RESEARCH ARTICLE

Community acquired versus hospital acquired acute kidney injury; causes and outcome

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Abstract

Objective: To evaluate causes of community-acquired and hospital-acquired acute kidney injury and the factors associated with increased inpatient mortality.

Method: The observational prospective study was conducted at the Aga Khan University Hospital, Karachi, from September 2018 to March 2019, and comprised patients having acute kidney injury either at the time of admission in group A or developed it after 48 hours of hospital stay in group B. The patients were followed up for 12 weeks and outcomes were categorised as recovered, developed chronic kidney disease, died or remained dialysis-dependent. Data was analysed using SPSS 19.

Results: Of the 400 patients, 347(86.8%) were in group A; 190(54.8%) males and 157(45.2%) females with an overall mean age of 57.2±17.0 years. The remaining 53(13.3%) were in group B; 31(58.5%) males and 22(41.5%) females with an overall mean age of 58.5±16.3 years. Urinary tract infection 105(30.3%) was the most frequent cause in group A, followed by volume depletion 73(21%). The causes in group B were multiple, with nephrotoxic antibiotics vancomycin 21(39.6%) and polymyxin 20(37.7%) being the most common. At 12 weeks, 224(56%) patients recovered, 55(13.8%) died, 82(20.5%) and 38(9.5%) developed new onset and progressive chronic kidney disease, respectively, and 1(0.25%) patient remained dialysis-dependent. Chronic liver disease, renin angiotensin system inhibitors, infection, shock, invasive ventilation and increasing length of stay were associated with increased inpatient mortality ($p<0.05$).

Conclusion: Acute kidney injury was largely community-acquired, and infection was the leading cause with better outcome in contrast to hospital-acquired acute kidney injury which was mostly multifactorial.

Keywords: Acute kidney injury, Chronic kidney disease, Haemodialysis, Sepsis. (JPMA 72: 1128; 2022)

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Introduction

Acute kidney injury (AKI) is one of the most frequently encountered problems in a hospital setting. The incidence of AKI is around 15% in hospitalised patients which significantly increases to more than 60% in critically ill patients admitted to intensive care unit (ICU).[1-3]

Many factors, such as chronic kidney disease (CKD), diabetes mellitus (DM) and increasing comorbidity, predispose an individual to an increased risk of developing community-acquired AKI (CA-AKI). However, hospital-acquired AKI (HA-AKI) is not found to be associated with underlying comorbid conditions, and the risk profiles are different from CA-AKI.[4] In recent years, drugs, especially antibiotics, have been increasingly recognised as the major culprit causing HA-AKI with estimated incidence of about 24% in patients aged >60 years.[5]

AKI is not just a simple disorder, rather it is a disease which not only involves patient factors including their geographical features and socioeconomic status (SES). This diversity has a great influence on prevalence, causes and outcome of AKI, and, hence, the aetiology of AKI varies widely among different regions and the outcome is affected by their environment.[6,7]

There is scarcity of data on AKI from South Asia where the causes and outcome may be entirely different owing to the lack of resources and other factors mentioned above. The current study was planned to evaluate the causes and outcomes of AKI, and to assess factors associated with mortality.

Patients and Methods

The prospective study was conducted at the Aga Khan University Hospital (AKUH), Karachi, from September 2018 to March 2019. After approval from the institutional ethics review committee, the sample size of 300 was found sufficient, by using WHO sample size calculator,[8] for the identification of risk factors with 80% power, 95% confidence interval (CI) and odds ratio (OR) 1.90 with estimated risk factor prevalence of 30% in CA-AKI.[4] After taking written consent, all adult inpatients with AKI for

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whom nephrology consultation was sought were included. Patients aged <18 years, those having advanced malignancy, terminal illness, stage 5 CKD and kidney transplant were excluded, and so were those who refused to volunteer. AKI was defined using the Kidney Diseases Improving Global Outcome (KDIGO) criteria as a rise in serum creatinine (Cr) by 0.3 mg/dl within 48 hours or an increase of 1.5 times from baseline within seven days.[9] On the basis of KDIGO criteria, the patients were categorised into stage1, stage 2 and stage 3 AKI. Patients who had AKI at the time of hospital admission were labelled as CA-AKI, and patients who developed AKI after 48 hours of hospital stay were labelled as HA-AKI.

For baseline serum Cr, the most recently available Cr either from prior hospital discharge or clinic visit within one year was used. In cases where baseline Cr was not available, the patients were included if they had acute presentation and history, and laboratory parameters were suggestive of AKI. The baseline Cr was estimated by Modification of Diet in Renal Disease (MDRD) formula assuming glomerular filtration rate (GFR) of 75 ml/min per 1.73m^2.[9]

A detailed history was taken regarding comorbid conditions and drugs, especially renin angiotensin system (RAS) inhibitors, non-steroidal anti-inflammatory drugs (NSAIDS) and diuretics. The patients who developed acute kidney injury and had a definite medication history available were included in the analysis. The reason for admission and the hospital course with special attention to the use of nephrotoxic drugs / contrast, any cardiac event, hypotensive episodes, development of new infection, invasive ventilation, length of stay, need and duration of haemodialysis were recorded.

Cardiac event was defined as the new-onset myocardial infarction (MI), including both ST elevation MI (STEMI) and non-ST elevation MI (NSTEMI), or any new onset rhythm abnormality with haemodynamic instability.

All patients were followed up for 12 weeks for the outcome of AKI. Complete recovery meant Cr reverted to baseline or below. Partial recovery meant patients had >50% reduction in Cr from the maximum admission level, or became dialysis-free. When Cr failed to reach baseline in case of normal baseline renal function, it was taken as new onset CKD, and when Cr showed progression from the baseline at 12 weeks in case of underlying CKD, it was taken as progressive CKD. The other outcomes were dialysis dependency and death.

Data was analysed using SPSS 19. Continuous variables with normal and non-normal distributions were reported as mean ± standard deviation and median with inter-quartile range (IQR). Continuous and categorical variables between the groups were compared using independent sample t test, Mann-Whitney U test and chi-square test as appropriate. To determine the independent risk factors, OR and their 95% CIs were estimated using logistic regression. The likelihood ratio test was used to assess the association between the explanatory variables and the outcome variables. Multivariable models were constructed, including variables that showed an effect in the prediction of risk factors in the univariable analyses, and the significance was set at $p<0.05$.

Results

Of the 400 patients, 347(86.8%) were in group A; 190(54.8%) males and 157(45.2%) females with an overall mean age of 57.2±17.0 years. The remaining 53(13.3%) were in group B; 31(58.5%) males and 22(41.5%) females with an overall

Table-1: Baseline characteristics of patients with community-acquired (CA) and hospital-acquired (HA) acute kidney injury (AKI).

Characteristics	Total patients n=400 (%)	CA-AKI; n=347 (86.8%)	HA-AKI; n=53 (13.3%)	p value
Age in years	57.4 ± 16.9	57.2 ± 17.0	58.5 ± 16.3	0.6
Gender no. (%)				
Male	221 (55.3)	190 (54.8)	31 (58.5)	0.65
Female	179 (44.8)	157 (45.2)	22 (41.5)	
Pre-existing CKD No. (%)	118 (29.5)	113 (32.6)	5 (9.4)	<0.001
Comorbid				
Diabetes no. (%)	194 (48.5)	171 (49.3)	23 (43.4)	0.4
Hypertension No. (%)	246 (61.5)	217 (62.5)	29 (54.7)	0.3
IHD no. (%)	95 (23.8)	80 (23.1)	15 (28.3)	0.4
CLD no. (%)	12 (3.0)	12 (3.5)	Nil	0.4
Kidney stone disease No. (%)	23 (5.8)	23 (6.6)	Nil	0.06
Medication history				
RAS Inhibitors† No. (%)	29/118 (24.6)	28/83 (33.7)	1/35 (2.9)	<0.001
NSAID† No. (%)	21/115 (18.3)	14/80 (17.5)	7/35 (20)	0.8
Diuretics† No. (%)	14/116 (12.1)	11/80 (13.6)	3/36 (8.3)	0.5
Admission Cr (mg/dl) [IQR]	3.2 [1.9-4.9]	3.6 [2.3-5.2]	0.9[0.8-1.2]	<0.001
Maximum Cr (mg/dl) [IQR]	3.7 [2.6-5.3]	3.8 [2.6-5.6]	3.1 [2.4-4.3]	0.04
Stage of AKI No. (%)				
I	60 (15)	55 (15.9)	5 (9.4)	0.2
II	95 (23.8)	76 (21.9)	19 (35.8)	0.02
III	245 (61.3)	216 (62.2)	29 (54.7)	0.3
Renal replacement therapy No. (%)	93 (23.3)	84 (24.2)	9 (17.0)	0.24
Invasive ventilation No. (%)	71 (17.7)	49 (14.1)	22 (41.5)	<0.001
Length of hospital[IQR]; days	7 [5-11]	7 [4-10]	13 [9-20]	<0.001*

CKD: Chronic kidney disease.
IHD: Ischemic heart disease.
CLD: Chronic liver disease.
RAS: Renin angiotensin system.
NSAID: Non-steroidal anti-inflammatory drugs, CR: Creatinine, IQR: Interquartile range.
*Mann- Whitney U Test.
† Only those patients who had a definite history of RAAS inhibitors, NSAIDS and diuretics were included in analysis.

Table-2: Causes of community-acquired (CA) and hospital-acquired (HA) acute kidney injury (AKI).

Community acquired AKI				Hospital acquired AKI	
Causes	**Number (%)**	**Causes**	**Number (%)**	**Causes**	**Number (%)**
Urosepsis (UTI)	105 (30.3)	RPGN/GN	11 (3.2)	Vancomycin	21(39.6)
LRTI	88 (25.4)	HRS	11 (3.2)	Polymyxin	20 (37.7)
Other infections	77 (22.1)	Rhabdomyolysis	7 (2)	Cardiac event	20 (37.7)
Volume loss	73 (21)	Pregnancy related	7 (2)	Infection	14 (26.4)
Cardiac event	69 (19.9)	Dengue	3 (0.8)	Shock/Hypotension	13 (24.5)
Contrast induced	35 (10.1)	Poisoning	2 (0.6)	Contrast induced	7 (13.2)
Malaria	14 (4)	Heat stroke	2 (0.6)	Amphotericin	4 (7.5)

*LRTI: Lower respiratory tract infection. *RPGN: Rapidly progressive glomerulonephritis. *GN: Glomerulonephritis. *HRS: Hepato-renal syndrome. UTI: Urinary tract infection.

Table-3: Univariable and multivariable analysis of factors associated with mortality.

Characteristics	Mortality		Odds ratio (95% CI)	P value	Adjusted Odd ratio (95% CI)
	Yes; n= 55(%)	No; = 345 (%)			
Age, years	57.7 ± 16.1	57.4 ± 17.1	1.001(0.98-1.01)	0.9	-
Gender					
Male	33(60)	188(54.5)	1.0	0.44	-
Female	22(40)	157(45.5)	0.79(0.44-1.42)		
CKD	12(21.8)	106(30.7)	0.62(0.31-1.24)	0.18	
CLD	6(10.9)	6(1.7)	6.91(2.14-22.30)	0.001	10.5 (3.0-35.8)
Infection	47(85.5)	244(70.7)	2.43(1.11-5.33)	0.02	-
UTI	10(18.2)	102(29.6)	0.52(0.25-1.09)	0.08	-
LRTI	28(50.9)	84(24.3)	3.22(1.79-5.77)	<0.001	3.3 (1.7-6.1)
Abdominal infection	10(18.2)	39(11.3)	1.74(0.81-3.73)	0.15	-
Shock	25(45.5)	50(14.5)	4.91(2.67-9.04)	<0.001	-
Infection related	24(43.6)	38(11)	6.25(3.32-11.75)	<0.001	-
Cardiac causes	14(25.5)	20(5.8)	5.54(2.60-11.82)	<0.001	-
RAS inhibitors	1(4.5)	28(29.2)	0.11(0.01-0.90)	0.04	
Polymyxin	12(54.5)	35(36.8)	2.05(0.80-5.25)	0.13	-
Vancomycin	14(63.6)	31(32.6)	3.61(1.37-9.51)	0.009	
Amphotericin	6(28.6)	5(5.3)	7.20(1.94-26.59)	0.003	-
Hospital stay, days	11.8 ± 7.3	8.6 ± 6.7	1.05(1.01-1.09)	0.004	-
Days on invasive ventilation	10.8 ± 7.2	4.4 ± 3.2	1.28(1.11-1.49)	0.001	-
Stage of AKI					
I	5(9.3)	55(15.9)	1.0		-
II	13(24.1)	82(23.7)	1.74(0.58-5.16)	0.31	
III	37(67.2)	208(60.3)	1.89(0.71-5.05)	0.2	

*CKD: Chronic kidney disease. *CLD: Chronic liver disease. *UTI: Urinary tract infection. *LRTI: Lower respiratory tract infection. *ICU: Intensive care unit.
RAS: Renin angiotensin system, LRTI: Lower respiratory tract infection, CI: Confidence interval.

mean age of 58.5±16.3 years (Table-1). Among CA-AKI patients, 113(32.6%) had underlying CKD. Having underlying CKD and taking renin angiotensin system (RAS) inhibitors were found to be independent predictors for the development of CA-AKI (p=0.01 and p=0.02).

Haemodialysis was performed in 93(23.3%) patients and the difference between the groups was non-significant (p=0.24). Of these patients, 72 77.4%) required it for <2 weeks.

Urinary tract infection (UTI) 105(30.3%) was the most frequent cause in CA-AKI group, followed by volume depletion 73(21%). The causes in the HA-AKI group were multiple, with nephrotoxic antibiotics Vancomycin 21(39.6%) and Polymyxin 20(37.7%) being the most common (Table-2).

At 12 weeks, 224(56%) patients recovered, 55(13.8%) died, 82(20.5%) and 38(9.5%) developed new onset CKD and progressive CKD, respectively, and 1(0.25%) patient remained dialysis-dependent. Mortality was high in HA-AKI group 42(12.1%) compared to the CA-AKI group 13(24.5%) (p=0.01). The combined mortality of stage I and II AKI was 18(32.7%) which rose to 37(67.2%) for stage III

AKI. There was no significant mortality difference among patients requiring haemodialysis as opposed to those who did not (p>0.05).

Chronic liver disease, RAS inhibitors, infection, shock, invasive ventilation and increasing length of hospital stay were associated with increased inpatient mortality (Table-3).

Discussion

The current study found that majority of patients had CA-AKI compared to HA-AKI, which is in line with literature.[7,10] Infection was the leading cause of CA-AKI, followed by volume depletion in the current study, which has been reported earlier as well.[7] A study in Malawi reported that sepsis and volume depletion together accounted for 86.9% of AKI patients,[11] and the main causes of infection were gastroenteritis (GI) and tuberculosis (TB), while lower respiratory tract infection (LRTI) and UTI accounted for only 10% and 0.7% patients, respectively. The current study had UTI and LRTI among the leading causes of infection and AKI. The difference could be explained by the age difference as the mean age of patients was 58 years compared to 40 years, and 48% had diabetes opposed to 6% in Malawi.[11] In another local study, urosepsis was the leading aetiological factor in diabetic patients presenting with AKI.[12]

In most developing countries, including Pakistan, volume depletion is still one of the major causes of AKI,[13] but the numbers are declining with time, and this could be explained by the improvement in health structure in the country. Although volume depletion was the second most frequent cause in the current study, the true percentage is not representative as nephrology consultation was not sought in all the patients because of good response to hydration and rapid improvement in kidney function.

With regards to HA-AKI, the causes were multifactorial and it was difficult to find out the exact cause. Nevertheless, Vancomycin and Polymyxin were most frequently used in patients who developed HA-AKI. Similar results were reported by a study in which multiple risk factors were found for HA-AKI, but half of the cases were related to drugs only.[14] Studies conducted to this date have shown Vancomycin to be an important cause of HA-AKI associated with high mortality.[15] It is, however, not established if Vancomycin is the most common drug to cause it.

The current study showed an overall mortality of 13.8% which increased as the severity of AKI went up. Nevertheless, patients with CA-AKI turned out to be more resilient than patients with HAAKI. Despite more patients with CA-AKI progressing to stage III, they had shorter length of stay and a lower in-hospital mortality (12.1%) compared to those with HA-AKI (24.5%). A report demonstrated significant mortality of 47.1% in HA-AKI compared to 15.6% in CA-AKI.[16] Similarly, a recent study from Latin America revealed in-hospital mortality of 20.2% and 43.8% for CA-AKI and HA-AKI, respectively.[17] This could be reflective of the overall outcome as HA-AKI occurs in many critically ill patients. However, a study showed the opposite trend, with more in-patient deaths in CA-AKI compared to HA-AKI.[7]

The current study found multiple independent risk factors for in-hospital mortality, such as infection, shock, Vancomycin, amphotericin and mechanical ventilation. In addition to these poor prognostic factors, which have been proved by other studies also,[11,17] the current study also found significant mortality in patients who were taking RAS inhibitors, patients with LRTI and those with lengthy hospital stay of >7 days. Nevertheless, the study did not find haemodialysis as a risk factor for raised mortality. A study in Brazil found haemodialysis to be associated with marginally increased mortality.[18]

A number of studies[19-21] have shown increased risk of new onset CKD and progressive CKD following AKI episodes. In the current study, despite the fact that the follow-up period was short, nearly one-fourth of the patients developed new onset CKD or progressive CKD.

The current study has several limitations. The findings cannot be generalised as it is a single-centre study. Secondly, the patients were only followed for 12 weeks, and no long-term consequences of AKI can be assessed on this basis. Finally, although drugs contributed to HA-AKI the most, this was not the only contributory factor as majority of these patients also had infection and were hypotensive.

Conclusion

AKI occurred mostly in the community due to infections with relatively better outcome opposed to HA-AKI which was caused by multiple factors, most importantly nephrotoxic antibiotics.

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