ICU as compared to those not developing AKI during stay in hospital. The increase in duration of total stay was primarily because of an extended stay in ICU since the stay in hospital after being shifted out of ICU was not different amongst the two groups. The presence or absence of AKI did not influence the need for mechanical ventilation or mortality. Kaplan-Meier estimator showed that the presence of AKI did not affect the probability of getting shifted out of ICU alive (p=0.184). The survival curves are shown in Figure 1. Comparison of outcomes amongst patients with various stages of AKI did not reveal any statistically significant differences, as shown in Table 3.

Table 2: *Comparison of Outcomes Amongst Patients with and without AKI*

	AKI (n=27)	No AKI (n= 136)	*p*
Duration of ICU stay (days)	5(1- 9)	2 (1- 5)	0.013
Duration of post-ICU stay (days)	3(0- 8)	2 (1-5)	0.606
Duration of total hospital stay (days)	11(10- 18)	8 (4-15)	0.044
Need for mechanical ventilation	4(14.81%)	22 (16.18%)	1.000
Mortality	8(29.63%)	29 (21.32%)	0.347

AKI= acute kidney injury; ICU= intensive care unit

Table 3: *Comparison of Outcomes amongst Patients with different Stages of AKI*

	Stage 1 (n=6)	Stage 2 (n=2)	Stage 3 (n=19)	*p*
Duration of ICU stay (days)	3 (1- 6)	1 (1- 1)	7 (3- 17)	0.092
Duration of post-ICU stay	7 (2-8)	1(1- 1)	3 (0- 11)	0.696
Duration of total hospital stay (days)	12(10-15)	3(3- 3)	11 (11- 19)	0.157
Need for mechanical ventilation	0 (0.00%)	0(0.00%)	6(31.58%)	0.372
Mortality	1 (16.67%)	1(50.00%)	4(21.05%)	0.632

AKI= acute kidney injury; ICU= intensive care unit

Discussion

This study focused on documenting the frequency of AKI in critically ill patients as well as its impact on length of hospital stay and in- hospital mortality. It has shown that AKI is a major problem in our ICU, affecting

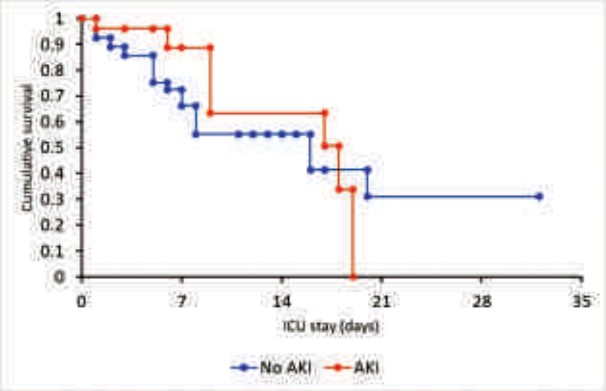

Figure-1: *Kaplan- Meier Curve Showing Survival in Intensive Care Unit.*
AKI= acute kidney injury; ICU= intensive care unit

one in every six patients. It lengthened the duration of stay in ICU as well as the overall timespan of stay in hospital. Similarly, mortality rate was also significant in this cohort, with one out of every four to five patients dying in the hospital. However, it was not related to the development of AKI or otherwise. Need for mechanical ventilation was also not influenced by AKI.

It is heartening to know that the frequency of AKI in our cohort was significantly lower than that reported elsewhere. In a study from our hospital done four years ago, AKI was seen in 31.4% surgical patients with traumatic injuries admitted to the ICU.[9] However, the pool of patients was not as diverse as in this study. Using RIFLE criteria, Hussain et al found that AKI occurred in 68.55% patients admitted to a tertiary care medical ICU at Islamabad.[10] In the multinational AKI-EPI study, 57.3% of ICU patients from 33 countries had AKI, though not all of them developed this during ICU stay.[11] The most probable reason for a lower incidence in our cohort is the greater variety of patients admitted, many of whom were not septic. Renal replacement therapy was required in 6.75% of our patients. This is quite similar to 4.3% reported by a multicenter, multinational study published many years ago.[12] Direct comparisons in this regard are obviously difficult because of differences in criteria used for initiation of renal replacement therapy. Timing for initiation of renal replacement therapy in AKI had also remained a contentious issue till recently, when some clarity has been added by latest published evidence.[13]

Development of AKI was associated with an extended length of stay in ICU and overall stay in hospital amongst our patients. This is in accordance with results from many other studies done previously. Amongst 1500 patients admitted to an ICU in Brazil, the median duration of stay in ICU was 5 days longer amongst patients with AKI.[14] In a retrospective audit of 745 patients, Challiner et al have shown that patients with

AKI had a length of stay in hospital almost two and a half times longer than those without AKI.[15]

It has been shown that AKI is associated with higher mortality in ICUs. Hashemian et al described mortality rates of 19.7% versus 0.7% for those with and without AKI amongst 200 patients from Iran.[16] In a retrospective observational study involving 2823 patients admitted to an ICU in Seoul, Korea over a six years period, the hazard ratio of death associated with AKI ranged from 2.08 to 5.14, depending on the stage of AKI.[17] However, this was not the case in our group of patients. Khan, et al also did not find any difference in mortality amongst 100 patients with different stages of AKI admitted to an ICU at Karachi.[18] Considering the objectives of our study, it is very much possible that most cases of AKI were picked up very early and were then treated aggressively, something that could have easily affected the outcomes. This potential bias at subconscious level can only have been removed by retrospective analysis of data from our setup.

There was no difference in outcomes amongst patients with different stages of AKI. This is most probably because of the fact that only a few patients developed stage 1 or 2 AKI. However, the study was adequately powered as far as its primary goals were concerned. The overall frequency of AKI was much lower than what we had anticipated at the time this study was designed. Yet, we had an acceptable number of patients with AKI included in the cohort. In a study comparing the outcomes between hospital and community acquired AKI, Khan et al also found that the mortality rates were not related to the stage of AKI amongst 200 patients treated at Agha Khan University Hospital Karachi.[19]

An important strength of this study is the diverse group of patients included for analysis. Our hospital has a single ICU catering for the needs of patients from different specialties. A major limitation of this study is that we did not follow up the patients after being discharged from the hospital, so that data on resolution of AKI and the time period required for this is not documented for every patient. There is evidence to suggest that the duration of AKI is directly related to negative in-hospital outcomes, including mortality.[20] Critically ill patients often have AKI as part of multiorgan failure. However, we did not record data regarding functional status of other vital organs and this was not catered for during statistical analyses. We are thus not sure how this could have influenced our results. This dataset was from a single center only, such that the extrapolation of results to other setups with different types of patients might not be practically possible.

Conclusion

AKI is a significant problem in critically ill patients, associated with an extended length of stay in ICU. However, it does not affect mortality or the need for invasive mechanical ventilation.

Conflict of Interest: *None*

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