ORIGINAL ARTICLE

OUTCOMES OF VARIOUS STAGES OF ACUTE KIDNEY INJURY IN CRITICAL CARE PATIENTS

Quratulain Khan[1], Ejaz Vohra[1]
[1]Department of Critical Care Medicine, Ziauddin Hospital, Karachi

ABSTRACT

Background: Acute Kidney Injury is not a single disease but rather a syndrome comprising of multiple clinical conditions. The high rate of morbidity associated with AKI poses a burden on both the public as well as private sector. Small changes in serum creatinine concentrations associated with a substantial increase in the risk of morbidity. Therefore, detection of even small changes in kidney injury has an important prognostic value to avoid chances of hemo-dialysis and the associated risks which can result in both better outcomes as well as lowering financial burden on the patient as well as the state.

Methods: A sample size of 100 patients was included as calculated by taking reported incidence of 36%. Patient's baseline and maximum creatinine was taken during ICU stay together with urine output monitoring during first 48 hours. Staging of acute kidney injury (AKI) was done by Acute Kidney Injury Network (AKIN) criteria. Outcome of renal failure was assessed on the basis of full, partial and no recovery.

Results: Out of 100 patients, 52% were in stage 1, 32% were in stage 2 and 16% were in stage 3. AKI was common in females; present in 37 males and 63 females; (p value <0.05). Full renal recovery was achieved in 62 patients (62%) of AKI; 25 patients (25%) were partial recovered, and in 13 patients (13%) recovery could not be achieved. Recovery was significantly lower (25%) and potentially greater in stage1 (79%).The chi square between outcome and acute kidney injury revealed statistical significant value (p value <0.001). Hemodialysis requirement was significantly higher in AKI stage3 (62%) than AKI stage1 (4%); (P < 0.001). There were no significant differences in duration of ICU stay, age and mortality.

Conclusion: Our study showed the morbidity and mortality associated with rising creatinine with increasing stages of acute kidney injury. Recovery in stage 1 was significantly higher and lower in stage 3 and therefore emphasis is required on early diagnosis and timely management of AKI that can prevent patients from distressing and life threatening problems.

KEY WORDS: Acute Kidney Injury Network, Risk Injury Failure Loss End-Stage Kidney classification, Acute Kidney Injury, End-stage renal disease, Glomerular filtration rate, Renal Replacement Therapy.

INTRODUCTION

Acute kidney injury (AKI) is a common clinical problem in Envisioned Intensive Care Unit (ICU) patients and independently predicts poor outcome [1, 2]. Multiple trials have shown the occurrence of acute kidney injury in 36% of patients admitted in intensive care unit [3, 4].

The etiology of AKI in critically ill patients is often multifactorial. However, sepsis has consistently been found to be a leading contributing factor to AKI in critical illness [5, 6]. Discriminating between AKI of septic and non septic origin may have clinical relevance[7]. Evolving data suggests that septic AKI may be characterized by a distinct pathophysiology [8, 9]. For that reason, septic AKI may be associated with important differences in terms of patient characteristics, response to interventions and clinical outcomes when compared with non septic precipitants of AKI [9].

Small changes in serum creatinine concentration are associated with a substantial increase in risk of death. AKI is not a sole entity but relatively conditions encompassing numerous clinical situations. Outcomes from AKI depend on underlying disease, severity and duration of renal impairment, and patient's renal baseline condition[10]. The progression of AKI is the result of intricate communications amid

Corresponding Author: Quratulain khan*

the real insult and ensuing inflammation and coagulation.

Loss of renal function can occur without histological signs of tubular damage or even necrosis. The detrimental effects of AKI are not limited to classical well-known symptoms such as fluid overload and electrolyte abnormalities. AKI can also lead to problems that are not readily appreciated at the bedside and can extend well beyond the ICU stay, including progression of CKD and impaired innate immunity.

In recent years the Acute Dialysis Quality Initiative (ADQI) group and the Acute Kidney Injury Network (AKIN) published the diagnostic criteria for AKI, defined as an abrupt (within 48 h) reduction in kidney function signified by an absolute increase in serum creatinine of ≥0.3 mg/dl (or ≥26.4 µmol/liter), an increase in Serum creatinine of ≥50% (1.5-fold from the baseline level), or a reduction in urine output. An AKIN criterion was found to be more sensitive than others in determining the frequency of AKI, however no difference in hospital mortality was found. Jiang et al found incidence of AKIN to be 25.8% compared to Risk, Injury, and Failure, and Loss, and End-Stage criteria RIFLE (Risk Injury Failure Loss End-Stage Kidney) 18.1% [11]. Chang et al also found more patients identified by AKIN criteria 68% than by RIFLE 60% [12], but no significant difference was found between the two criteria in determining the total hospital mortality by (37.9% vs. 34.1%)[12]. Chen et al [13] found increased mortality in patients with increased severity score of AKI. Local recent data lacking in determining frequency, follow up and outcomes of critically ill patients with acute kidney injury. The objective of the study is to determine outcomes of various stages of Acute Kidney Injury in critical care patients with normal renal function at baseline.

METHOD

The Prospective Observational Cohort study was carried out from January 2015 to June 2015 on 100 patients admitted in critical care unit of Ziauddin university hospital. All males and females with age more than 18 years who were admitted in ICU with any illness and remain in ICU for more than 48 hrs, also patients who had AKI according to AKIN criteria during ICU stay were included in the study. Acute kidney injury was defined as sudden deterioration of renal function i-e; within 48 h. Staging system for acute kidney injury according to AKIN Criteria was used with both Serum creatinine criteria and Urine output (UO) criteria applied. According to Serum Creatinine criteria, Stage 1 included patients with Absolute increase in serum creatinine of ≥0.3 mg/dl or increase to 1.5–2.0-fold from baseline, Stage 2 included patients with Serum creatinine increases >2.0–3.0-fold from baseline. Stage 3included Serum creatinine increase >3.0-fold from baseline or serum creatinine of ≥4.0 mg/dl with an acute increase of at least 0.5 mg/dl.According to Urine output (UO) criteria, Stage 1 included patients with UO < 0.5ml/kg/hr for 6 hours, Stage 2 included UO< 0.5ml/kg/hr for 12 hours and Stage 3 included patients with UO <0.3 ml/kg/h for 24 h or anuria for 12 h or need for Renal Replacement Therapy. In our study serum creatinine concentration as criteria to assign a category in AKIN classification was used. The Outcomes was defined by full recovery: serum creatinine concentration fell to baseline in cases of AKI during ICU stay, partial recovery with serum creatinine level decreased after treatment but did not reach to baseline in case of AKI during ICU stay and no recovery with serum creatinine level did not decrease OR increased in serum creatinine level observed during ICU stay. Patients included all males and females who were admitted in ICU with any illness, age more than 18 years, Patients remain in hospital for more than 48 hrs and Patients who had AKI according to AKIN criteria during hospital stay. Patients below 18 years of age, who have prior history of chronic renal insufficiency, were excluded.

Data was collected by taking informed consent to be included in the study and approval from ethical committee of the hospital was taken. Complete base line labs including complete blood count (CBC), liver function tests (LFTs), renal function tests (RFTs) and other workup related to their illness was done. Serum creatinine above 1.35mg/dl was considered abnormal. Standard of care treatment was given according to their diagnosis, co-morbidities and active issues. Monitoring of vitals and urine output was done on hourly bases. Patients were followed on daily basis including urine output, vital monitoring and renal functions.

The statistical analysis was performed by using SPSS.20. Descriptive statistics were presented as means ± SD like sex, age, ICU stay. The quantitative variables were expressed as frequencies and percentages. Chi square was applied to determine relationship between categorical variables and $p<0.05$ was considered significant. Binary logistic regression was used to predict effect of maximum creatinine level on patient's mortality. Outcomes were determined by full recovery, partial recovery

and no recovery.

RESULTS

Patients (n=100) selected for the study. 93 patients developed renal insult during the course of their illness within ICU stay but 07 patients had normal renal functions at time of admission but developed renal injury within ward and later shifted to ICU. There were 63 females and 37 males with a sex ratio of female vs. male 1.7:1 (table 1). The chi square between gender and acute kidney injury revealed statistical significant difference (p value 0.029). Mean age in year for patients with AKI was 63.2+15 with an average age among males was 69 years and of females was 59 years. Among 100 patients who selected, 52% were in stage 1, 32% were in stage 2 and 16% were in stage 3. Full renal recovery was achieved in 62 patients of AKI; 25 patients were partially recovered, and in 13 patients no renal recovery seen. Out of 62 patients who fully recovered, 41(79%) were in stage I, 17(53%) were in stage II and 4(25%) were in stage III. Out of 25 patients who partial recovered, 9(17%) were in stage I, 11(34%) were in stage II and 5(31%) patients were in stage III. Out of 13 patients who did not recover 2(4%) were in stage I, 4(12%) were in stage II and 7(44%) patients were in stage III. Recovery in stage3 was significantly lower and potentially greater in stage1 ($P < 0.001$). The chi square between outcome and acute kidney injury showed statistical significant value (p value <0.001) with mean duration in days was 6.68+3.62 and P value of (0.64). The limitation of our study was that it is solely ICU based study so renal outcome of patients were not followed when shifted out of ICU and secondly it was not reported at regular interval as patients were either expired or shifted out before that interval.Most patients who received Hemodialysis were in stage 3 i.e.62% while in stage 1 it was required only in 4% patients; ($P < 0.001$) secondary to refractory pulmonary edema and metabolic acidosis hyperkalemia. So early recognition of patients with kidney injury can prevent patients from Hemodialysis.

In our study, mortality is not related to the severity of renal injury as patient's primary illness and its severity with co morbids are also contributing factor. Out of 71 patients who alive, comorbids seen in only 23 patients and while out of total 29 patients who expired, comorbids were present in 20 patients, with significant p value 0.001. Similarly ventilator requirement in alive patients were found only in 20 patients while out of total 29 patients who expired, ventilator requirement were in 19 patients. Some patients have more than 01 co morbid along with current illness.

Ventilator requirement in stage 1 was 23.1%, in stage 2 was 34.4% and in stage 3 was 56.3% with significant association with severity of renal injury i.e. p value of 0.043 while inotropes requirement in stage 1 was 34.6%, in stage 2 was 53.1% and in stage 3 was 81.3% with significant association with staging of renal injury having p value of 0.004

Mortality in stage1 was 23%, stage2 was 31% and stage3 was 37% but p value (0.470) indicated statistical no significant difference. Out of 12 patients who expired in stage 1, 10 patients achieved full renal recovery before their death. In stage 3 out of 07 patients who expired, 03 were failed to show renal recovery but 02 had full renal recovery and 02 were partial recovered at time of death. Out of 10 patients who expired in stage 2, 07 were partial recovered and 03 had no renal recovery at time of death. Logistic regression analysis also showed an independent association of rising creatinine on mortality [Odds Ratio 1.20(95% CI (0.727–1.982)] p=0.476. The mortality however was not predicted with improvement in creatinine due to multiple co-morbidities.

Table 1: Demographic variables

Variables	Patients with AKI n=100
Age(years) Mean ± SD	63±15,003
Female / Male Ratio (total)	1:7:1 (63/37)
Baseline creatinine mg/dl Mean ± SD	0.94±0.351

Co-morbids:	
Asthma	4%
DM	5%
DM/HTN	6%
DM/IHD	1%
HTN	6%
HTN/IHD	2%
CLD	1%
Follicular lymphoma	1%
COPD	2%
COPD/HTN	2%
Ca prostrate	5%
Ca check	1%
Ca cheek/IHD	1%
IHD	4%
Multiple myeloma	3%
No comorbids	56%
Inotropic support (yes/no)	48%:52%
Ventilator support % yes/no	32%:68%

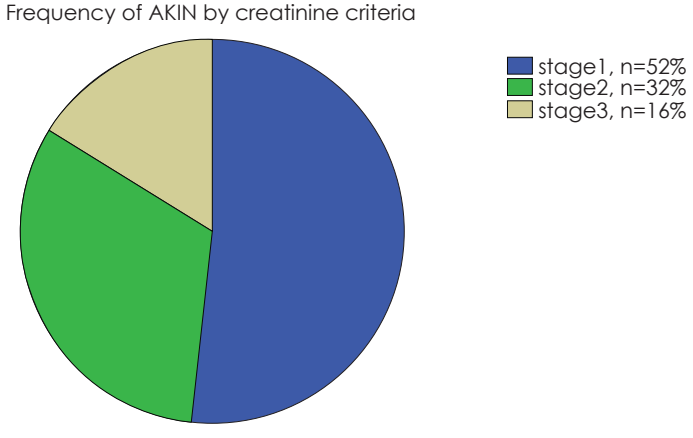

Figure 1: Frequency of AKIN by creatinine criteria

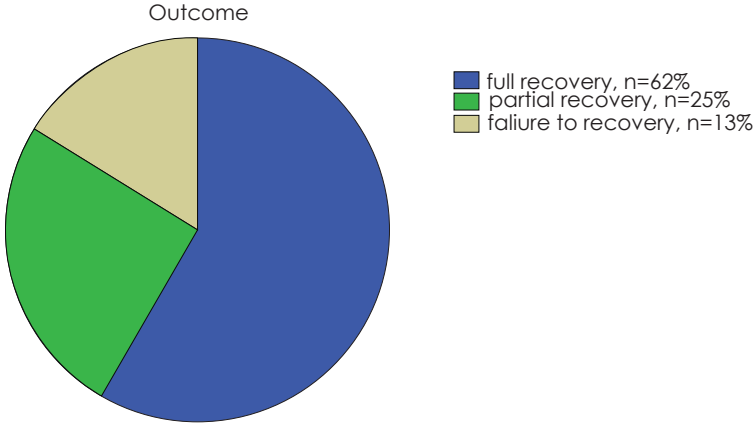

Figure 2: Outcomes of acute kidney injury

Table 2: Characteristics of patients with AKI

Characteristics		Patients with AKI (n=100)				
		Stage1	Stage2	Stage3	Total	P value
N		52	32	16	100	
OUTCOME	Full recovery (n%)	41(79)	17(53)	4(25)	62	<0.001
	Partial recovery ([n%])	9(17)	11(34)	5(31)	25	
	No recovery ([n%])	2(4)	4(12)	7(44)	13	
Age [yr;(mean)]		28-90 (63.7+15.2)	28-83 (62.1+13.8)	40-89 (63.8+17.0)	28-90 (63.2+15.0)	0.62
Hospital (ICU) stay[days;(mean)]		3.0 to 14 (6.23+2.96)	3.0-21 (7.16+4.58)	3.0-15 (7.19+3.48)	3.0-21 (6.68+3.62)	0.64
Gender(n[%])	Male	13(25)	15(47)	9(56)	37	0.02
	Female	39(75)	17(53)	7(44)	63	
Mortality (n[%])	Alive	40(77)	22(69)	10(62)	72	0.47
	Expired	12(23)	10(31)	6(37)	28	
Dialysis(n[%])	Required	02(4)	06(19)	10(62)	18	<0.001
	Not Required	50(96)	26(81)	06(37)	82	

Table 3: Comparison of Characteristics of patients of AKI (stage 1 and stage 3

Characteristics		Patients with AKI			
		Stage1	Stage3	Total	P- value
N		52	16	68	
1-Outcome	Full recovery (n[%])	41(79)	04(25)	45	<0.001
	Partial recovery(n[%])	09(17)	05(31)	14	
	No recovery(n[%])	02(04)	07(44)	09	
2-Age [yr;(mean)]		28-90 (63.7+15.2)	40-89 (63.8+17.0)	28-90 (63.7+15.5)	0.27
3-Gender	Male (n[%])	13(25)	9(56)	22	0.01
	Female (n[%])	39(75)	7(44)	46	

4-Mortality(n[%])	12(23)	6(37)	18	0.25
5-Hospital (ICU) stay[days;(mean)]	3.0 to 14 (6.23+2.96)	3.0-15 (7.19+3.48)	3.0-15 (6.46+3.09)	0.66
6-Dialysis(n[%])	2(04)	10(62)	12	<0.001

DISCUSSION

Acute Kidney Injury is one of the most vulnerable issues in critically ill patients contributing to high mortality of 50-70%. It is responsible for 25% of all intensive care admissions and 7% of all hospital admissions[14-19]. This high rate of morbidity poses a burden on developing countries where limited resources are available and thus leading to high mortality. Therefore, detection of even small changes in kidney injury has an important prognostic value to avoid chances of Hemodialysis that is not only economical burden on patient but also a source of infection associated with catheter insertion [20]. This high morbidity rate is consistent with hospital admissions reported in literature [20]. Varying rates of tubular injury have been found with highest reported were 7- 83% [16].

Recent advances in detection of AKI worldwide have improved the outcome of the patients but in developing countries this approach is lacking with loss of opportunities due to unawareness and non practicing progress. Early recognition and need for dialysis can narrow down the mortality rate and prevent further morbidity.

In our study, most of the patients were females with female to male ratio was 1.7:1 and elderly age being more affected. The incidence of AKI was highest among patients admitted with septicemia (36%) while remaining other admissions were due to pneumonia (13%), myocardial infarction (15%) acute gastroenteritis (11%), dengue shock syndrome (8%), heart block (5%), pancreatitis (5%), left ventricular failure (5%) and chronic liver disease (2%). Data from previous studies also reveals that AKI is a constant finding in patients with severe sepsis and sepsis contributes to 30-50% of cases [17- 19]. Most of the patients were in stage 1 of AKI (52%) detected by AKIN creatinine criteria and these criteria were found to be useful method of early recognition of patients with kidney injury. The overall mortality rate was 28%. Lafrance et al in a large cohort trial found 90 day survival rate was higher among patients with AKI severity class[16]. Previous studies have analyzed that mortality increased in patients with increasing severity and longer hospital stays [17]. This was not consistent with our findings. Rising creatinine had no significant relation to mortality in our study.

Another trial by Gammelager and colleagues found 15% patients presenting to ICU had AKI [18]. In our study, patients presenting with AKI at the time of ICU admission were 12%. Mostly patients with AKI recovered without Hemodialysis and were shifted to ward and then discharged. Among the non survivors also, very few required Hemodialysis. Most of the patients who received Hemodialysis were in stage 3. The patients with complete improvement to baseline creatinine were 62% while the remaining had creatinine either partially recovered or not recovered with resulting either morbidity or mortality. The mortality however was not correlated with the improvement in creatinine due to primary illness and multiple co-morbidities.

CONCLUSION

We conclude that detection of even small changes in kidney injury has an important prognostic value to prevent patients from short and long term complications and AKI diagnostic criteria is a useful method of early recognition of patients with kidney injury and should be practically applied in critical care unit to prevent patients from distress and life threatening problem.

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