

Original Research Article

Volume 4, Issue 4 -2018

DOI: <http://dx.doi.org/10.22192/ijcrms.2018.04.04.010>

Comparative Clinical Profile and Outcome of Cases of Acute Kidney Injury in a Tertiary Care Centre

**Dr Ashutosh Ojha¹, Maj (Dr) Yatharth Dixit²,
Gp Capt(Dr) V R Muzeeb³, Col(Dr) Arun Kumar⁴, Dr Varsha Mundley⁵,
Surg Cd (Dr) Anuj Singhal⁶**

¹ Asstt Prof, Department of Medicine, Armed Forces Medical College, Pune, India

² Resident, Department of Medicine, AFMC& Command hospital (Southern Command), Pune, India

³ Professor, Department of Medicine, AFMC& Command hospital (Southern Command), Pune, India

⁴ Prof Medicine & Sr Advisor Nephrology, Army Hospital (R&R) New Delhi.

⁵ Medical Officer, Pune

⁶ Associate Prof, Department of Medicine AFMC, Pune

Corresponding Author: **Dr Ashutosh Ojha**, Asstt Prof, Department of Medicine,
Armed Forces Medical College, Pune-411040, India

E mail: ashutosh8116@gmail.com

Abstract

Acute Kidney Injury (AKI), earlier termed Acute Renal Failure, is a very common entity affecting patients suffering from a wide variety of illnesses worldwide.

It is characterized by a rapid decrease in renal excretory function with increase in levels of urea and creatinine and decreased urine output. It has a variety of etiologies. It is mostly preventable and easily treatable entity. Initial preventive measures and timely institution of therapy can save a number of cases. Today in the era of No Death due to AKI, still we face a sizable mortality and morbidity in developing countries. In the initial stages of AKI these patients can be easily managed. However, AKI in the setting of multiple co-morbidities is very challenging to manage and has a potentially fatal complication. The etiological factors are so diverse that it has been varying in most of the studies done at different geographical area and time frame.

Hence this study was conducted to analyse the incidence, types, etiological factors, management protocol and mortality secondary to AKI in a tertiary care hospital. 172 patients admitted in the hospital were included in the study. Patients were selected if their serum creatinine level on the day of admission was more than 1.5 times of the baseline serum creatinine or the urine output was less than 0.5 ml/kg/h for 6 h or the GFR was less than 25 % from the baseline. Patients were classified as pre-renal, renal or post-renal AKI based on history, clinical findings and investigation results.

Out of 172 patients with AKI, 35 patients had chronic kidney disease. Infection accounted for 48.8% of all cases followed by volume loss (17.4%) and drugs (12%). Other important causes were altered renal hemodynamics (6.3%), and obstructive uropathy (4%). Pre-renal cause accounted for 84 cases, Renal cause for 79 cases and Post-renal cause for 7 cases. Out of 172 patients, 83 belonged to the Risk category, 57 developed Kidney Injury and 32 developed

kidney failure(RIFLE). None of the cases were Obstetric related AKI. A total of 52 (30.5%) patients required renal replacement therapy. Out of these 35 underwent hemodialysis,12 underwent peritoneal dialysis and 5 required CVVHD.The outcome of study was compared with different published studies.

Keywords: AKI, GFR, Pre-Renal, Renal, Post-Renal, Renal Replacement therapy in AKI, No Obstetric related AKI.

Introduction

Acute kidney injury (AKI), previously known as acute renal failure is characterized by the sudden impairment of kidney function resulting in the retention of nitrogenous and other waste products normally cleared by the kidneys. AKI is not a single disease but, rather, a designation for a heterogeneous group of conditions that share common diagnostic features: specifically, an increase in the blood urea nitrogen (BUN) concentration and/or an increase in the plasma or serum creatinine (SCr) concentration often associated with a reduction in urine volume. AKI can range in severity from asymptomatic and transient changes in laboratory parameters of glomerular filtration rate (GFR), to overwhelming and rapidly fatal derangements in effective circulating volume regulation and electrolyte and acid-base composition of the plasma. Acute Kidney Injury (AKI), earlier termed Acute Renal Failure, is a very common entity affecting patients suffering from a wide variety of illnesses.(1)

Many studies have found the incidence of AKI between 3 to 5%. It refers to a clinical entity characterized by a rapid decrease in renal functions. excretory function with increase in levels of urea and creatinine and decreased urine output. Other abnormalities include accumulation of metabolic acids, increased potassium and phosphate concentrations. It is now understood that a continuum of kidney injury exists long

before the loss of kidney function can be measured with standard laboratory tests. This led to a definition of acute kidney injury (then known as Acute Renal Failure) by the Acute Dialysis Quality Initiative (1). They also proposed a classification system for AKI known as the RIFLE criteria. These RIFLE (risk, injury, failure, loss, end stage) criteria have also been supported by the Acute Kidney Injury Network. Both definitions have now been validated by multiple studies and in thousands of patients (2).

Aims & Objectives:

This study was conducted to analyse the incidence, types, etiological factors, management protocol and mortality secondary to AKI in a tertiary care hospital.

Materials and Methods

172 patients admitted in the hospital were included in the study. Patients were selected if their serum creatinine level on the day of admission was more than 1.5 times of the baseline serum creatinine or the urine output was less than 0.5 ml/kg/h for 6 h or the GFR was less than 25 % from the baseline.

GFR (Creatinine Clearance Rate) was estimated by using the Cockcroft-Gault formula which is as under

$$\text{GFR (ml/min)} = \text{Sex} * ((140 - \text{Age}) / (\text{Serum Creatinine})) * (\text{Weight} / 72) (*\text{Sex- Male- 1, Female-0.85})$$

All the patients were asked about history of volume depletion (diarrhea, vomiting, blood loss etc.), exposure to nephrotoxic drugs, recent trauma/major surgery, cardiovascular/renal/chronic liver disease prior to admission. Then they underwent necessary

hematological, biochemical and radiological investigations as per the approved protocol. Serum creatinine was measured by kinetic Jaffe's method using semi-automated analyzer. Ultrasonography of the kidneys, ureter and bladder was done in all patients. Size of kidneys,

echogenicity, cortico-medullary differentiation and obstruction if any were recorded. Contracted kidneys were defined by kidney size less than 7.5 cm. Urine for spot sodium was done and fractional excretion of sodium (FENa) was calculated in all patients.

Patients were classified as pre-renal AKI if they had history of volume depletion (history of poor fluid intake, acute diarrhea, vomiting or blood loss from the body etc.), evidence of dehydration on examination, urine for spot sodium less than 20 mEq/l, blood urea nitrogen to creatinine ratio more than 20 and fractional excretion of sodium less than one percent.

Intrinsic AKI was evaluated after excluding the pre-renal and post renal causes. A diagnosis of glomerulonephritis was considered if the patient had recorded hypertension, hematuria and urine examination revealed red cell cast, dysmorphic RBCs and spot urine albumin-creatinine ratio more than 300 mg/g. Hemolytic uremic syndrome was considered if the patient had anemia, evidence of hemolysis on peripheral blood smear, thrombocytopenia and raised serum LDH.

Patients were classified as having Acute Tubular Necrosis if they had history of recent blood loss, fluid loss, history of exposure to nephrotoxic drugs or radio-contrast dye and laboratory investigations showed fractional excretion of sodium more than one percent and urine for spot sodium was more than 20 mEq/l. Rhabdomyolysis was considered as a cause of acute tubular necrosis if patient had history of trauma, prolonged immobilization, raised serum creatinine kinase and positive urine for hemoglobinuria with no evidence of hematuria.

The diagnosis of acute interstitial nephritis was considered if patient had history of exposure to certain medications (sulphonamides, quinolones, rifampicin, NSAIDs etc.) and microscopic examination of urine showed WBC casts and eosinophiluria.

Sepsis was defined as systemic inflammatory response syndrome that has a proven or suspected infectious etiology. Systemic inflammatory response syndrome was defined by presence of two or more of the following: (1) Fever (oral temperature $> 38\text{ C}$ [$> 100.4^{\circ}\text{F}$]) or hypothermia ($< 36^{\circ}\text{C}$ [$< 96.8^{\circ}\text{F}$]); (2) tachypnea (> 24 breaths/min); (3) tachycardia (heart rate > 90 beats/min); (4) leukocytosis ($> 12000/\text{mm}^3$), leucopenia ($< 4000/\text{mm}^3$), or $>10\%$ bands on Peripheral Blood smear .

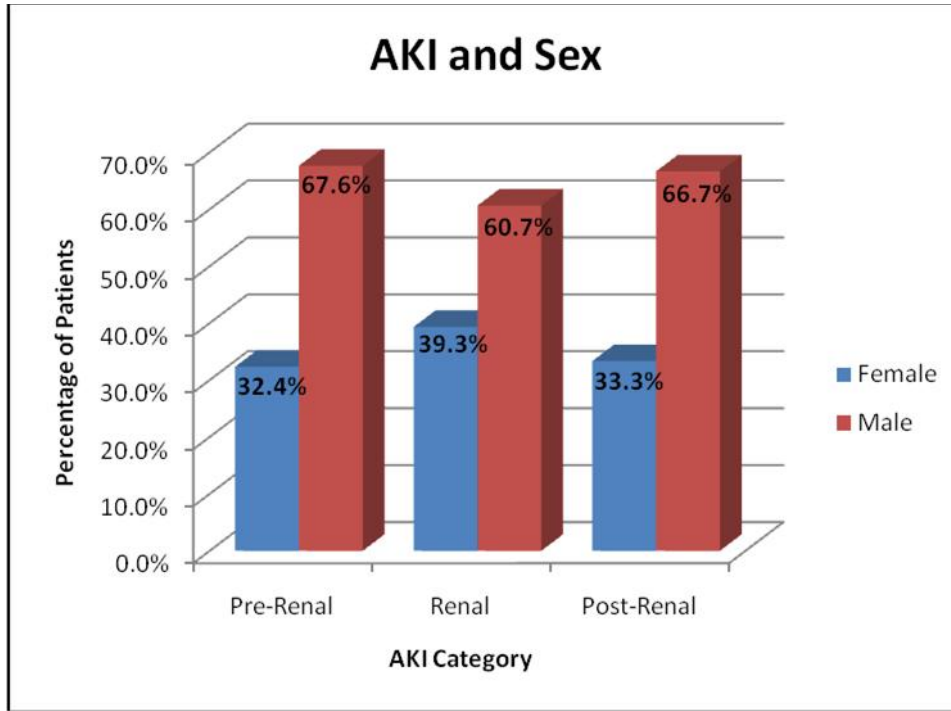
Evaluation for medical conditions such as severe pulmonary disorder, severe cardiovascular disorders, portal hypertension, evidence of liver cirrhosis, hepatic encephalopathy and neurological, metabolic and gastrointestinal disorders was also made.

Renal replacement therapy was offered to patient who had acute renal failure associated with hyperkalemia, fluid overload, encephalopathy, metabolic acidosis, or uremic pericarditis. The patients were followed up at 3 months and 6 months' interval to assess renal function and progression to ESRD as per the RIFLE criteria. The requirement of long term Renal Replacement Therapy was also determined.

Statistical analysis The Data was compiled in Excel sheet and was analysed using IBM SPSS v22. One way ANOVA and t test were used for quantitative variables while chi-square test and Fisher's Exact test were used for qualitative variables. Graphs and Charts were made for better understanding. P value less than 0.05 was considered significant.

Results

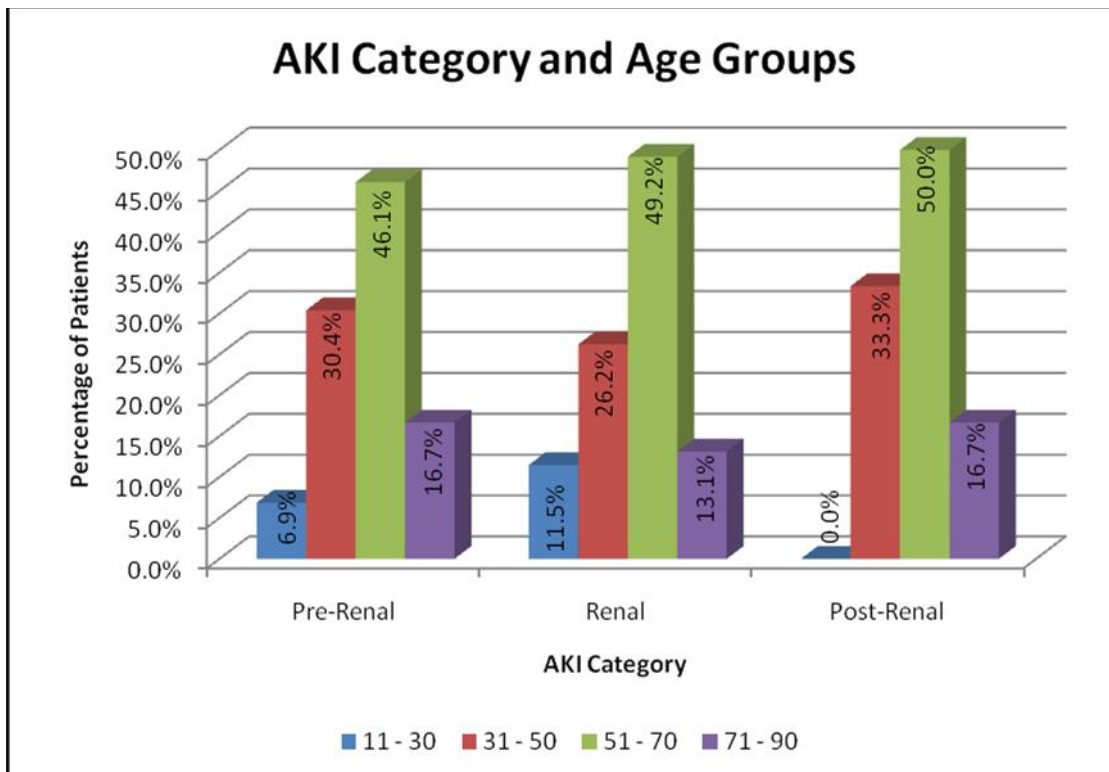
Epidemiology of AKI Total number of patients included in the study was 172. 111 (64.5%) were males and 61 (35.5%) were females (Bar Diagram-1).



Bar Diagram 1- Sex- wise Incidence of AKI

Age Distribution

Maximum patients were in the age group 51-70 years (Bar Diagram- 2). The mean age of study group was 54.77 years.



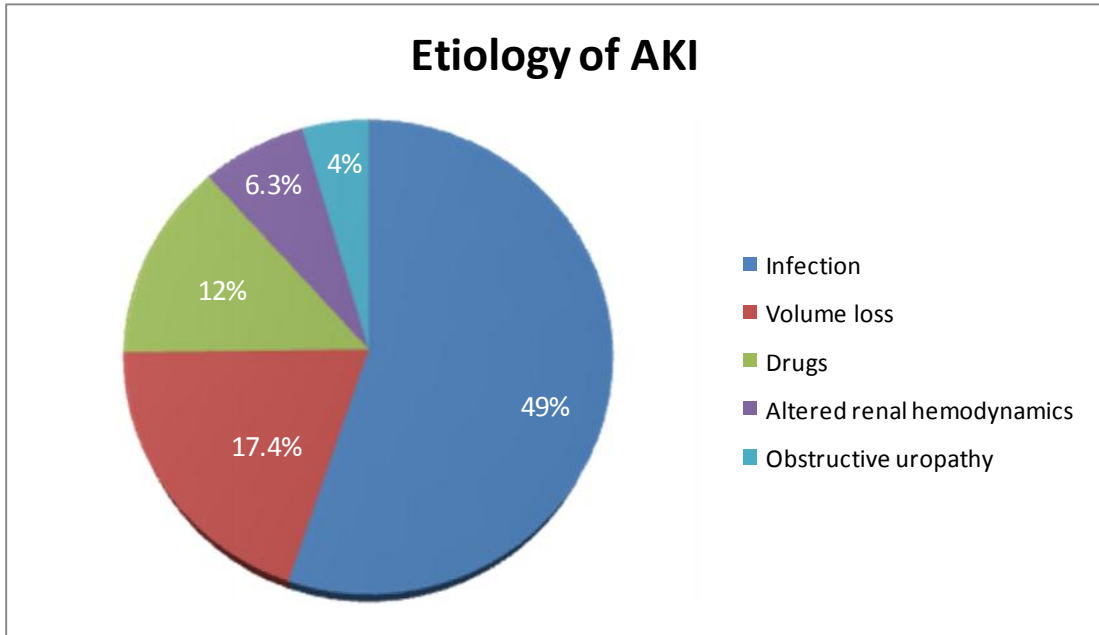
Bar Diagram 2- Age- wise Incidence of AKI

Comorbidities

Average baseline serum creatinine on the day of admission was 1.4 mg/dl. Average peak serum creatinine during admission was 3.3 mg/dl. Hypertension was the most common comorbidity followed by Type 2 Diabetes Mellitus. Chronic liver disease, stroke and malignancy were the other common comorbidities.

Etiology of AKI

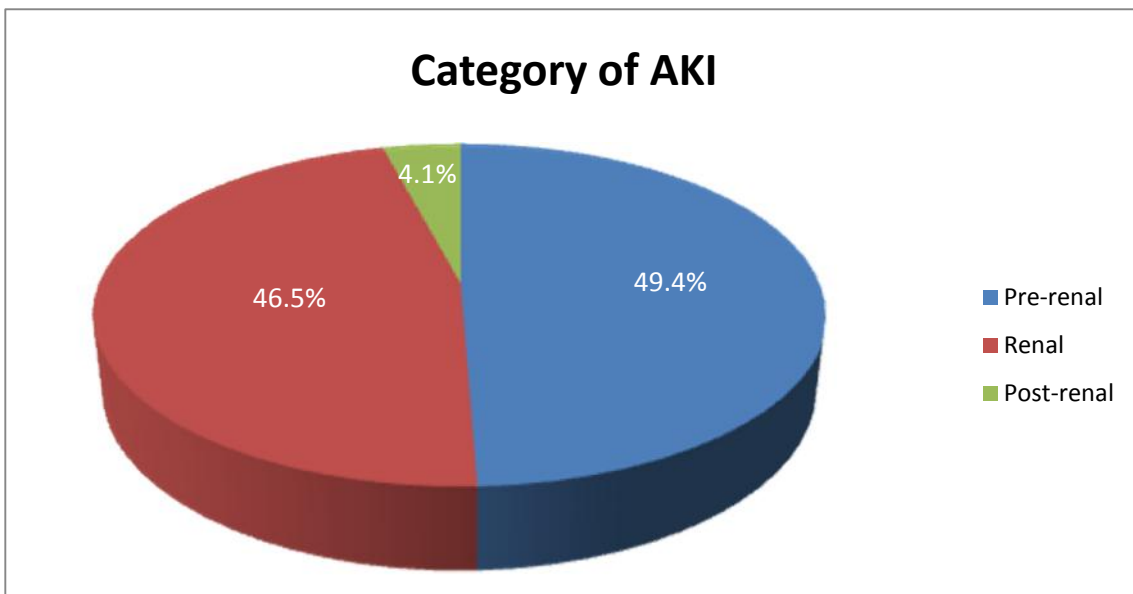
Out of 172 patients with AKI, 35 patients had chronic kidney disease. Infection accounted for 48.8% of all cases followed by volume loss (17.4%) and drugs (12%). Other important causes were altered renal hemodynamics (6.3%), and obstructive uropathy (4%)



Pie chart of Etiology of AKI

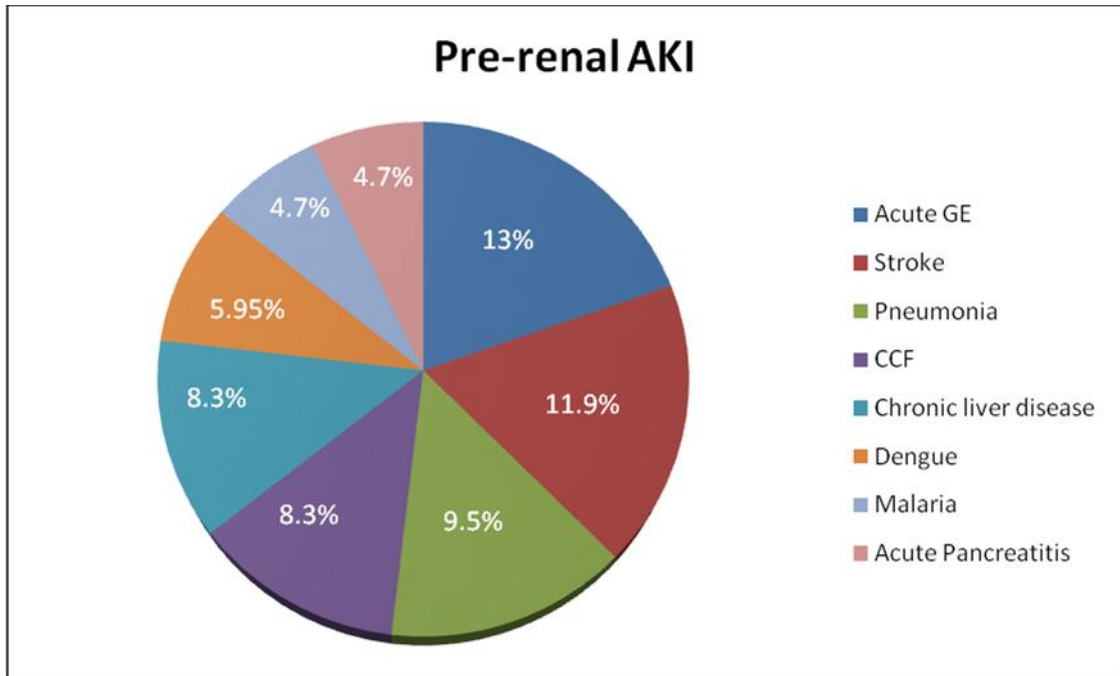
Category of AKI

Pre-renal cause accounted for 84 cases, Renal cause for 79 cases and Post-renal cause for 7 cases.



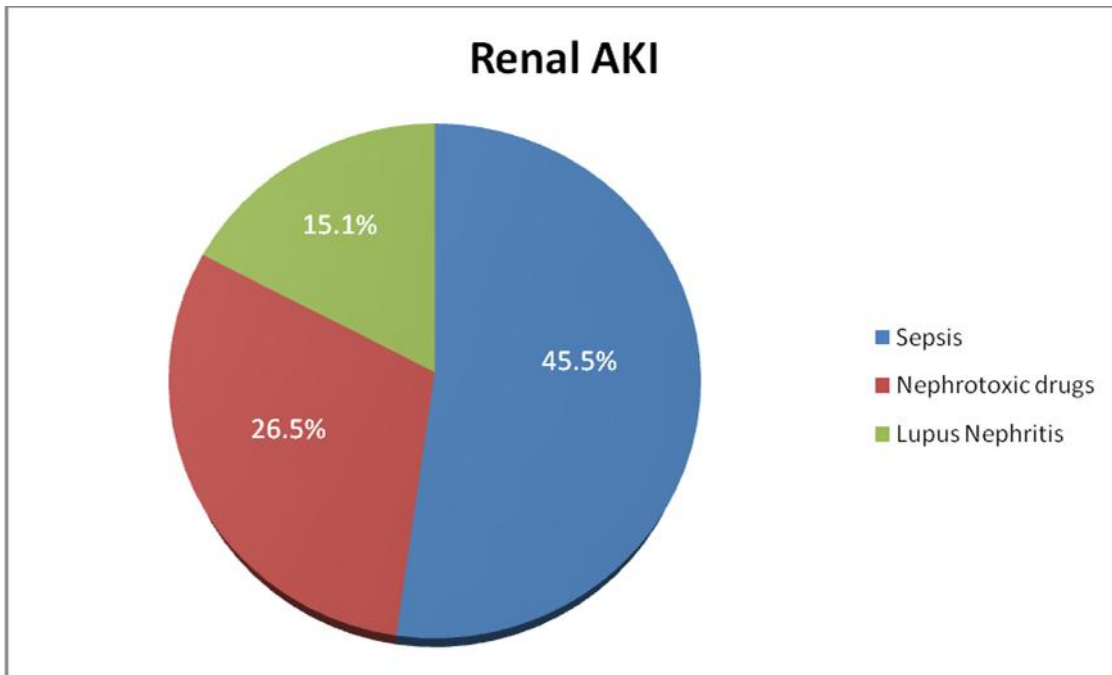
Pie chart1 of category of AKI

Etiological factors in Pre Renal AKI



Pie chart 2.Pre Renal AKI

Etiology of Renal AKI

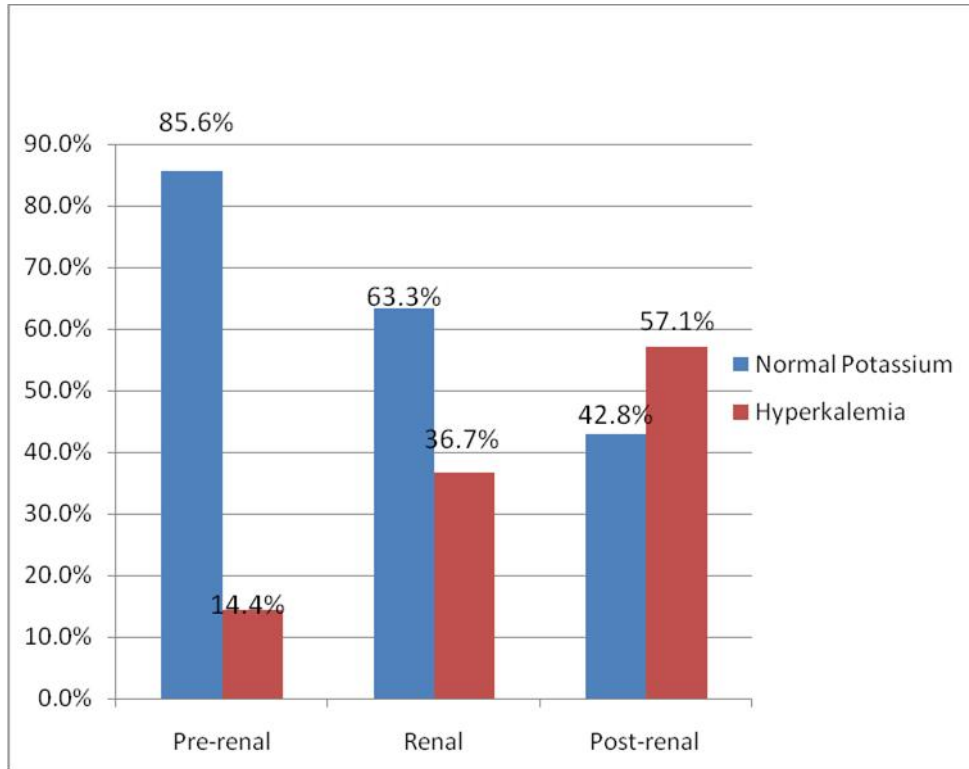


Pie chart 3 - Predominant renal causes were Sepsis-36 (Urinary tract infection-22, Pneumonia-6, Septic shock-5, sepsis-3), Nephrotoxic drugs-21 and miscellaneous (Lupus Nephritis-4, Contrast induced Nephropathy-3, Warfarin induced Nephropathy-2, Hemolytic uremic syndrome-1, Organophosphorus poisoning-1 and Paraphenylene diamine poisoning-1) (Pie Chart3).

Clinical and laboratory parameters Most common finding was pallor seen in 113 (66.4%) patients followed by pedal edema in 78 (45.8%), Hypotension in 37 (21%) and Oliguria in 37(21%) patients. A total of 45 (26.16%) patients developed hyperkalemia (Serum potassium > 5.5 mEq/l) which consisted of 12 from pre-renal

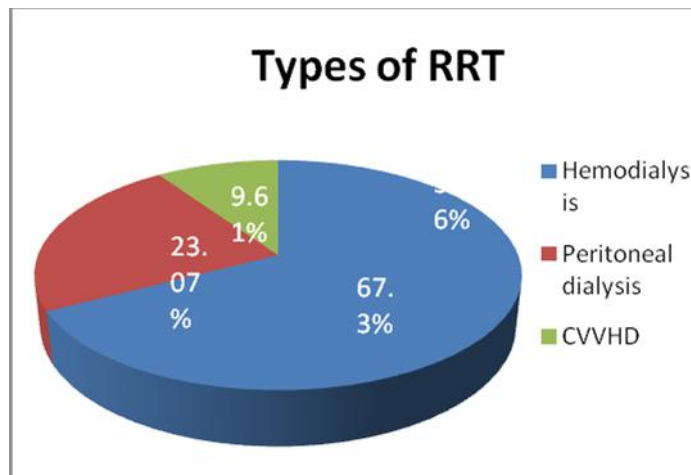
category, 29 from renal category and 4 from post renal category.

Hyperkalemia in different category of AKI – it was the most common cause of Renal Replacement therapy followed by Acidosis and fluid overload.

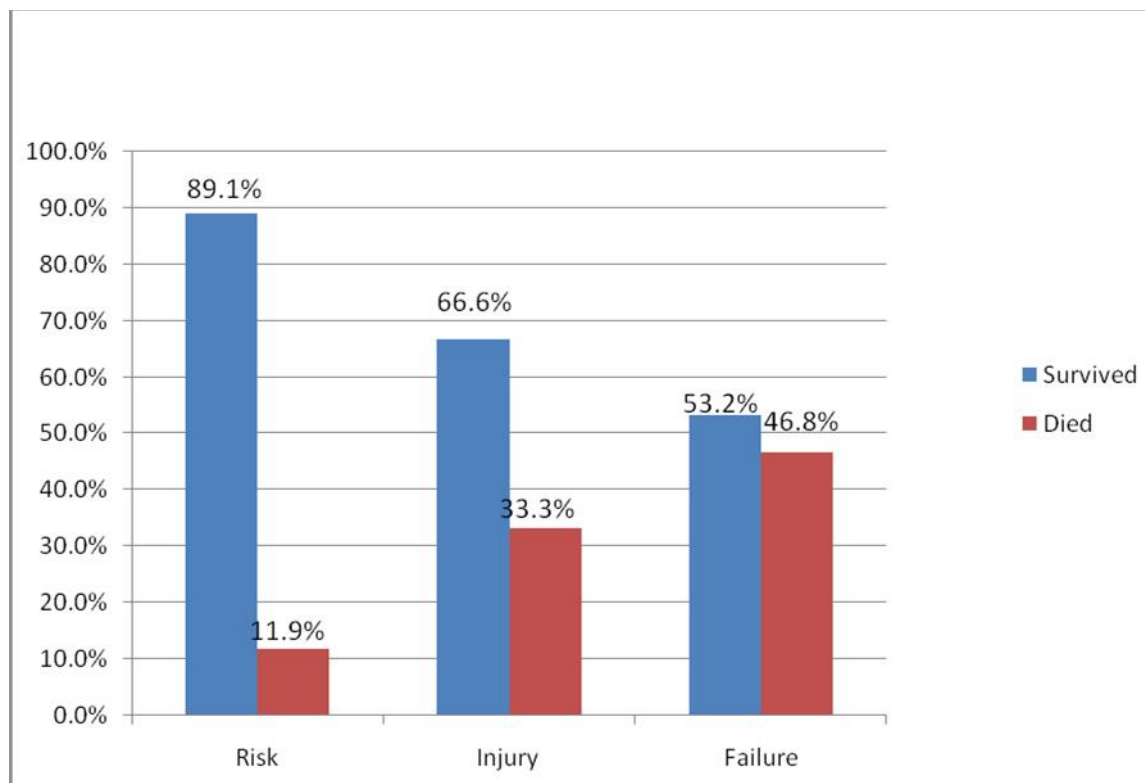


Renal Replacement Therapy in AKI - A total of 52 (30.5%) patients required renal replacement therapy. Of these 35 patients had underlying CKD. Indications for RRT included hyperkalemia (Serum potassium>6.5 mEq/l) in 15 patients, fluid

overload in 32 patients and metabolic acidosis in 5 patients. At the end of 3 months follow up, 44 patients died. Out of these 10 belonged to the risk category, 19 belonged to the injury category and 15 belonged to the Failure category.



Mortality in AKI - The most common cause of death was sepsis.



Discussion

Many studies have found the incidence of AKI between 3 to 5%. A study conducted by Bagshaw et al. which consisted of 91,254 patient admissions to the 20 study ICUs, found that AKI developed in 4,754 cases with an estimated incidence of 5.2% (3). A study conducted by Prakash et al. found the incidence of AKI in ICUs to be around 3.79% (4). Our study shows similar results with an incidence of 4.3% in the study period. In our study, necessarily all cases admitted for any reason and having AKI as per RIFLE criteria were included. While in other studies, mostly ICU patients were included.

AKI was predominantly encountered in the elderly age group. In the study conducted by Bagshaw et al. maximum number of patients belonged to more than 75 year age group and the incidence of AKI was also highest in them (3). However mean age of the patients, in the study by Prakash et al. was 44 ± 17 year (4). Similarly, in a study conducted by Eswarappa et al. in South India, the mean age of patients was 55.5 year (5). Our study agrees with other Indian studies showing mean age of patients as 54 year. Age has been consistently shown to be a risk factor for AKI (6).

Our study confirms the earlier finding that AKI is more common in male sex. Majority of patients with AKI had co morbidities with hypertension (21) and Type 2 Diabetes Mellitus (18) being the most common. Other significant co-morbidities were chronic liver disease, stroke and malignancy. These findings are in agreement with a review study by Rodrigo *et al.*, which demonstrated a significantly increased risk of AKI in critically ill patients with older age, diabetes, hypertension and multiple other risk factors (6).

Majority of cases of AKI were accounted for by pre-renal causes (48.8%) while the renal causes were responsible for 45.9% of the cases. Infection accounted for 48.8% of all cases followed by volume loss (17.4%) and drugs (12%). In a study conducted by Liano et al (Madrid Acute Renal Failure Group) the most frequent causes of ARF were Acute Tubular Necrosis (45%), pre-renal (21%), acute-onset chronic renal failure (12.7%) and obstructive ARF (10%) (7). Studies by Jha et al., and Prakash et al., which evaluated AKI irrespective of ICU setting had shown that nephrotoxic drugs were the most common cause of AKI (8, 9). In a similar study at Chandigarh,

they mention a sizable number of cases of obstetric related cases and abortions. None was noted in our study. Probably better obstetric services and awareness has been the reason.

However, a study conducted in South India by Krishnamurthy et al. also published that infection (55%) was responsible for majority of cases of AKI in children (10) and many studies conducted both in India, Sri Lanka and world over have found sepsis as the most common cause of AKI (5,11). In our study, urinary tract infection was the most common cause of AKI. Nephrotoxic drugs accounted for 12% of the cases. In this continuation of ACE inhibitor as noted in 7% and NSAID inappropriate use in 4% cases. This is in contrast to a study by Bagshaw et al., which found that the predominant sources of sepsis were chest and abdominal infections (54.3%) (12).

This difference may be due to a greater number of patients with Diabetes Mellitus as they are prone to urinary tract infections. In our study the second most common infectious cause of AKI was Pneumonia. Malaria, dengue, heat stroke and snake bite accounted for nearly 1% of cases.

In our study, a total of 52 (30.5%) patients required renal replacement therapy. Previous Indian studies by Prakash et al. and Singh et al. reported that 54.3% and 25.5% of the cases respectively, required RRT (9, 13). Out of these 35 underwent hemodialysis, 12 underwent peritoneal dialysis due to compelling reasons hemodynamic instability and poor vascular access and 5 required continuous venovenous hemodialysis (CVVHD).

At the end of 3 months follow up, 44 (25.8%) patients died. In the study conducted by Prakash et.al. the mortality was 63% and in that conducted by Eswarappa et al. and Singh et al. the mortality was 37.2% and 37.2% respectively (61, 63, 66). Our study shows lower mortality as compared to previous Indian studies. This could be due to inclusion of less severe AKI cases taken from acute wards. Out of these 10 (12%) belonged to the risk category, 19 (33%) belonged to the injury category and 15 (46%) belonged to the Failure category. This could be due to higher incidence of

multi-organ failure seen with worsening of kidney function. This is in contrast to the study of Singh et.al. in which the mortality was maximum in RIFLE-I group (n=7) in medical patients and RIFLE-R group (n=22) in ICU patients (66). However similar results were seen in a study by Bagshaw *et al.* which found that the mortality rates were 17.9% in the risk group, 27.7% in injury group and 33.2% in failure group (12).

All patients who underwent CVVHD died. In first instance this may suggest that hemodialysis is a better modality. However, on closer study it becomes obvious that only those patients underwent CVVHD, who were hemodynamically unstable. It would be, therefore, incorrect to consider hemodialysis as better modality of dialysis. There are many controversial results about the influence of renal replacement therapy (RRT) on outcome of patients with AKI in intensive care units. Early onset of RRT in critically ill patients reduces the mortality of intensive care unit patients with AKI independent of underlying diseases (14). However, there is no difference between intensive and less intensive RRT as regards decrease in mortality, recovery of kidney function, or reduction in the rate of non-renal organ failure (15).

Conclusion

AKI is a common entity complicating the hospitalized patients. A myriad of pre, intrinsic and post renal causes are responsible of AKI. The key to management lies in high index of suspicion and early intervention while the injury is still reversible. With increase of longevity, the patient group has become older. Sizable number of cases had preventable causes as dehydration and inappropriate nephrotoxic drug use.

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Ashutosh Ojha, Maj, Yatharth Dixit, Gp Capt V R Muzeeb, Col Arun Kumar, Varsha Mundley, Surg Cd Anuj Singhal. (2018). Comparative Clinical Profile and Outcome of Cases of Acute Kidney Injury in a Tertiary Care Centre. *Int. J. Curr. Res. Med. Sci.* 4(4): 67-76.
DOI: <http://dx.doi.org/10.22192/ijcrms.2018.04.04.010>