Original article

Clinical Profile of Acute Kidney Injury in Intensive care unit: a prospective observational study from a rural tertiary care centre in North India

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Abstract:

Introduction: Acute Kidney Injury is characterized by an acute and potentially reversible deterioration of renal function, which results in failure of the kidney to excrete nitrogenous waste products and to maintain fluid and electrolyte balance. There is marked variation in epidemiological data of Acute Kidney Injury depending upon the definitions used, population being studied and the clinical settings. ***Aims and Objectives*****:** This study was designed to determine the clinical profile of adult patients with Acute Kidney Injury (AKI) admitted in the medical ICU at a rural tertiary care centre in North India. ***Materials and Methods*****:** This prospective observational study was conducted on 70 patients of Acute Kidney Injury admitted in the Medical Intensive Care Unit in Department of Medicine at M. M. Institute of Medical Sciences and Research, Mullana, Ambala. AKI was diagnosed and staged for severity according to the KDIGO criteria. ***Results and Observations:*** Amongst the 70 cases of AKI, 32 cases (45.7%) were females while 38 cases (54.3%) were males. The mean age at presentation was 55.22 ± 14.91 years. Sepsis was found to be the major cause of AKI. Out of 70 patients in our study, 45 (64.2%) cases were attributed to sepsis. Mortality rate seen in this study was 40% (n=28). ***Conclusion:*** Acute Kidney Injury is a common clinical problem encountered in critically ill patients, especially in the medical ICU. Early detection and adequate management is important to reduce AKI related as well as all- cause mortality in critically ill patients.

Keywords: Acute Kidney Injury; KDIGO criteria; Critically ill, Sepsis; Mortality

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Introduction

Acute kidney injury (AKI) has now replaced by the term acute renal failure. AKI is characterized by an acute (over hours to days) and potentially reversible deterioration of renal function, which results in the failure of the kidney to excrete nitrogenous waste products and to maintain fluid and electrolyte balance. If left untreated, it may progress to irreversible renal damage leading to Chronic Kidney Disease. Acute Kidney Injury has been shown to be an independent predictor of mortality[1].

Over the recent years there has been increasing recognition that relatively small rises in serum creatinine in a variety of clinical settings are associated with worse outcomes[2]. Therefore, AKI is now considered to include the entire spectrum of the syndrome from minor changes in markers of renal function to requirement for renal replacement

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therapy (RRT). Accordingly, efforts have been made to establish standard criteria for defining and grading Acute Kidney Injury. It started with development of RIFLE criteria in 2004 by the Acute Dialysis Quality Initiative (ADQI) group[3]. With this system three severity grades are defined (Risk, Injury and Failure) and two outcome classes- Loss and End-Stage Renal Disease (ESRD). In 2007, a modified form of RIFLE criteria was proposed by the Acute Kidney Injury Network (AKIN) group with an aim to improve the sensitivity of diagnostic criteria of AKI[4]. This was further modified by the Acute Kidney Injury Working Group of KDIGO (Kidney Disease: Improving Global Outcomes) which diagnoses AKI by an absolute increase in Serum Creatinine, at least 0.3 mg/dL within 48 hours or by a 50% increase in Serum Creatinine from baseline within 7 days, or a urine volume of less than 0.5 mL/kg/h for at least 6 hours [5].

There is marked variation in epidemiological data of Acute Kidney Injury depending upon the definitions used, population being studied and the clinical settings6,7. In the critically ill patients in different ICU settings, incidence of AKI varies from 20% to 50% with mortality rates of more than 50%[8,9]. There is significant difference in the epidemiological and clinical profile of AKI between developed and developing nations. AKI in developed nations occur mainly in hospitalized patients of older age group, whereas in developing countries, children and younger adults are more commonly involved. Infections and volume depletion are more common causes of AKI in developing countries[10,11].

With the advent of newer standards for definition and classification of AKI, analysis of epidemiological and clinical data at the regional level is important for understanding the magnitude of the problem and adequate allocation of health care resources. Also, significant regional variations exist with regard to the epidemiology of Acute Kidney Injury. Limited data is available regarding clinical and epidemiological profile of patients with AKI in developing countries like India, using these newer defining criteria. Presence of Acute Kidney Injury in the critically ill patients has also been shown to be important predictor of increased long term morbidity and mortality. Therefore, this study was designed to study the clinical and epidemiological profile of adult patients with Acute Kidney Injury (AKI) admitted in the medical ICU at a rural tertiary care centre in North India.

Materials and Methods

This prospective observational study was conducted on 70 patients of Acute Kidney Injury admitted in the Medical Intensive Care Unit in Department of Medicine at M. M. Institute of Medical Sciences and Research, Mullana, Ambala**.** The study was done over a period of 18 months (September 2015 to March 2017) after approval from the Institutional Ethics Committee.

Inclusion Criteria

All patients who were older than 18 years and were admitted to Medical intensive care unit during the observational period were considered for study inclusion. From this population, only patients who fulfilled predefined KDIGO criteria for AKI were included in the study. AKI was defined as

- Increase in SCr by 0.3 mg/dl (26.5 µmol/l) within 48 hours; or
- Increase in SCr to 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume 0.5 ml/kg/h for 6 hours

Exclusion Criteria

Patients who were diagnosed cases of CKD, Acute on CKD, those on maintenance hemodialysis and those with transplanted kidney were excluded from the study.

After verification of the patients for fulfilling the inclusion and exclusion criteria, a detailed history of all the selected patients was recorded. Presence of chronic co-morbid conditions (Diabetes, Hypertension, Chronic Liver Disease etc) and history of nephrotoxic drugs/toxins, if any was recorded. Complete physical examination including vital signs was performed. Demographic details including age, gender, residence (rural/urban) was recorded. All patients were subjected to laboratory investigations including Hemogram, Peripheral Blood Smear, Random Blood Sugar, Liver Function Tests, Renal Function Tests. Glomerular Filtration Rate (GFR) was measured according to estimated Creatinine Clearance based on Cockcroft Gault Equation.

AKI was staged for severity according to the following criteria (KDIGO)

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ≥0.3 mg/dl (≥26.5 µmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ≥12 hours
3	3.0 times baseline OR Increase in serum creatinine to ≥4.0 mg/dl (≥353.6 µmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m2	<0.3 ml/kg/h for ≥24 hours OR Anuria for ≥12 hours

Patients with confirmed AKI were followed up until the AKI resolved or till the patient was discharged from the hospital or till he/she expired. The possible etiology (prerenal, renal and postrenal) and contributing factors to development of Acute Kidney Injury were identified in all patients. Complications including development of Oliguria, Hyperkalemia, Uremic Encephalopathy, Volume Overload, etc were noted. Other relevant data including need of Renal Replacement Therapy (Hemodialysis) and final outcome (survival/death) was recorded.

Statistical Analysis

The data collected was compiled on excelsheet and was analyzed statistically by using SPSS software version 21.0. Chi Square test and Fisher Exact test were used for qualitative variables. Mean and Standard Deviation were calculated for quantitative variables. p value < 0.05 was taken as significant.

Ethical Clearance: Cleared by the Institutional Ethical Committee

Results and Observations

The study was conducted at M. M. Institute of Medical Sciences and Research, Mullana, Ambala in 70 patients admitted in the Medical intensive care unit who developed acute kidney Injury with an aim to profile the overall presentation, clinical course and outcome.

Table 1 shows the demographic and clinical characteristics of the study population. Amongst the 70 cases of AKI documented, 32 cases (45.7%) were females while 38 cases (54.3%) were males. The mean age at presentation was 55.22 ± 14.91 years. The majority of patients in our study were in the age range of 41-60 years (n=39 patients, 55.7%). 27.1% of patients belonged to the elderly population (more than 60 yrs of age). Total duration of hospital stay was 7.91 ± 3.89 days. Mean stay in the Medical Intensive Care Unit was 4.98 ± 2.56 days. Majority of the patients had an MICU stay of <4 days i.e. 44.28 (31 patients). 31.4% (22 patients) had a stay of 4-7 days. Only 24.28% (17 patients) stayed for > 7 days. Mean GFR at presentation was 49.04 ± 19.09. As per KDIGO staging, 41.4% patients were in Stage 3 of Acute Kidney Injury. The common co-morbid conditions seen were Diabetes Mellitus (27.14%), COPD (15.72%), Chronic Liver Disease (5.71%) and Hypertension (11.43%). RRT was initiated in 40% (n=28) patients in the form of haemodialysis (HD), while 60% (n=42) patients did not receive RRT.

Table 1 showing the demographic and clinical characteristics of the study population

Parameter	Patient Characteristics
Age (yrs), Mean ± S.D.	55.22 ± 14.91
Gender (n, %) Males Females	 38 (54.3%) 32 (45.7%)
Co-Morbid Conditions (n, %) Diabetes Mellitus COPD Chronic Liver Disease Hypertension	 19(27.14%) 11(15.72%) 4(5.71%) 8(11.43%)
Length of ICU Stay (days), Mean ± S.D.	4.98 ± 2.56
Total Hospital Stay (days), Mean ± S.D.	7.91 ± 3.89
GFR	49.04 ± 19.09
SBP (mm Hg), Mean ± S.D.	121.43 ± 12.57
DBP(mm Hg), Mean ± S.D.	78.84 ± 11.63
Peak S Creatinine (mg/dl), Mean ± S.D.	5.25 ± 2.10
CKD Stage(KDIGO) Stage 1 (n, %) Stage 2 (n, %) Stage 3 (n, %)	 28(40%) 13(18.6%) 29(41.4%)
APACHE II Score, Mean ± S.D.	13.00 ± 5.41
RRT (Hemodialysis) Initiated (n, %)	28 (40%)
Need for Mechanical Ventilation (n, %)	16 (22.8%)
No of Deaths (n, %)	28 (40%)

Table 2 showing the major clinical manifestations at presentation in patients with Acute Kidney Injury

Clinical features	Number	Percentage of Cases
Fever	50	71.4%
Nausea/Vomiting	22	31.4%
Loose stools	26	37.1%
Oliguria	46	65.7%
Polyuria	9	12.9%
Odema	17	24.3%
Dyspnea	21	30%
Encephalopathy	16	22.9%

Table 2 shows the major clinical manifestations at presentation in patients with Acute Kidney Injury. The most common presenting symptoms were fever in 50 patients (71.4%), oliguria (65.7%), loose stools (37.1%), nausea and vomiting (31.4%), dyspnea (30%), edema (24.3%) and altered sensorium (22.9%). The etiological causes leading to Acute Kidney Injury in the medical ICU are shown in **Table 3**. Sepsis was found to be the major cause of AKI. Out of 70 patients in our study, 45 (64.2%) cases were attributed to sepsis. Major sources of sepsis in our patients were complicated Urinary Tract Infections and Respiratory Tract Infections. The other etiological factors responsible for AKI were Hypovolumic Shock (24.2%), Nephrotoxic Drug Intake (4.2%), Renal Stone Disease (2.8%) and Poisoning (1.4%).

Table 4 shows the complications occurring in patients with Acute Kidney Injury. The most common complications recorded were Hyperkalemia (25.7%), Metabolic Acidosis (44.2%), Encephalopathy (47.1%) and Oliguria (65.7%). Mechanical ventilation in view of respiratory compromise was needed in 22.8% patients.

Table 3 showing etiological causes leading to Acute Kidney Injury in the medical ICU

Etiology	Number	Percentage of Cases
Ac. Gastroenteritis/Hypovolumic Shock	17	24.2%
Infections Sepsis - Urinary Tract Infections - Respiratory Tract - Ac Pancreatitis - Diabetic Foot with sepsis - Septicemia - Malaria - Others	 45 8 14 4 2 8 3 6	 64.2% 11.4% 20% 5.7% 2.8% 11.4% 4.2% 8.6%
Drug intake	3	4.2%
Poisoning	1	1.4%
Renal Stone Disease/Obstructive Uropathy	2	2.8%
Multifactorial	2	2.8%

Table 4 showing complications seen in patients with Acute Kidney Injury

Complication	Number	Percentage of Cases
Oliguria	46	65.7%
Hyperkalemia	18	25.7%
Metabolic Acidosis	31	44.2%
Encephalopathy	33	47.1%
Arrhythmia	2	2.8%
Respiratory Distress	16	22.8%

Table 5 shows the comparison of clinical profile, laboratory investigations and complications between Survivors and Non-survivors. Longer total duration of stay in the hospital (> 7 days) and longer ICU stay (≥ 4 days) was significantly associated with increased mortality. Presence of complications including Oliguria and Encephalopathy were also associated with significantly higher mortality. GFR< 60 and KDIGO Stage 3 were also associated with significantly higher mortality. No significant association was found between mortality and factors like age, gender, type of AKI and renal replacement therapy.

Table 5 showing the comparison of clinical profile, laboratory investigations and complications between Survivors and Non-survivors

Parameters	Survivors (n=42)	Non – survivors (n=28)	P-value
AGE			
21-40	6 (14.3%)	6 (21.4%)	0.334 NS
41-60	22 (52.4%)	17 (60.7%)	
>60	14 (33.3%)	5 (17.9%)	
SEX			
Male	24 (57.1%)	14 (50%)	0.557 NS
Female	18 (42.9%)	14(50%)	
TOTAL HOSPITAL STAY			
≤7 days	33 (78.6%)	3 (10.7%)	< 0.01 *
>7 days	9 (21.4%)	25 (89.3%)	
ICU STAY			
< 4 DAYS	29 (69.04%)	2 (7.14%)	<0.01 *
4-7 DAYS	8 (19.04%)	14 (50%)	
>7 DAYS	5 (11.90%)	12 (42.85%)	
APACHE II SCORE			
Score ≤10	17 (40.5%)	8 (28.6%)	0.308 NS
Score >10	25 (59.5%)	20 (71.4%)	
ENCEPHALOPATHY			
Present	11 (26.2%)	22 (78.6%)	< 0.01 *
Absent	31 (73.8%)	6 (21.4%)	
OLIGURIA			
Present	20 (47.6%)	26 (92.9%)	< 0.05 *
Absent	22(52.4%)	2 (7.1%)	
SEPSIS			
Present	26 (61.9%)	19 (67.9%)	0.611 NS
Absent	16 (38.1%)	9 (32.1%)	
TYPE OF AKI			
Pre Renal	7 (16.7%)	4 (14.4%)	0.377 NS
Renal	33(78.6%)	20 (83.3%)	
Post Renal	2 (4.1%)	4 (14.3%)	
KDIGO AKI			
Stage 1	26(61.9%)	2 (7.1%)	<0.01 *
Stage 2	8 (19.0%)	5 (17.9%)	
Stage 3	8 (19.0%)	21 (75%)	
GFR			
≤60	14 (33.3%)	24 (85.7%)	<0.01 *
>60	28 (66.7%)	4 (14.3%)	

(* - significant, NS- Non significant)

Discussion

Acute Kidney Injury is a common presentation in hospitalized patients, especially those who are admitted in the ICU with critical illness. With recent changes in definition and advancement in the diagnostic and treatment modalities, it is important to study the incidence and clinical profile of patients with AKI in different populations. Availability of adequate and recent epidemiological data helps in optimum use of health care resources at the regional level. Some of the recent studies on AKI in ICU patients have shown a wide variation in its incidence across different populations and patient groups[6,8,12].

The majority of patients in our study were in the age group of 41-60 years (55.7%). This is consistent with previous data from developing countries which shows that AKI in these countries is seen at a comparatively younger age, as compared to the developed nations where it is more common in the elderly population[13,14].

The etiological spectrum and pattern of AKI is quite variable. In the present study, Intrinsic Renal diseases were the most common etiology leading to AKI (69.8%), followed by pre-renal (24.2%) and post renal causes (2.8%). Majority of cases of AKI was attributed to Sepsis (64.2%). Source of sepsis included Respiratory tract infections, Urinary tract infections, Septicemia, complicated malaria, and other infections. Other important etiologies for AKI included Acute Gastroenteritis**,** Drug Intake, Renal Stone Disease and Poisoning. In a multicentric study (54 hospitals in 23 countries) of acute renal failure in critically ill patients, septic shock accounted for 47.5% of the patients[15]. In a retrospective analysis done in 500 critically ill Indian patients with Acute Kidney Injury, Eswarappa et al[16] showed that Sepsis was the most common cause of AKI (accounting for 38.6% of patients). Although recent data has shown that incidence of sepsis as a cause of AKI has decreased in the developed world, it is still a major factor contributing to AKI in the developing countries.

The mortality rates reported in patients of AKI in ICU settings vary widely with some studies showing more than 50 % mortality[8]. This is again dependent upon the study population, socioeconomic status, underlying etiologies for AKI and the management facilities available at the hospital. In a multinational multicenteric study of 29269 critically ill patients with Acute Kidney Injury, Uchino et al[15] reported an overall hospital mortality of 60.5%. In a recent observational study on incidence, prognostic factors and outcome of Acute Kidney Injury in ICU patients conducted in South India, Korula et al[12] reported a 28 days mortality of 49.5%. Similarly, in a retrospective study of Intensive Care Unit patients with acute kidney injury requiring renal replacement therapy, the mortality rate reported was 49% [17]. In our study, 28 patients with AKI expired; mortality rate was 40%. Higher mortality was seen in patients with Sepsis related AKI (19 out of 45, 42.2 %) as compared to

patients without sepsis (9 out of 25, 36%). In our study most of the patients were found to be in KDIGO stage 3 AKI comprising 41.4% (29 patients) of the total, with a mortality of 21 patients (72.41%).

On comparison of various clinical parameters between survivors and non-survivors, the factors which showed significant effect on mortality included total hospital stay, total stay in ICU, presence of oliguria and encephalopathy, baseline GFR and KDIGO Stage. Presence of Oliguria was seen as an important determinant of mortality. Of 70 patients, oligouria was present in total of 46 patients, out of which 26 expired (56.6%) while 20 survived (43.4%). In Non oliguric patients (n=24), mortality occurred in only 2 patients (8.4%).

Acute Kidney Injury is a commonly encountered problem in critically ill patients and also increases the economic burden on health care resources, which is especially significant in recourse limited settings seen in developing countries like India. Early diagnosis and prompt management is the key to prevent mortality and long term morbidity.

The present study had some limitations. As it was only an observational study about clinical profile of AKI, we did not compare ICU patients having AKI with those who did not develop AKI. Secondly, our study was limited only to clinical profile of AKI patients during the hospital stay. Long term follow up of patients to study development of any chronic complications or need of maintenance RRT was not included in the study. Another limitation may be the smaller sample size of the study. Further studies with long term follow up may be needed to ascertain changing epidemiological and clinical profile of patients with Acute Kidney Injury at regional level.

Conclusion

Acute Kidney Injury is an important common clinical problem encountered in critically ill patients, especially in the medical ICU. Sepsis and Volume depletion are still the most common etiological factors resulting in AKI. It is now considered as an independent predictor of mortality. Early detection and adequate management including renal replacement therapy (wherever indicated) is important to reduce AKI related as well as all- cause mortality in critically ill patients.

Authors Contribution

Data gathering and idea owner of this study: Shashwat Jindal, Sandeep Joshi

Study design: Sandeep Joshi, Ruby Sharma, Chander Mohan Adya

Data gathering: Shashwat Jindal, Nitin Gupta

Writing and submitting manuscript: Sandeep Joshi, Ruby Sharma, Nitin Gupta

Editing and approval of final draft: Shashwat Jindal, Sandeep Joshi, Ruby Sharma, Chander Mohan Adya, Nitin Gupta

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