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Original Article

Internal Medicine Section

Evaluation of Aetiology and Outcome of Acute Kidney Injury in a Tertiary Care Hospital of India- A Prospective Observational Study

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ABSTRACT

Introduction: The Acute Kidney Injury (AKI) is a rapid decline in renal filtration function. The aetiological spectrum, prevalence of AKI and outcome is highly variable. This variation exists due to the difference in the criteria used, study population and demographic features. Huge differences are noted when AKI is compared in developing and developed countries. Hence, it is important to analyse the spectrum of AKI to facilitate earlier diagnosis and treatment which shall help in improving the outcome.

Aim: To study the prevalence, aetiology and outcome of AKI in the medical intensive care.

Materials and Methods: This was a prospective observational study conducted in a medical intensive care for 18 months where 1490 patients were screened and 403 patients were included as AKI by KDIGO criteria. History, examination, appropriate investigations and treatment details including dialysis were noted. The serum creatinine levels were obtained every day, to know the time of onset of AKI, at the time of death or discharge, and after one month for patients who turned up for follow-up. Patients were categorised based on outcome as survivors and nonsurvivors. Survivors were divided into as fully recovered and partially recovered and those who left the Intensive Care Unit (ICU) against medical advice were termed as lost to follow-up.

Results: A total of 403 patients (27.04% of 1490) of medical intensive care admissions were found to have AKI. Sepsis was the most common cause of AKI. At the end of the month, 78.4% of AKI patients fully recovered, 1.2% partially recovered and the mortality was 14.9%. Mortality was higher in AKI associated with chronic medical conditions like cardiac failure, chronic liver disease and stroke.

Conclusion: If treated early, AKI is mostly reversible. Regional differences in AKI should be studied extensively and local guidelines should be formulated by experts for prevention and early treatment, to improve the disease outcome.

Keywords: Acute renal failure, Creatinine, Mortality, Sepsis

INTRODUCTION

AKI, previously called acute renal failure is characterised by sudden impairment of kidney function causing accumulation of nitrogenous and other waste products which are normally excreted by the kidneys. The earlier term acute renal failure has been shunned by nephrologists worldwide as a person having AKI may not have permanent loss of renal function and is often completely reversible [1].

AKI is classified based on underlying mechanism into prerenal, renal and postrenal types [2]. It is observed that the age group, aetiology and outcome differ between developed and developing countries and between centres within countries [3-5]. Studies have also identified a drastic change in the trend of aetiologies of AKI. There was a significant drop in the incidence of surgical, and obstetric related AKI, whereas there was a rise in the incidence of AKI due to sepsis, drugs and chronic diseases [3,4]. The prevalence of AKI in hospital set up varies between 17 to 50% in various studies [5-7]. Our country lacks a central registry of AKI, thereby epidemiology of AKI is in grey area and highly variable. Since the impact of AKI on all-cause mortality and cost of healthcare is significant in developing countries like India, it is essential to implement effective strategies for prevention, early diagnosis and treatment of AKI, according to changing trends specific to our geographical area. Studies specific to southern part of India are limited in this regard [8-10]. This study helps in better understanding of prevalence, current trend of aetiological pattern and outcome of AKI in our geographical area, which may help in improving the outcome of AKI patients.

MATERIALS AND METHODS

This was a prospective observational study conducted in medical intensive care in a tertiary hospital of India for a period of 18 months (January 2017 to June 2018). Patients of age above 18 years, who were admitted in ICU with AKI or who developed AKI within 48 hours of admission into ICU by the Kidney Disease Improving Global Outcomes (KDIGO) criteria were recruited for the study [11].

AKI is defined as any of the following:

Increase in Serum creatinine by ≥0.3 mg/dL within 48 hours; or

Increase in Serum creatinine 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 with known pre-existing renal disease like interstitial nephritis, polycystic kidney disease, end stage renal disease, patients who received renal transplant, and surgical postoperative patients in medical ICU were excluded.

After obtaining ethical clearance from institutional ethical committee (937/IEC/2016), 1490 patients admitted in medical ICU in study period were screened and 403 patients were selected for study by convenient sampling method according to inclusion and exclusion criteria. The minimum sample size was calculated as 288 using sample size formula for single proportion with approximate prevalence as 25% from previous studies and 95% confidence interval [12-14]. They were subjected to detailed history and clinical examination. All the patients underwent the complete haemogram, fasting and postprandial sugars, serum bilirubin and liver enzymes, serum electrolytes, blood urea, serum creatinine, routine urine examination and microscopy, ultrasonography of abdomen and pelvis. Other specific investigations based on individual patients like blood culture, renal biopsy, CT abdomen were also performed. Treatment

details including dialysis were noted. The serum creatinine levels were obtained every day, to know the time of onset of AKI, at the time of death or discharge, and after one month for patients who turned up for follow-up. Serum creatinine estimation was done by modified Jaffe method using autoanalyser [15]. AKI staging was done according to KDIGO into stage I, II and III based on rise in serum creatinine.

The urine output criteria were not utilised in this study due to practical constraints. Patients were categorised based on outcome as survivors and nonsurvivors. Survivors were divided into as fully recovered and partially recovered and those who left the ICU against medical advice were termed as lost to follow-up (n=22).

STATISTICAL ANALYSIS

The collected data was analysed with IBM SPSS statistics version 20 software. Continuous data are expressed as mean±standard deviation, and the means of the survivor and nonsurvivor were compared using an unpaired t-test. Nominal data are expressed as frequencies or proportions, and the Chi-square test was used to compare the differences in frequency between the two study groups. A p-value ≤0.05 was considered statistically significant.

RESULTS

During the study period, 1490 patients admitted in the ICU were screened and 403 patients who developed AKI which accounted for 27.04% of the total ICU population. The mean age among the cases was 56±16 years. The maximum number of patients belonged to the age group of 51-65 years (32.7%). The prevalence of AKI was more in male patients (62% in males versus 38% in females). Diabetes was the most common comorbidity associated and there were no comorbidities in 147 patients constituting 36.5% of study population [Table/Fig-1].

Sepsis was the most common aetiology of AKI in our study (33.7%) followed by other causes such as cardiac failure (13.3%), stroke (11.9%), chronic liver disease (9.4%), Post renal causes (8.4%) and diarrheal diseases (7.9%). The aetiologies which constituted less than 5% each were acute glomerulonephritis (1.9%), drug induced AKI (4.4%), snake bite (4.4%), undiagnosed AKI (1.4%) and miscellaneous causes (2.7%) which comprised of HELLP syndrome (Haemolysis, elevated liver enzymes and low platelets), sick sinus syndrome, carcinoma of the breast, metastatic cervical carcinoma, myasthenic crisis, severe pulmonary hypertension, benzodiazepine poisoning, Organophosphate compound poisoning, Oleander seed poisoning, multiple myeloma and hypertensive emergency. Among the total study population, 58 patients required dialysis, accounting for 14.4% of the AKI cases [Table/Fig-2].

Groups	Frequency (Percentage of total study population)	Survivor, N (%)	Nonsurvivor N (%)	p-value comparing survivor and nonsurvivor	Lost to follow-up N (%)
Age group in (years)					
18-35	45 (11.1%)	38 (84.4%)	2 (4.4%)	0.181	5 (11.1%)
36-50	105 (26.0%)	83 (79.0%)	17 (16.2%)		5 (4.8%)
51-65	132 (32.7%)	106 (80.3%)	19 (14.4%)		7 (5.3%)
66-80	99 (24.5%)	75 (75.8%)	20 (20.2%)		4 (4%)
>80	22 (5.4%)	19 (86.4%)	2 (2%)		1 (4.5%)
Sex					
Male	250 (62%)	196 (78.4%)	40 (16.0%)	0.412	14 (5.6%)
Female	153 (38%)	125 (1.7%)	20 (13.1%)		8 (5.2%)
Comorbidities					
Diabetes	91 (22.6%)	77 (84.6%)	9 (9.9%)	0.12	5 (5.5%)
Hypertension	53 (13.2%)	43 (81.1%)	8 (15.1%)	0.88	2 (3.8%)
Coronary artery disease	29 (7.1%)	26 (89.6%)	3 (10.4%)	0.40	Nil

[Table/Fig-1]: Distribution of age, sex and co-morbidities of study population with comparison of survivor and nonsurvivor group. (Chi-square test was used to calculate p-value).

Parameter	Total, N (Percentage of total study population)	Survivor, N (%)	Nonsurvivor N (%)	p-value comparing survivor and nonsurvivor	Lost to follow-up N (%)
AKI stages based on KDIGO					
I	183 (45.4%)	179 (97.8%)	2 (1.1%)	<0.001*	2 (1.1%)
II	118 (29.2%)	90 (76.3%)	12 (10.2%)		16 (13.6%)
III	102 (25.3%)	52 (51%)	46 (45.1%)		4 (3.9%)
Aetiology of AKI					
Sepsis	136 (33.7%)	112 (82.3%)	17 (12.5%)	0.32	7 (5.2%)
Diarrhoeal disease	32 (7.9%)	28 (87.6%)	2 (6.2%)	0.15	2 (6.2%)
Cardiac failure	54 (13.3%)	36 (66.6%)	15 (27.7%)	0.004*	3 (10.7%)
Chronic liver disease	38 (9.4%)	30 (78.9%)	8 (21.1%)	0.34	-
Acute glomerulonephritis	8 (1.9%)	7 (87.5%)	-	-	1 (12.5%)
Stroke	48 (11.9%)	35 (72.9%)	13 (27.1%)	0.02*	-
Drug induced	18 (4.4%)	15 (83.3%)	-	-	3 (16.7%)
Postrenal	34 (8.4%)	30 (88.2%)	3 (8.8%)	0.27	1 (3%)
Snake bite	18 (4.4%)	16 (88.8%)	-	-	2 (11.2%)
Others	11 (2.7%)	8 (72.7%)	2 (18.2%)	0.7	1 (9.1%)
Undiagnosed	6 (1.4%)	4 (66.7%)	-	-	2 (33.4%)
Total	403 (100%)	321 (79.6%)	60 (14.8%)	-	22 (5.6%)
Dialysis	58 (14.4%)	21 (36.2%)	36 (62%)	<0.001*	1 (1.7%)

[Table/Fig-2]: Distribution of staging of AKI, aetiologies and dialysed patients with comparison of survivor and nonsurvivor group. Chi-square test was used to calculate p-value. *p-value significant at 95% confidence interval.

The postrenal causes were renal calculi, benign prostatic hyperplasia, stricture urethra complicated by urinary tract infection.

Among 403 patients of AKI, 321 (79.6%) recovered and 60 patients (14.8%) died. A total of 22 patients (5.4%) patients were lost to follow-up as they left the ICU against medical advice. Among survivors (n=321), 316 patients had complete recovery (78.4%) and 5 patients had partial recovery (1.2%) [Table/Fig-3]. Patients progressing to CKD could not be ascertained in this study as the patients were followed-up only after 1 month. The highest observed mortality rate (20.2%) was in the 66-80 age group [Table/Fig-1]. There was significant difference in mortality among the various stages of AKI. Mortality in stage I, II and III AKI were 1.1%, 10.2% and 45.1%, respectively [Table/Fig-2].

Survival	Group based on recovery	Frequency	Percentage
Survivors (n=321)	Fully recovered at end of 1 month	316	78.4%
	Partially recovered at end of 1 month	5	1.2%
Nonsurvivors	-	60	14.8%
Lost to follow-up	-	22	5.4%

[Table/Fig-3]: Outcome of AKI at the end of 1 month.

Among the various aetiologies, mortality was significantly higher in AKI with cardiac failure (27.7%), and stroke (27.1%). Survivors and nonsurvivors were compared statistically and it was found that mortality significantly increased as the staging of AKI increased (p-value <0.001). Cardiac failure and stroke caused significant mortality (p-value=0.004 and 0.02 respectively). Among those patients who underwent dialysis, the mortality was 62% [Table/Fig-2].

DISCUSSION

This prospective observational study included 403 patients of AKI by KDIGO criteria and their aetiology and outcome were analysed at the end of one month. AKI was noted in 27.04% of medical intensive care admissions. The prevalence of AKI in intensive care setup is highly variable from studies all over the world. In a multinational study done by Hoste EAJ et al., in the intensive care setup, 57.3% of ICU admissions had AKI [5]. Case J et al., observed that AKI was noted in patients ranged from 20% to 50% with lower incidence seen in elective surgical patients and higher incidence in sepsis patients [12]. Similarly in an Indian study by Avasti G et al., AKI was noted in 17.2% of medical ICU patients compared to 3.1% in surgical ICU [13]. Korula S et al., noted AKI in 16.1% of medical ICU patients [14]. This is comparable with prevalence of our study done in medical intensive care.

The mean age of study population was 56±16 years and 32.7% of the total cases/population belonged to 51-65 years of age. Studies of AKI conducted in India by Eswarappa M et al., Thabah M et al., and Avasti G et al., showed that majority of patients belong to 40-60 years similar to our study [8,9,13].

Males were found to be affected more compared to females (62% versus 38%) similar to other studies [4,9,14,16]. Diabetes (22.6%) was the commonest comorbidity followed by hypertension (13.2%) and coronary artery disease (7.19%). Eswarappa M et al., Thabah M et al., and Korula S et al., also noted diabetes as the most common comorbidity followed by hypertension [8,9,14].

The percentage of the study population in stage I, stage II and stage III AKI were 45.4%, 29.2% and 25.3%, respectively. Hence, majority of study population belonged to less severe, potentially reversible form of AKI like other studies on AKI [16,17].

The most common aetiology of AKI in the present study was sepsis (33.7%). The major cause of sepsis was urinary tract infection, followed by pneumonia and aspiration pneumonitis. Sepsis is found to be the most common aetiology all over the world witnessed by multiple studies [8,9,14,16-18]. Urogenital sepsis was noted as most common cause by Eswarappa M et al., Thabah M et al., and Shah P et al., but Bagshaw SM et al., observed that the predominant sources of sepsis were chest and abdomen [8,9,17,18]. Priyamvada PS et al., found skin was the most common source of sepsis [16]. Prakash J et al., and Singh TB et al., observed drugs as the most common aetiology of AKI [4,19].

The other aetiologies of AKI observed were cardiac failure (13.3%), stroke (11.9%), chronic liver disease (9.4%), postrenal causes (8.4%) and diarrhoeal diseases (7.9%). The aetiologies of AKI observed by Priyamvada PS et al., were 18% due to neurological causes, 14% due to cardiac causes and 4% due to hepatic causes [16]. This pattern of aetiology was similar to that of study by Eswarappa M et al., except that cardiac causes and stroke leading to AKI is higher in our study comparatively [8]. A study by Tsagalis G et al., showed that nearly 1 in 4 patients with stroke developed AKI [20].

The cardiac causes noted were predominantly acute decompensated heart failure secondary to myocardial infarction, dilated cardiomyopathy and hypertensive heart disease. The most common cause of AKI in liver disease was volume responsive prerenal azotemia in this study, followed by hepatorenal syndrome and acute tubular necrosis similar to a study done by Russ KB et al., [21]. Drugs implicated with AKI in our study were NSAIDS (27.7%), aminoglycoside (22.2%), contrast agents (16.6%), ACE inhibitors (11.1%), unknown native medicines (11.1%), Amlodipine overdose (5.5%) and Cyclosporine (5.5%). Priyamvada PS et al., observed that 30% of AKI was due to drugs and toxins. NSAIDs and aminoglycosides were the most common culprit similar to our study [16]. A total of 14.4% of study population required dialysis. Thabah M et al., observed 21.5% required dialysis and Priyamvada PS et al., observed 30% required dialysis [9,16]. Mortality was observed in 14.8% of total study population where as 78.4% of patients completely recovered at the end of 1 month and 1.2% of patients had partial recovery (creatinine level did not fall back to normal reference range). The mortality rates of AKI reported by other studies in India are higher than that of our study. Ali T et al., reported 33% in hospital mortality and full recovery in 92.5% of survivors [22]. The mortality rates reported by Umesh L et al., Priyamvada PS et al., and Kashinkunti MD et al., were 52.5%, 28.3% and 9.61%, respectively [10,16,23]. Hoste EAJ et al., in a multinational study on AKI using KDIGO criteria reported around 18% mortality rate [5]. This variability in mortality rates can be explained by varying demographical characteristics of patients, inclusion of surgical intensive care patients, comorbid conditions and different study designs. Higher mortality was observed in males and age more than 65 years. Stage III AKI showed higher mortality (45.1%) compared to stage I AKI and stage II AKI similar to study by Hoste EAJ et al., and Bagshaw SM et al., [5,17]. The mortality in patients who underwent dialysis was 62%. AKI associated with cardiac failure and stroke showed significantly higher mortality.

In the two multicentric studies on AKI by Cerda J et al., and Bouchard J et al., AKI in developed countries were found to be associated with multiorgan failure and sepsis, high mortality, and occurrence in older populations. Similar results were noted in urban centres of developing countries. Mortality was higher in developed countries than developed countries (27.6% versus 17.65%). AKI in rural areas of developing countries were found to occur in younger population, due to single disease and lesser mortality [3,24]. Our centre is situated in semi urban area. Though sepsis was the most common cause of AKI in our centre, the mean age is lesser and outcome is better when compared to developed countries. The local guidelines on treatment strategies of AKI which specifically caters our pattern of disease should be developed by experts to improve the outcome.

Strength(s)

This study enlightens about the changing spectrum of AKI in South India and prospective studies using KDIGO criteria which are limited in the area studied.

Limitation(s)

Urine output criteria were not used in the study due to practical constraints which would have missed few cases of AKI and the progression to chronic kidney disease is not studied at the end of three months.

CONCLUSION(S)

AKI was noted in 27.04% of medical intensive care admissions and the prevalence increased with age. Sepsis was the most common cause of AKI. Major proportion of AKI patients recovered at the end of 1 month and the mortality observed in this study was 14.9%. Mortality was higher in AKI associated with chronic medical conditions and multiple comorbidities. Hence, it is important to identify the aetiology for early initiation of treatment as AKI is predominantly a potentially reversible disease.

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