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Clinicoetiologic Profile of Acute Kidney Injury in a Tertiary Hospital Of North India

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ABSTRACT
We aimed to study the epidemiology and outcome of acute kidney injury (AKI). This is a prospective study of adults aged 18 years or above diagnosed with AKI over a period of 12 months at a tertiary care hospital. One hundred and fifty patients had AKI. The observed incidence of AKI was seven per 1000 admissions. About 90% had community-acquired AKI (CA-AKI), and in 10% it was hospital-acquired AKI (HA-AKI). Etiological factors for AKI were medical in 87.4% of the cases, surgical in 9.4%, and obstetric 3.2%. Sepsis was the most common (52%) etiology of AKI among the medical cases. Among sepsis, scrub typhus, urosepsis, and pneumonia were the most common causes of AKI. Hypovolemia (14.6 %), biological toxins (6.6%), nephrotoxic drugs and chemicals (11.8 %), cardiac causes (3.3 %), and acute glomerulonephritis (1.3%) were other medical causes of AKI. Nearly 40.6 % had multiorgan failure, 14 % required vasopressors, 8 % required Intensive Care Unit support, and 23.3% required dialysis. Mortality was 8.6 %. Anemia, use of vasopressor agent, and need for intensive care support were independent predictive factors for mortality. AKI is common in hospitalized adults in India and leads to significant in-hospital mortality. AKI is largely a CA-AKI and the lesser percentage is due to HA-AKI. Many causes are potentially preventable. Early fluid resuscitation, effective anti-infective treatment, appropriate antidotes, and timely referral of established AKI patients to centers with dialysis facilities can improve AKI outcomes.

Keywords: NIL

INTRODUCTION

Acute kidney injury (AKI) is a disorder which is commonly associated with high morbidity and mortality worldwide. Epidemiology of AKI is determined by the difference in climate, ethnicity, culture, socioeconomic, and development status. hence,the epidemiology of AKI differs from one country to another, and from one center to another within the same country. Characteristics of patients with AKI encountered in tertiary care hospitals in large cities of high-income countries are mostly the elderly, critically ill with multiorgan failure, have chronic comorbidities, and the main AKI causes are ischemia, sepsis, and nephrotoxic drugs. By contrast, Community aquired AKI in smaller urban areas distant from large cities and in rural zones are secondary to diarrhea, tropical infectious diseases, animal venoms, use of native medicines, and poor obstetric care, among young individuals who are previously healthy .[1],[2],[3]

Hospital-acquired AKI (HAAKI) are typically drug-induced, sepsis-related, post contrast administration, post-surgical, and caused by hemorrhage.[1] HAAKI mainly forms the bulk of AKI in developed nations whereas in tropical countries like India, AKI is mostly community acquired (CAAKI), i.e., occurs outside the hospital setting, the causes of which are mentioned above .[2] The demographics and

etiology of CAAKI is known to vary from country to country. Within the Indian subcontinent, there is variation in the etiology of CAAKI reported between different centers, which are geographically distant, and the etiologic spectrum has been seen to change with passage of time. For example, in the study by Prakash *et al.* from the eastern part of India comparing AKI between 1983–1995 and 1996–2008, it was found that the incidences of obstetrical, surgical, and diarrheal AKI decreased significantly, whereas AKI associated with malaria, sepsis, nephrotoxic drugs, and liver disease increased.[3] The incidence of renal cortical necrosis also reduced significantly.[4] From the northern part of the country, in the study from Chandigarh involving 1862 patients over a period of 21 years (1965–1986), the bulk of AKI cases were medical causes (60%), whereas obstetric and surgical constituted 15% and 25% causes of AKI, respectively.[5] Diarrheal diseases-related AKI drastically reduced, whereas drug-related and sepsis-related AKI increased. Similarly, obstetric causes of AKI reduced. These studies also highlighted that the pattern of AKI in India is different from industrialized nations in that there is a significant component of CAAKI. While the etiologic spectrum of AKI in northern India varies from the etiology and outcomes of CAAKI from southern India. A study from Chennai reported diarrhea as the most common cause of AKI, followed by drugs, glomerulonephritis, sepsis, snakebite, leptospirosis, malaria, and copper sulfate as other common causes.[6]

Mahatma Gandhi Medical College Hospital, jaipur is one of the largest tertiary care hospital in the state of Rajasthan in Northern India . We prospectively studied the epidemiology and outcome of AKI at this hospital over a period of 12 months.

MATERIALS AND METHODS

This was a prospective study done over a period of 12 months at mahatma Gandhi Medical College, jaipur. The study participants were hospitalized adults aged 18 years or above. The inclusion and exclusion criteria were defined as follows.

Inclusion criteria

1. Presence of uremic symptoms or oliguria or anuria of recent onset
2. AKI as defined using the Kidney Disease – Improving Global Outcomes (KDIGO) criteria based on serum creatinine (increase in serum creatinine by ≥0.3 mg/dL within 48h or increase in serum creatinine to ≥1.5 times baseline), which is known or presumed to have occurred within the prior 7 days.
3. Staging of AKI was serum creatinine 1.5 to 1.9 times base-line or ≥0.3 mg/dL increase (stage 1); 2.0 to 2.9 times baseline (stage 2); and 3.0 times baseline or increase in serum creatinine to ≥4.0 mg/dL or initiation of renal replacement therapy (stage 3).[9] It was presumed that the patient had normal renal function if the serum creatinine was 1.5 mg/dL or below .

Exclusion criteria

1. Preexisting kidney disease (serum creatinine >1.5 mg/dL or ultrasonography of the abdomen suggestive of bilateral small kidneys/loss of corticomedullary differentiation/obstructive nephropathy/other renal pathology)
2. Patients with acute on chronic kidney disease or renal failure attributed to chronic kidney disease.

Patients who had AKI on admission were considered as community acquired-AKI (CA-AKI). Those who developed kidney injury after at least 24 h of admission were considered as hospital acquired-AKI (HA-AKI).

All patients were subjected to a detailed history, clinical examination, laboratory investigations, and ultrasound imaging of the kidneys. Patients were provided supportive care and given dialysis as per standard hospital protocol. Daily follow-up was done until discharge or death. Patients remaining oliguric or anuric or whose serum creatinine did not decrease satisfactorily at the end of four weeks of treatment, unexplained AKI, and those with features suggestive of systemic and glomerular disease, were subjected to kidney biopsy which was examined with light and immunofluorescence microscopy. Outcomes of the requirement of vasopressor drugs, and Intensive Care Unit (ICU) support, treatment with dialysis, survival at discharge, and in-hospital mortality were studied. The survival and nonsurvival were compared to see

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the difference in clinical characteristics and laboratory features between the two groups.

The patients included in the study were explained in detail about the purpose of the study, and informed consent was obtained. The study was approved by the Institutional Ethics Committee.

Continuous data are expressed as means ± standard deviation, and the means of the two study groups were compared using an unpaired t-test. Nominal data are expressed as frequencies or proportions, and the Chi-square test and Fisher's exact test were used to compare the differences in frequency between the two study groups. For nonnormal data, a Mann-Whitney U-test was performed. Multi-variate binary logistic regression analysis was done for factors predictive mortality. A P <0.05 was considered statistically significant. All statistics were carried out using the Statistical Package for Social Sciences (SPSS) version 16.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

The total number of patients hospitalized over the study period was 20,000. Of them, 150 (0.75%) had AKI with an incidence of 8 per 1000 admissions or six per 1000 admissions per year. One hundred and thirty six (90.6%) had CA-AKI with an incidence of 7.2/1000 admissions. 14(9.3%) had HA-AKI with an incidence of 0.6/1000 admissions. AKI occurred in medical, surgical, and obstetric setting in 84.6%, 8.6%, and 6.6%, respectively

Demographic and clinical characteristics of the study patients (n=150).

GENDER	n(%)
MALE	85(56.6%)
FEMALE	65(43.3%)
AGE (YEARS)	
MEAN (+/-SD)	49+-18.2
RANGE	18-90
TYPE OF AKI	
COMMUNITY-ACQUIRED,n(%)	136(90.6%)
HOSPITAL-ACQUIRED,n(%)	14(9.3%)
SETTING OF AKI	
MEDICAL,N(%)	127(84.6)
SURGICAL,N(%)	13(8.6)
OBSETRICAL,N(%)	10(6.6)
HEMOGLOBIN(G/DL)	10.5+/-2.3
UREA	140+/-65
CREATININE	3.5+/-2.2
KDIGO STAGE	
STAGE1	38(25.3)
STAGE2	60(40)
STAGE 3	52(34.6)
OLIGURIA	60(40)
HYPERKALEMIA	37(24.6)
METABOLIC ACIDOSIS	30(20)
MULTIORGAN FAILURE	61(40.6)
VASOPRESSOR SUPPORT	21(14%)
ICU SUPPORT	12(8%)
DIALYSIS	35(23.3)
OUTCOME	
survived	137(91.3)
died	13(8.6)

TABLE 1

Demographic and clinical characteristics

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[Table 1] shows the demographic and clinical characteristics of the study patients. Mean age was 49 ± 18.1 years, 86 (27.8%) patients were of age 60 years or above, and the majority were men. In about two-third, AKI was KDIGO stage 1 or 2, and in other one-third, it was stage 3. Oliguria was seen in 40%, fluid overload in 6.1%, anemia in 42.5%, hypoalbuminemia in 48.5%, hyperkalemia in 29.4% and metabolic acidosis in 19.1%. Encephalopathy was seen in 9%, and 38.2% had a multi-organ failure. Comorbid conditions seen were as follows: chronic obstructive pulmonary disease (14.2%), hypertension (10%), coronary artery disease (9.7%), chronic liver disease (9.4%), diabetes mellitus (9.4%), malignancy (3.2%), and pulmonary tuberculosis (2.9%).

Etiology of acute kidney injury

Sepsis, hypovolemia, toxins, cardiac, and acute glomerulonephritis were the medical causes of AKI [Table 2]. Sepsis was the leading (52%) cause of AKI in our study. Sepsis was secondary to scrub typhus (6.1%), urinary tract infection (15.3%), pneumonia (5.3%), H1N1 influenza (6%), infected diabetic foot (5.3%), viral hepatitis (6.1%), leptospirosis (1.3%), febrile neutropenia(3.3), and secondary bacterial peritonitis 2% each. Hypovolemia due to diarrheal illness (11.3%) and acute pancreatitis (3.3%) was the cause of AKI in 14.6% of patients.

SEPSIS	78(52%)
SCRUB TYPHUS	10(6.1)
UTI	23(15.3)
PNEUMONIA	8(5.3%)
H1N1INFLUENZA	9(6)
INFECTED DIABETIC FOOT	8(5.3)
VIRAL HEPATITIS	10(6.1)
FEBRILE NEUTROPENIA	5(3.3)
BACTERIAL PERITONITIS	3(2)
LEPTOSPIROSIS	2(1.3)
HYPOVOLEMIA	22(14.6)
DIARRHEAL ILLNESS	17(11.3)
ACUTE PANCREATITIS	5(3.3)
BIOLOGICAL TOXINS	10(6.6)
NEPHROTOXIC DRUGS	15(10)
CARDIAC CAUSES	5(3.3)
ACUTE GLOMERULONEPHRITIS	2(1.3)
SURGICAL CAUSES	
OBSTRUCTIVE UROPATHY	6(4)
POST OPERATIVE	4(2.6)
OBSTETRICAL CAUSES	
PUERPERAL SEPSIS	4(2.6)
SEVERE PREECLAMPSIA	2(1.3)
PPH	2(1.3)

TABLE-2

Toxins such as nephrotoxic drugs, contrast, chemicals, and biological toxins were observed to be a cause of AKI in 16.6% patients [Table 3]. Drugs such as aminoglycosides, platinum compounds, nonsteroidal anti-inflammatory drugs (NSAIDs), acyclovir, amphotericin B, and angiotensin receptor blocker were etiology of AKI in 9.2%. Contrast caused AKI in 2.6%. Chemical causes (1.9%) of AKI were paraquat and aluminium phosphide. Snakebite (2%), multiple wasp stings (0.6%), were the biological toxins leading to AKI.

Cardiac causes such as acute myocardial infarcttion and complete heart block leading to cardiogenic shock were the implicated as a cause of AKI in 3.3% of patients. In 1.3 % patients AKI was due to acute glomerulonephritis.

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Obstructive uropathy (4%) and postoperative AKI (2.6%) were the surgical causes of AKI. Puerperal sepsis (2.6%), severe preeclampsia (1.3 %), and postpartum hemorrhage (1.3%) were the obstetrical causes of AKI.

TOXINS	N-25
DRUGS	
AMINOGLYCOSIDES	2(1.3%)
NSAIDS	8(5.3%)
AMPHOTERICIN	1(0.6)
ANGIOTENSIN RECEPTOR BLOCKER(ARB)	3(2%)
CONTRAST	4(2.6%)
CHEMICALS	
PARAQUAT	2(1.3)
ALUMINIUM PHOSPHIDE	1(0.6)
BIOLOGICAL TOXINS	
SNAKE BITE	3(2%)
MULTIPLE WASP STINGS	1(0.6%)

TABLE 3

Renal histology

Kidney biopsy was done to determine the etiology of AKI in 15 (10%) patients. On renal histology diffuse proliferative glomerulonephritis (0.6%), IgA nephropathy (0.6%) and necrotizing crescentic glomerulonephritis (0.6%) were found to be etiology of AKI. Acute tubular necrosis (ATN) (4%), acute interstitial nephritis (AIN) (1.3%), myeloma cast nephropathy(0.6) and renal cortical necrosis (RCN) (0.6%) were causes of AKI in other patients [Table 4]. The renal histology revealed ATN in four and RCN in one among AKI due snake bite. ATN associated AIN was seen in a patient with AKI due to wasp stings.

TABLE-4

BIOPSY DIAGNOSIS	N(%)
Diffuse proliferative GN	1(0.6)
Iga nephropathy	1(0.6)
Necrotizing cresentric GN	1(0.6)
Acute tubular necrosis(ATN)	6(4)
Acute tubulo interstitial nephritis (ATIN)	2(1.3)
ATN+ATIN	2(1.3)
Myeloma cast nephropathy	1(0.6)
Renal cortical necrosis	1(0.6)

Clinical outcomes

14 % of the patients, required treatment with vasopressor drugs, 8% ICU support and 23.3% required dialysis. One hundred and thirty seven (91.3%) patients survived and thirteen (8.6%) patients died [Table 1].

Comparison between survival and nonsurvival group

[Table 5] shows the comparison between the clinical characteristics of the two outcome groups. The proportion of patients with oliguria (P = 0.001), fluid overload (P = 0.001), encephalopathy (P = 0.006), multi-organ failure (P = 0.001), anemia (P = 0.001), metabolic acidosis (P = 0.001), requirement of vasopressors (P = 0.001, need for ICU support (P = 0.001) and dialysis (P = 0.015) was significantly higher in patients who died. As compared to the survival group, the hemoglobin was significantly lower (P = 0.001) in patients who died. There were no significant differences in other demographic and clinical characteristics between the groups. In multivariate binary logistic regression analysis, the presence of anemia, use of vasopressor drugs and requirement of ICU support were predictive factors for mortality.

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Variables	Survived (n=282)	Died (n=27)	P
Oliguria, n (%)	116 (41.1)	24 (88.9)	0.001[a]
Fluid overload, n (%)	10 (3.5)	9 (33.3)	0.001[a]
Encephalopathy, n (%)	21 (7.4)	7 (25.9)	0.006[a]
Multi organ failure n (%)	95 (33.7)	23 (85.2)	0.001[a]
Hemoglobin (g/dL)	10.9±2.4	8.6±2.1	0.001[b]
Urea (mg/dL)	143±68	148±63	0.716[b]
Creatinine (mg/dL)	3.7±2.4	4.8±4.1	0.242[c]
Anemia, n (%)	108 (38.3)	23 (85.2)	0.001[a]
Hypoalbuminemia, n (%)	132 (46.8)	18 (66.7)	0.07[a]
Metabolic acidosis, n (%)	42 (14.9)	9 (33.3)	0.001[a]
Vasopressor support, n (%)	40 (14.2)	22 (81.5)	0.001[a]
Intensive care support, n (%)	3 (1.1)	16 (59.3)	0.001[a]
Dialysis, n (%)	60 (21.3)	12 (44.4)	0.015[a]

[a]Chi-square with Fisher's Exact test Exact sig. (2-sided), [b]Independent samples t-test, Sig. (2-tailed), [c]Mann–Whitney U-test, Sig. (2-tailed) nonparametric independent samples test.

VARIABLES	SURVIVED(n=137)	DIED(n=13)
OLIGURIA,n(%)	30(21.8)	11(84.6)
FLUID OVERLOAD	4(2.9)	6(46.1)
ENCEPHALOPATHY	10(7.2)	5(38.4)
MULTI-ORGAN FAILURE	46(33.5)	4(30.7)
HEMOGLOBIN	10.5+-2.5	8.6+-2.1
UREA	140+-65	148+-60
CREATININE	3.5+-4	4.8+-4.0
ANEMIA	48(35)	12(92.3)
HYPOALBUMINEMIA	68(49.6)	10(76.9)
METABOLIC ACIDOSIS	20(14.5)	4(30.7)
VASOPRESSOR SUPPORT	19(13.8)	10(76.9)
INTENSIVE CARE SUPPORT	3(2.1)	7(53.8)
DIALYSIS	27(19.7)	6(46.1)

Discussion

In developed countries, AKI is primarily Hospital aquired,while it is mainly community aquired in developing countries.[2] Our study found that AKI was largely a CA-AKI and lesser percentage was due to HA-AKI. The incidence AKI was eight per 1000 admissions or six per 1000 admissions per year. Data on CA-AKI from the developing world is scanty, different definitions of AKI are used in different regions, and it often originates in a single center of an urban location. True estimation of CA-AKI in developing countries is difficult to make because most patients do not go to urban hospitals, where they would have been included in the incidence estimation.[5] Further, it is likely that gross under-reporting results in the apparently lower incidence of AKI in the developing world due to insufficient monitoring of renal function in hospitalized patients due to poor resources and lack awareness among attending doctors.[2],[10] The incidence of CA-AKI in this study was 7.2 per 1000 admissions was higher than that reported in the earlier studies.[4],[5],[11],[12] The age of our study patients was higher, a significant proportion was elderly, and many had the burden of chronic comorbidities, which could explain the higher incidence observed in the current study. Further, an increased awareness, recognition, and diagnosis of AKI in recent years might have contributed to higher incidence observed.

In our study, 87.4% of the patients were having AKI related to medical causes, 9.4% from surgical causes and 3.2% of patients were having obstetrical causes for AKI. Previous studies have shown that medical, surgical and obstetrical causes accounted for 77.5%–

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87.6%, 8.3%–8.9%, and 3.4%–14.2% cases, respectively.[4],[13] Our observation thus stands comparable to the previous Indian data.

Sepsis is the most common cause of AKI in critically ill patients.[14],[15] It was a major (53.1%) cause of AKI in our study. Scrub typhus is caused by the bacterium Orientia tsutsugamushi and is transmitted to humans by infected Leptotrombidium mite larva (chiggers). It is an important cause of acute undifferentiated febrile illnesses in the Indian subcontinent, and it should be part of the differential diagnosis of acute febrile illness with AKI. AKI is thought to be a consequence of multiorgan dysfunction secondary to sepsis.[7] The AKI is frequent, ranging from 20% to up to 60%.[16] Scrub typhus emerged as a leading (18.5%) cause of sepsis-associated AKI in our study.

Leptospirosis, a spirochetal zoonosis was responsible for AKI in 1.6% of patients. In two-third (66.7%) the AKI was nonoliguric. The incidence of AKI in leptospirosis varies from 10% to 60%, depending on the severity of the disease, age, and definition of AKI. AKI in leptospirosis is primarily nonoliguric. Several factors are involved in AKI in leptospirosis, including the direct nephrotoxic action of the leptospira, hyperbilirubinemia, rhabdomyolysis, and hypovolemia.[17].

Five (1.6%) patients had AKI post-acute viral hepatitis. Although AKI is common in patients with fulminant hepatitis due to hepatitis A/E virus, it has been recognized as a rare complication of nonfulminant acute viral hepatitis.[18] Two of the five patients with viral hepatitis associated AKI had a fulminant hepatic failure; one of them was secondary to documented viral hepatitis A infection and the other was secondary to documented viral hepatitis E infection. In one patient acute viral hepatitis led to decompensation of his chronic liver disease leading to AKI. In two other patients, nonfulminant form of viral hepatitis E was associated with AKI; one of these had associated glucose-6-phosphate dehydrogenase (G6PD) deficiency with accompanying evidence of intravascular hemolysis, and other had normal G6PD levels. Intravascular hemolysis secondary to G6PD deficiency should be suspected in patients with acute viral hepatitis E with marked bilirubinemia and anemia.[19] However, AKI in acute hepatitis E can occur even in the absence of G6PD deficiency due to hyperbilirubinemia and retained biliary nephrotoxic substances along with a possible direct toxicity of the virus.[20]

UTI was another major causes of sepsis-associated AKI in our study accounting for 14% cases. A study from India reported UTI to be the most common source of AKI associated sepsis in critically ill patients.[21] UTI may cause sudden deterioration in renal function. Further, hypovolemia, hypotension, sepsis, the use of nephrotoxic drugs, contrast media and urinary obstruction are AKI risk factors in UTI patients.[22],[23]

Next, the most common source of sepsis in our study was the lungs (9.1%). Murugan et al reported AKI in 34% of patients with community-acquired pneumonia (CAP) and AKI was also found to be common in nonsevere categories of CAP.[24] Our study had 3.9% of patients of AKI associated with sepsis secondary to H1N1 influenza. Few studies have investigated AKI in patients infected with the 2009 pandemic influenza A (H1N1) virus. A study from India found that the 19.4% prevalence of AKI in patients with H1N1[25] whereas a study from Brazil found AKI in 53% of the H1N1-infected patients[26] AKI in H1N1-infected patients involves multiple mechanisms, including hemodynamic instability, hypoxia, and a direct effect of the H1N1 virus on the kidney.

Hypovolemia due to diarrheal illness was the cause of AKI 6.5% of patients in this study. This was less than the earlier reported incidence of 20.6% from our institute.[12] The decline in the incidence of AKI secondary to diarrheal illness could be due to improvements in hygiene, patient education in oral rehydration and health infrastructure in our state wherein most of these patients are adequately managed at the primary level leading to less number of referrals to our tertiary center. Similarly, a significant decline in diarrhea-related AKI has been also reported from India by Prakash et al.[5]

Acute pancreatitis accounted for 2.9% of the cases in our study. AKI is one of the most common complications in patients with severe acute pancreatitis. Its incidence rate ranges from 14% to 42%.[27],[28] AKI due to severe acute pancreatitis is the result of hypoxemia, the release of pancreatic amylase from the injured pancreas with impairment of renal microcirculation, decrease in renal perfusion

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pressure due to abdominal compartment syndrome, intraabdominal hypertension or hypovolemia.[29]

Toxins were observed to be a cause of AKI in 15.5%. It included snake and wasp envenomations (6.8%), nephrotoxic medications (4.8%), poisonous chemicals (1.3%), contrast (1.3%), and poisonous mushrooms (1.3%).

AKI due to snake bite is an important cause of CA-AKI in tropical countries. About 12%– 30% of patients bitten by venomous snakes, primarily vipers, develop AKI. Hemorrhage, hypotension, disseminated intravascular coagulation, intravascular hemolysis, and rhabdomyolysis contribute to the development of AKI. Enzymatic activities of snake venoms account for direct nephrotoxicity. Immunologic mechanism plays a minor role. Mortality in snake bite-induced AKI is 1%–20%.[30],[31] Early administration of anti-snake venom (ASV) is a vital therapeutic measure. Treatment of established AKI is largely supportive in nature, renal replacement therapy being the cornerstone.[31]

Our snakebite victims were referred from farflung rural areas. Most of the patient visited the traditional healers first or waited to become severely symptomatic. There were delays in seeking treatment at health centers and getting treatment with ASV due to its nonavailability at peripheral health centers. Majority of the patients first received ASV at our center. Most (90%) patients with snake bite-induced AKI were KDIGO AKI stage 3 and required dialysis. There was no mortality.

More than half of the victims who experience multiple wasp or bee stings develop AKI due to intravascular hemolysis, rhabdomyolysis, shock, and the direct toxic effects of the venom, and most of these patients need dialysis. The mortality rate of patients who experience AKI has been reported to be as high as 25%. Since there is no antivenom, treatment in all such cases is essentially supportive.[32],[33] Two patients developed AKI secondary to multiple wasp stings and required dialysis. One patient died.

Accidental consumption of poisonous wild mushrooms was a cause of AKI in four patients. The species of mushrooms consumed could not be ascertained. All had AKI as a component of multiorgan dysfunction. The mortality rate was 75%. Accidental ingestion of certain wild mushrooms (Amanita species, Galerina species) leads to gastrointestinal and hepatic toxicity. AKI occurs around 10-14 hours after exposure. The latter is usually severe, with up to 50% mortality.[34]

In the current study,, 6.1% of patients developed AKI secondary to nephrotoxic drugs. The majority (84.2%) of them developed AKI during a hospital stay. The drugs accounted for 66.7% of cases of HA-AKI. Drug-induced AKI accounted for 20% of all AKI in an Indian study; aminoglycosides accounted for 40% of such cases.[35] The decreased incidence in our study done 20 years later reflects the increasing awareness of nephrotoxic medications among the medical professionals and the general public. Nephrotoxic drugs in our study included aminoglycosides, contrast, platinum compounds, NSAIDs, acyclovir, amphotericin B and angiotensin receptor blockers. The etiology of drug-related AKI in our country has changed. In the past, antibiotics were the most common causes, followed by analgesics and contrast media. AKI due to antibiotics has declined while other new causal agents have emerged including NSAIDs, angiotensin converting enzyme inhibitors, chemotherapeutic and antiviral medications.[5] The variety of drugs associated with AKI in our study show consistence with the changing epidemiology of drug-related AKI observed by Prakash et al.[5]

Paraquat poisoning was a cause of AKI in 1% patients. All the patients had multi organ failure and died. A study of six cases of paraquat poisoning from India reported AKI in all the cases and mortality of 66%.[36] The multiorgan involvement with circulatory collapse is associated with 100% mortality.[37] This observation and late referral to our center may account for the 100% mortality rate seen in our patients.

Cardiac causes such as myocardial infarction, heart block were the causes of AKI in 7.4%of our patients. Acute glomerulonephritis was a cause of AKI in 1.9% of patients as compared to 9.3% reported in a previous study from India.[5]

Surgical causes accounted for AKI in 9.4% patients which is comparable to the incidence reported in other studies.[4],[12] Of these 6.5% patients had obstructive uropathy, and other 2.9% were

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postoperative AKI. Whereas trauma, drugs and cardiovascular surgery are the leading causes of AKI in the surgical setup in the developed nations, obstructive uropathy constitutes a major cause of surgical AKI in developing nations like India. Obstructive uropathy was secondary to renal or ureteric calculi, carcinoma cervix, and prostatic enlargement. Postoperative AKI accounted for 25% of all cases of HA-AKI in our study.

AKI is one of the most challenging complications of pregnancy in developing countries and is frequently related to suboptimal antenatal care, out-of-hospital delivery in rural areas, and unsafe abortions conducted by unqualified personnel or using insecure medicines.[10] Most cases of AKI occur during the third trimester and postpartum related to preeclampsia, eclampsia, placental abruption, postpartum hemorrhage, disseminated intravascular coagulation, and puerperal sepsis.[10]

In India, improvements in the antenatal medical care and obstetric care have decreased obstetric AKI to 10%–12%.[5],[38] Medical care for pregnant women is still deficient, and the timing of hospital referral in obstetric AKI is generally delayed. Renal ischemia, caused by hemorrhagic shock or hypotension due to sepsis, is the dominant factor leading to AKI. In our study, obstetric AKI was 3.2%, and the puerperal sepsis was the most common (70%) cause followed by severe preeclampsia and postpartum hemorrhage.

Luo et al have reported that as compared to other AKI diagnostic criteria, the highest incidence of AKI using the KDIGO criteria.[39] We used the KDIGO criteria in our study. Maximum patients (42.1%) were in KDIGO Stage 2 while KDIGO Stage 1 and 3 had 22.6% and 35.3% patients, respectively. Thakar et al found that increased severity of AKI associated with an increased risk of death independent of comorbidity.[40] In our study, the maximum proportion (48.1%) of patients who died was in AKI KDIGO Stage 3.

In contrast to the high mortality associated with AKI in developed nations, AKI-associated mortality is lower (10%–40%) in developing countries because AKI affects younger people and caused by a single disease, i.e., less commonly associated with multi-organ failure.[5],[10]Moreover, in developing countries, CA-AKI is commonly due to volume-responsive azotemia, which is rapidly reversible on volume correction. Conversely, the mortality is high in AKI with specific diseases when associated with multiorgan failure.[5],[10] The mortality rate in this study was 8.7%. The mortality rate with HA-AKI was 4.2% compared to 9.1% with CA-AKI patients. The major (92.6%) mortality was contributed by the medical group as compared to the surgical (3.7%) and obstetric (3.7%) group. The possible explanation for the lower mortality in the surgical and obstetrical patients is that they did not have multiple organ failure which was common among the medical group.

In our study, the proportion of patients with oliguria, fluid overload, encephalopathy, multiorgan failure, anemia, metabolic acidosis, the requirement of vasopressors, need for ICU support and dialysis was significantly higher among patients who died. A similar association of increased mortality with above factors has been observed by Kaul et al.[4] A multivariate binary logistic regression analysis showed that the presence of anemia, use vasopressor drugs, and requirement of ICU support were independent predictive factors for mortality in our patients.

In our study, we found that AKI was largely a CA-AKI and lesser percentage was due to HA-AKI. Sepsis, hypovolemia, envenomation, nephrotoxic drugs, and chemical were the main etiologies of AKI and were associated with significant mortality. Many causes are potentially preventable which requires adopting a public health approach, including provision of safe water, infection control, vector management, better obstetric care, and campaigns to raise awareness about safe use of drugs, pesticides, and chemicals. Early fluid resuscitation, effective anti-infective treatment, appropriate antidotes, and timely referral of patients with established AKI to centers with dialysis facilities will improve outcomes.

In summary, our study described the clinical and etiological spectrum of AKI among hospitalized adults at a tertiary care hospital in northern India and described the profiles of risk factors and in-hospital outcomes of AKI. This unique spectrum represents the CA-AKI from small towns and rural areas. Results from this study may help to clarify the epidemiologic characteristics and burden of AKI in India. Our study has certain limitations. First, because the study was carried out at tertiary care hospital, it

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does not truly reflect the etiological spectrum of AKI prevalent throughout the country. Second, pediatric patients were excluded. Finally, long-term outcome could not be studied in our patients due to lack of such follow up. Nevertheless, our study describes very relevant information on adult AKI spectrum encountered at a large tertiary care referral center in a developing country.

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