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Internal Medicine

IN-HOSPITAL MORTALITY OF ACUTE KIDNEY INJURY: AN EXPERIENCE FROM SOUTH RAJASTHAN.

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ABSTRACT **INTRODUCTION:** There are few studies on in-hospital mortality among medical intensive care unit (MICU) patients with acute kidney injury (AKI). We assessed the clinical characteristics of AKI at MICU admission, its impact on mortality during the current hospitalization, and whether the influence of AKI varied in subgroups of AKI patients.

METHODS: We identified all adult aged 12 years and above having medical etiology related community acquired AKI who were admitted to MICU at Pacific Medical College and Hospital, Udaipur, India; from 2015 to 2019. AKI was defined based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria; based on serum creatinine (SCr). Dialysis requiring AKI (D-AKI) was defined as needing acute dialysis at or after MICU admission. Among 2440 MICU patients; 516 patients (21.1%) had AKI. We analyzed in-hospital mortality for subgroups of AKI: stage1, stage2 and stage3: with different etiology, comorbidity levels, acute risk factors, primary hospital diagnosis, and treatment with mechanical ventilation, vasopressors and dialysis.

RESULTS: Maximum number of AKI patients (57.8%) were in KDIGO Stage3, while stage1 and stage2 had 17.8% and 24.4% respectively. 51.4% patients were male, median age was 54.81 years and average length of ICU stay was 11.73 days. The most common primary diagnosis and etiology was sepsis (31.4%), the most common acute risk factor was hypovolemia (18.8%), the common chronic comorbidity were diabetes (17.0%) and hypertension (10.0%). The most common presenting symptoms was oliguria (43.8 %), while commonest sign on admission was edema (28.1%). Common indications for dialysis were oliguria (75%), hyperkalemia (38.2%), refractory fluid overload (36.2%) and metabolic acidosis (35.2%). Overall common critical care treatment required in AKI patients were acute dialysis (58.9%), vasopressor support (16.5%) and ventilator support (14%). The requirement of dialysis was 0.0%, 4.8% and 100%; among stage1, stage2 and stage3 respectively. The overall AKI mortality was 9.9% (95% confidence interval (CI) 7% to 12%). The associations between AKI and mortality were 10.87% (95% CI 5% to 17%) for the AKI-stage1, 13.49% (95% CI 8% to 19%) for the AKI-stage2 and 8.05% (95% CI 5% to 11%) for the AKI-stage3. The mortality in D-AKI group was 8.6% (95% CI 5 % to 12 %) compared to the mortality in ND-AKI group 11.8% (95% CI 7 % to 16 %). The association between AKI and in-hospital mortality was evident in all subgroups of AKI; association was more pronounced in stage2 AKI, mostly due to worsening of complications which suggests that KDIGO stage2 AKI is a transition zone among D-AKI and ND-AKI groups. Further, it may be needed to lower the threshold for dialysis criteria in AKI.

CONCLUSIONS: Any degree of AKI was associated with increased mortality. Timely and early initiation of dialysis in AKI was an important prognostic factor for the reduction of in-hospital mortality.

KEYWORDS : acute kidney injury, AKI, medical intensive care unit, AKI stage, dialysis requiring AKI, critical care, in-hospital mortality.

INTRODUCTION

Kidney function plays a central role in critical illness because the kidneys help to regulate the composition and volume of extra cellular fluid, play an essential role in acid-base balance, remove waste material, and affect drug disposition [1].

In principle acute kidney injury (AKI) is one of the conditions that acutely affects kidney structure and function. For simplicity we refer to these conditions as acute kidney diseases and disorders (AKD), in contrast to chronic kidney diseases (CKD); and illustrate the relationship of AKI, AKD and CKD. Whereas CKD has a well established conceptual model and definition that has been useful in clinical medicine, research and public health, the definition of AKI is evolving and the concept of AKD is relatively new. A conceptual model of AKI and AKD is also evolving (figure 1) [2].

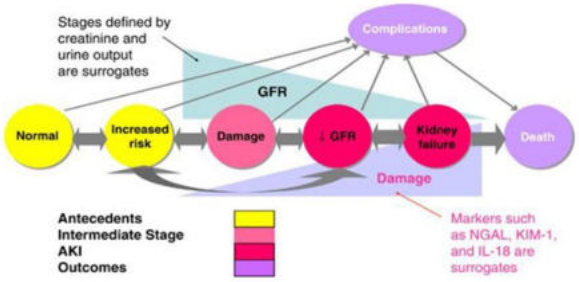

Figure 1: Conceptual Model of AKI. Adopted and modified from KDIGO Practice Guideline [3].

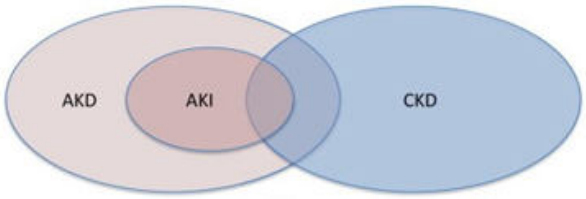

Figure 2: Integration of AKI, AKD and CKD Model. Adopted and modified from KDIGO Practice Guideline [3].

Conditions affecting kidney structure and function can be considered acute or chronic (figure 2), depending on their duration. AKI is one of a number of acute kidney diseases and disorders (AKD), and can occur with or without other acute or chronic kidney diseases and disorders.

The Syndrome of AKI

AKI is a clinical metabolic syndrome characterized by rapid decline of kidney excretory function. Primarily described in recent years using the widely accepted risk, injury, failure, loss of kidney function, and end-stage kidney disease (RIFLE) classification based on changes in serum creatinine (SCr) level and/or urine output [4,5]. Typically, AKI is diagnosed by surrogate markers of decreased glomerular filtration rate (GFR), such as retention of nitrogen metabolism waste products like

creatinine and/or decreased urine output [6,7]. It is a broad clinical syndrome encompassing various etiologies, including specific kidney diseases (e.g., acute interstitial nephritis, acute glomerular and vasculitis renal diseases); non-specific conditions (e.g, ischemia, toxic injury); as well as extrarenal pathology (e.g., prerenal azotemia, and acute postrenal obstructive nephropathy). More than one of these conditions may coexist in the same patient and, more importantly, epidemiological evidence supports the notion that even mild, reversible AKI has important clinical consequences, including increased risk of death [8]. Thus, AKI can be thought of more like acute lung injury or acute coronary syndrome. Furthermore, because the manifestations and clinical consequences of AKI can be quite similar (even indistinguishable) regardless of whether the etiology is predominantly within the kidney or predominantly from the outside stresses on the kidney, the syndrome of AKI encompasses both direct injury to the kidney as well as acute impairment of function.

Serum Creatinine, Glomerular Filtration Rate and Oliguria

It is widely accepted that GFR is the most useful and the best overall index of kidney function in health and disease; and changes in SCr and urine output are surrogates for changes in GFR. Although urine flow rate is a poor measure of kidney function, oliguria (urine output <500 ml/1.73 m2/24 hours in adult) generally reflects a decreased GFR. If GFR is normal (approximately 125 ml/min,corresponding to approximately 107 ml/kg/h for a 70-kg adult), then reduction in urine volume to <0.5 ml/kg/h would reflect reabsorption of more than 99.5% of glomerular filtrate. Such profound stimulation of tubular reabsorption usually accompanies circulatory disturbances associated with decreased GFR. Severe AKI is defined as urine output of less than 200 ml in 12 hours, blood urea nitrogen level higher than 84 mg/dl (30 mmol/l) or need for acute dialysis during admission.

Review of AKI Criteria

The first international interdisciplinary consensus for diagnosis of AKI were the RIFLE(risk, injury, failure, loss of kidney function, and end-stage kidney disease) criteria proposed by the acute dialysis quality initiative (ADQI). Two similar definitions by RIFLE and AKIN (acute kidney network) was based on serum creatinine (SCr) and urine output have been validated [9]. In 2012, the Kidney Disease Improving Global Outcome (KDIGO) collaboration combined the suggested criteria from both; and released a clinical practice guidelines (table 1) [10]. The KDIGO staging of AKI is more appropriate because, with increased stage of AKI, the risk for death and need for renal replacement therapy (RRT) increases [11-15]. Furthermore, there is now accumulating evidence of long-term risk of subsequent development of cardiovascular disease or CKD and mortality, even after apparent resolution of AKI [16-18].

Table 1: RIFLE, AKIN and KDIGO AKI diagnostic criteria.

AKI Class/ Stage	Serum Creatinine (SCr) Criteria			Urine Output (UO) Criteria
	RIFLE	AKIN	KDIGO	
R = 1	Increase × 1.5 from baseline or GFR decrease > 25%	Increase ≥ 0.3 mg/dl within 48 h or Increase 1.5-1.9 times from baseline	Increase ≥ 0.3 mg/dl within 48 h or ≥ 1.5- to 2 times from baseline	< 0.5 ml/kg/h for 6-12 h
I = 2	Increase × 2 from baseline or GFR decreased > 50%	Increase > 2-3 times from baseline	Increase 2.0-2.9 times from baseline	< 0.5 ml/kg/h for 12 h
F = 3	Increase × 3 from baseline or SCr > 4 mg/dl) with an acute rise > 0.5 mg/dl or GFR decreased > 75%	Increased > 300% (> 3 times) from baseline, or ≥ 4.0 mg/dl with an acute increase of ≥ 0.5 mg/dl or on RRT	3.0 times from baseline or increase in SCr to ≥ 4.0 mg/dl or initiation of RRT or, in patients < 18 years, decrease in eGFR to < 35 ml/min per 1.73 m^2	< 0.3 ml/kg/h for 24 h or anuria for 12 h

Note:The urine output (UO) criteria are similar for the three classification systems. Stage is based on the worse of either SCr/GFR or UO criteria.

Prevalence of AKI

AKI is an increasingly common complication of critical illness, with some researches showing that as high as 1 in 5 adults and 1 in 3 children experiencing AKI per hospital admission [19]. The prevalence of severe AKI with a requirement for acute dialysis is in most studies reported to occur in 4% to 6% of ICU patients [20,21].

Risk assessment of AKI

The kidney is a fairly robust organ that can tolerate exposure to several insults without suffering significant structural or functional change. For this reason, any acute change in kidney function often indicates severe systemic derangement and predicts a poor prognosis. Risk for AKI is increased by exposure to factors that cause AKI or the presence of factors that increase susceptibility to AKI. Factors that determine susceptibility of the kidneys to injury include dehydration, certain demographic characteristics, genetic predispositions, chronic comorbidities, and treatment. It is the interaction between susceptibility and the type and extent of exposure to insults that determines the risk of occurrence of AKI. AKI in India is unique in etiology and predominantly includes tropical infections, diarrhea, animal venom, chemicals, pesticides and anaemia among previously healthy young individuals [22-25].

Management of AKI

AKI is common, harmful, and potentially treatable. Indeed, recognition of patients at risk for AKI, or with possible AKI but prior to clinical manifestations; is likely to result in better outcomes than treating only established AKI. The management of AKI is mainly supportive, with dialysis being indicated when other medical management fails to treat the complications [26]. Therefore, the primary treatment is focused on diminishing or treating potential etiology, contributing risk factors, ensuring sufficient volume status and perfusion pressure, avoiding drugs and procedures that might further worsen kidney function. Immediate treatment of life threatening complications of AKI; such as hyperkalemia, volume overload and metabolic acidosis is a must. Depending on AKI severity and complications; renal support with dialysis is frequently needed [10].

Mortality of AKI

AKI is associated with 1.4- to 3.2-fold increased in-hospital mortality compared with ICU patients without AKI, depending on the ICU study population and AKI severity [27,28]. ICU studies of the association between maximum AKI severity during ICU stay and mortality have shown the similar results [14,29,30].

Epidemiology of the Current Study

Udaipur and surrounding districts of Rajasthan is known as south Rajasthan. Population in this area is a mixed cohort of tribal, rural, hilly and semi urban. Pacific Medical College and Hospital is a tertiary care teaching hospital having two standard intensive care unit and a dialysis unit since its inception. We get patients either by direct visit or referred from small health centers/hospitals in the periphery. This study is the first of its kind to describe the etiology, clinical profile and in-hospital mortality based outcome of AKI patients from this region. We prospectively studied the clinical characteristics and outcome of 516 AKI patients at our hospital over a period of 5 years.

The aim of the present study is to examine the epidemiology and prognostic implication of adult AKI ICU patients within subgroups of acute medical diagnosis.

MATERIALS AND METHODS

Settings

This is a hospital based prospective study done over a period of 5 years (2015-2019) at Pacific Medical College and Hospital (PMCH), Udaipur. PMCH is tertiary care teaching hospital in Rajasthan, India.The study participants were hospitalized in medical intensive care unit (MICU) adults aged 12 years or above. The patients included in the study were explained in detail about the purpose of the study, and informed written consent was obtained. The study was approved by the institutional ethics committee. The inclusion and exclusion criteria were defined as follows:

INCLUSION CRITERIA

1. AKI as defined using the KDIGO criteria based on serum creatinine (increase in SCr 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 [26].

2. Presence of uremic signs or oliguria/anuria of recent onset (within 1 week) in patients admitted to medical ICU with acute medical conditions.
3. The KDIGO staging: S1, S2 and S3 for severity of AKI was done [10].

EXCLUSION CRITERIA

1. Pre existing kidney disease (serum creatinine >1.5 mg/dL with ultrasonography of
the abdomen suggestive of bilateral small kidneys/loss of corticomedullary differen
tiation), including CKD/ESRD or patients on maintenance dialysis.
2. Patients with acute on chronic kidney disease or renal failure attributed to CKD.
3. It was presumed that the patient had normal renal function if the serum creatinine was =/<1.5 mg/dL.

A large study within a population-based hospital setting with complete history of pre admission acute illness, comorbidity and complete follow-up is needed to quantify the impact of AKI on mortality, including differential impacts in subgroups of the heterogeneous ICU population. Such information would extend our current knowledge of the clinical course of AKI and identify potentially preventable pre and post-discharge deaths.

OBJECTIVES

We therefore conducted a cohort study to (1) examine the prevalence and clinical lab characteristics of AKI patients in medical ICU, (2) examine whether the influence of AKI varied in subgroups of ICU patients with different risk factors, comorbidities, primary hospital diagnosis, and treatment with mechanical ventilation, or vasopressors; (3) to compare outcome among AKI subgroups, including acute dialysis requiring AKI (D-AKI) and dialysis not requiring AKI (ND-AKI); and (4) its impact on mortality during the hospital course,

AKI patients

We identified all (N=516) adult AKI patients in medical ICU admission from January 2015 to December 2019 in the current study. We used the primary medical diagnosis for the current hospitalization to identify the cause for ICU admission and classify patients into different medical diseases category. We used the serum creatinine (SCr) level to define the AKI; based on the KDIGO definition. AKI was defined as any of the following :
Increase in serum creatinine by 0.3mg/dL or more within 48 hours
Or
Increase in serum creatinine to 1.5 times baseline or more within the last 7 days.

All other ICU patients were classified as without AKI. For practical purpose we used only serum creatinine (SCr) criteria and dropped out the urine output criteria as urine output is affected by many confounding factors and treatment strategy in the critically ill patients. Patients who had AKI on admission or developed AKI within 48 hours of admission were considered for the study purpose. All patients were subjected to a detailed history, clinical examination, laboratory investigations, and ultrasound imaging of the kidneys. A detailed patient performa for clinical and lab data was filled and updated daily for each patient till discharge or death. Patients were treated and managed as per medical ICU protocol including dialysis and other supportive care. Outcomes of the requirement of vasopressor drugs, ventilatory support, and treatment with dialysis; survival at discharge, and in-hospital mortality were studied.

AKI Subgroups

In this study the exposure AKI was defined and staged by change in serum creatinine SCr according to the creatinine criteria in KDIGO classifications. Baseline and highest measured SCr was used as the main lab data of all AKI subgroups. Highest SCr was defined as the highest value of SCr during the current admission or within seven days prior to the admission [31]. We recorded the highest value of measured SCr only for classification of AKI. The SCr based AKI severity stage according to the KDIGO criteria was as: AKI stage1: SCr 1.5-1.9 times baseline or increase to ≥0.3 mg/dL ; AKI stage2: SCr 2.0-2.9 times baseline and; AKI stage3: SCr 3.0 times baseline or increase to ≥4 mg/dL or initiation of renal replacement therapy (acute dialysis). AKI stage 3 was considered the most severe category. AKI patients were further divided into two groups; dialysis requiring AKI (D-AKI) patients and AKI patients without the requirement of dialysis (ND-AKI). The D-AKI and ND-AKI were compared to see the difference in clinical characteristics and risk factors associated with mortality between the two groups. Patients receiving chronic dialysis treatment, post kidney transplant,and CKD were excluded from the study because the exposure under study was kidney dysfunction.

MORTALITY

In this prospective study, the outcome was in-hospital death. This information was entered in patient study performa kept in MICU.

Clinical and Demographic Characteristics

The study population comprised 2440 adults admitted to MICU in Pacific Medical College and Hospital, Udaipur during the five-year prospective observation period. Out of this 516 (21.1%) patients had AKI. In D-AKI group there were 304 (58.91%) patients and in ND-AKI group it was 212 (41.09%). Table 2, shows the detailed clinical and demographic characteristics of the study patients.

Table 2: Primary acute medical diagnosis, clinical characteristics and outcome of 516 AKI MICU patients, PMCH, Udaipur, India; 2015-2019.

Clinical Characteristics	KDIGO stage1, N=92 (17.8%)	KDIGO stage2 , N=126 (24.4%)	KDIGO stage 3, N=298 (57.8%)	Total AKI, N=516 (100%)
Median Age (IQR,years)	23	31.5	74.5	54.81
12-30	33 (35.87)	17 (13.49)	22 (7.38)	72 (13.95)
31-50	19 (20.65)	28 (22.22)	65 (21.81)	112 (21.71)
51-70	15 (16.3)	37 (29.37)	95 (31.88)	147 (28.49)
71-90	25 (27.17)	44 (34.92)	116 (38.93)	185 (35.85)
Gender(Total no.)	92	126	298	516
Male	48 (52.17)	71 (56.35)	146 (48.99)	265 (51.36)
Female	44 (47.83)	55 (43.65)	152 (51.01)	251 (48.64)
Charlson comorbidity index (CCI) Score				
Low score, 0	48 (52.17)	56 (44.44)	204 (68.46)	308 (59.69)
Medium score, 1-2	24 (26.09)	36 (28.57)	52 (17.45)	112 (21.71)
High score, > 3	20 (21.74)	34 (26.98)	42 (14.09)	96 (18.6)
Primary diagnosis, Sepsis	21 (22.83)	30 (42.03)	111 (42.03)	162 (31.4)
Primary diagnosis, Tropical Infections				
Malaria	15 (16.3)	7 (5.56)	9 (3.02)	31 (6.01)
Dengue	9 (9.78)	4 (3.17)	2 (0.67)	15 (2.91)
Scrub Typhus	3 (3.26)	4 (3.17)	9 (3.02)	16 (3.1)
Primary diagnosis, GIT diseases				
Acute GE	3 (3.26)	12 (9.52)	14 (4.7)	29 (5.62)
Acute hepatic failure	0 (0)	1 (0.79)	4 (1.34)	5 (0.97)
Acute Pancreatitis	1 (1.09)	1 (0.79)	5 (1.68)	7 (1.36)
Primary diagnosis, Chemical Toxins				
Organophosphorous	4 (4.35)	3 (2.38)	1 (0.34)	8 (1.55)
Aluminium Phosphide	0 (0)	0 (0)	2 (0.67)	2 (0.39)
Sulfos	0 (0)	0 (0)	2 (0.67)	2 (0.39)
Biological toxin, Snake bite	3 (3.26)	6 (4.76)	13 (4.36)	22 (4.26)
Primary diagnosis, CAP	5 (5.43)	5 (3.97)	11 (3.69)	21 (4.07)
Primary diagnosis, Acute MI	9 (9.78)	12 (9.52)	12 (4.03)	33 (6.4)
Primary diagnosis, Acute Stroke	5 (5.43)	9 (7.14)	26 (8.72)	40 (7.75)
Primary diagnosis,Trauma	1 (1.09)	2 (1.59)	8 (2.68)	11 (2.13)
Post renal Obstructive Sepsis	13 (14.13)	28 (22.22)	68 (22.82)	109 (21.12)
Primary diagnosis, Others				
NMDA Encephalitis	0 (0)	1 (0.79)	0 (0)	1 (0.19)
SJ Syndrome(drug induced)	0 (0)	1 (0.79)	1 (0.34)	2 (0.39)
Chronic comorbid conditions	19 (20.65)	47 (37.3)	142 (47.65)	208 (40.31)
Anaemia	43 (46.74)	59 (46.83)	99 (33.22)	201 (38.95)
Blood transfusion required				

PCV	40 (43.48)	59 (46.83)	97 (32.55)	196 (37.98)
RDP/SDP	4 (4.35)	10 (7.94)	38 (12.75)	52 (10.08)
Plasma/FFP	1 (1.09)	6 (4.76)	29 (9.73)	36 (6.98)
ICU treatments				
Mechanical ventilation	8 (8.7)	17 (13.49)	47 (15.77)	72 (13.95)
Inotropes/ vasopressors	1 (1.09)	6 (4.76)	78 (26.17)	85 (16.47)
Intermittent Hemodialysis	0 (0)	6 (4.76)	298 (100)	304 (58.91)
LOS, (range 1-25 days)	7	14	12	11.73
OUT COME				
Survived	82 (89.13)	109 (86.51)	274 (91.95)	11.73465 (90.12)
In-Hospital Death	10 (10.87)	17 (13.49)	24 (8.05)	51 (9.88)

Results are presented as number (percent) of patients unless stated otherwise. AKI: acute kidney injury; ICU: intensive care unit; IQR: interquartile range; GE: gastroenteritis; CAP: community acquired pneumonia; MI: myocardial infarction.

Statistical Analysis

Patient characteristics, including risk factors acute and chronic both, preexisting comorbidity, primary diagnosis and other information from the current hospitalization, were tabulated by KDIGO stage classification. We followed patients from ICU admission until discharge or death. We computed 95% confidence interval (95% CI) during the MICU stay period for age, gender, primary diagnosis, to compute mortality and estimate cumulative mortality. This was found appropriate in view of small numbers for calculations. To examine potentially differing effects of AKI on mortality in subgroups of patients, we stratified the analyses by age groups, etiology, acute risk factors, chronic comorbidity, primary hospital diagnosis, and treatment with mechanical ventilation, vasopressors or dialysis [32]. Finally in these subgroup analyses we combined patients with any degree of AKI into two groups based on requirement of acute dialysis. Outcome based detailed comparison of mortality and associated characteristics were done among the subgroups.

RESULTS

Descriptive data

Table 2 data shows that maximum patients (57.8%) were in KDIGO Stage3 while KDIGO Stage 1 and 2 had 17.8% and 24.4% respectively. Median age was 54.81 years, while 35.9% of patients were aged 71-90 years, and 51.4% patients were male. Average length of ICU stay (LOS) was 11.73 days (interquartile range 1-25 days). We obtained data on preexisting comorbidity (chronic risk factors) based on inpatient and outpatient diagnosis before the current hospitalization and used these to compute the Charlson Comorbidity Index (CCI) scores [33]. Patients were categorized as having low (score = 0), medium (score 1 to 2) and high (score ≥ 3) levels of comorbidity [34,35]. Kidney diseases were excluded from the CCI and addressed separately because the exposure under study was kidney dysfunction. For the same, CKD was excluded from covariate, defined as an estimated GFR (eGFR) below 60 ml/min per 1.73 m2 using the four-variable MDRD equation (stage 3 or higher CKD as per National Kidney Foundation guidelines) [36].

Table 3: Risk factors associated with AKI (N =516).

	Acute risk factors	No. (%)	Chronic Comorbidity	No. (%
1	Hypovolemia	97 (18.8)	DM	88 (17.0)
2	Acute hepatic derangement, HRS	33 (6.4)	HTN	52 (10.0)
3	post renal (obstructive) urosepsis	74 (14.3)	Stable CAD	17 (3.3)
4	Nephrotoxic drugs	2 (0.4)	CLD	11 (2.1)
5	DIC	22 (4.3)	COPD	17 (3.3)
6	Acute LVF (LVEF <35 %)/AMI	12 (2.3)	Cancer	9 (1.7)
7	Encephalopathy	14 (2.7)	Autoimmune diseases	4 (0.8)
8	Acute glomerulonephritis (AGN)	12 (2.3)	PVD(DVT+PAD)	10 (1.9)

HRS: hepatorenal syndrome.

The most common diagnosis was sepsis (31.4%), post renal obstuctive urosepsis (21.1%), tropical infectious diseases (most common malaria) (12.0%), acute stroke (7.8%), acute MI (6.4%), acute gastroenteritis (5.6%), snake bite envenomation (4.3%); and CAP (4.0%).Younger patients had less preexisting comorbidity, shorter ICU stay and less mortality as compared with older patients. Snakebite was the only biological toxin leading to AKI. Anaemia was prevalent (38.9%) comorbidity and severe anaemia was common in severe AKI and D-AKI patients. Overall 37.9% AKI patients required blood transfusion, while platelets transfusion was required in 10.0% of the patients. Most (73.0%) of the platelets were required in AKI stage 3 patients.

Table 4: Main Clinical Symptoms & Signs on admission, AKI Patients (N=516).

	Clinical characteristics	No.	%
1	Fever	115	22.3
2	Oliguria	226	43.8
3	Vomiting	128	24.8
4	Diarrhoea	32	6.2
5	Breathlessness	88	17.0
6	Abdominal Pain	72	14.0
7	Edema	145	28.1
8	Jaundice	66	12.8
9	Hypotension (SBP < 90mmHg)	86	16.7
10	Coma/Decreased Sensorium	53	10.3

One patient had NMDA (N-Methyl D-Aspartate) autoimmune encephalitis who required dialysis in the form of plasmapharesis.

Table 5: Indications for Acute Dialysis (N =304).

	Indication type	No.	%
1	Refractory fluid overload	110	36.2
2	Uremic signs	106	35.2
3	Hyperkalemia	115	38.2
4	Metabolic acidosis	106	35.2
5	Oliguria, Anuria	224	75.0
6	Sepsis	98	32.3
7	Trauma	13	4.4

Prognostic Outcomes and In-Hospital Mortality

Out of 516 AKI patients, 304 (58.91%) required dialysis while 212 (41.08%) did not required dialysis. The overall AKI mortality was 9.9% (95% confidence interval (CI) 7% to 12%) while 465 (90.1%) patients survived. AKI subgroup mortality was 10.9 % (95% CI 5 % to 17 %) for the KDIGO stage1; 13.5% (95% CI 8 % to 19 %) for the KDIGO stage2; and 8.1% (95% CI 5% to 11%) for the KDIGO stage3. In our study, 47.0% of patients who died was in AKI KDIGO Stage3; but it was due to more number of patients were by default recruited in this subgroup (table 2). The corrected mortality in stage 3 was 8.1% only. As expected D-AKI patients were more often required mechanical ventilation 16.5 % and vasopressors 26.6 % as compared to ND-AKI patients 10.4%, and 1.9 % respectively (table 2, 6). The mean SCr and haemoglobin of AKI was 3.37 mg/dl and 8.7 gm/dl respectively.

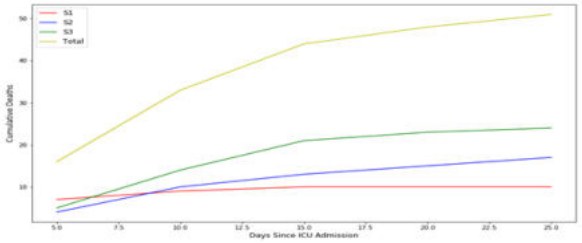

Figure 3: Cumulative in-hospital mortality by AKI stage; PMCH, Udaipur 2015-2019.

Figure 3 shows that maximum number of deaths in KDIGO stage1 were in the first five days compared to KDIGO stage2 and 3; where the parallel rise of deaths found from day 7 to day 10 of medical ICU admission.

SUBGROUPANALYSIS

Table 6 shows the in-hospital mortality comparison between the two groups. Acute dialysis required AKI (D-AKI) group was compared with AKI without requirement of acute dialysis (ND-AKI) group. The relative impact of D-AKI was most pronounced in patients aged 71 to

90 years; the mortality of patients in this subgroup was 13.6%, compared to 4.5% for patients with any degree of D-AKI in 31-50 years; and 8.3% in 12-30 years. The relative impact of AKI was also more pronounced among chemical toxins (Sulfos,Aluminium phosphide) 100%; and among acute myocardial infarction 15.4%, with 95% CI of 4% to 35%. We had two patients each of Sulfos poisoning and Aluminium phosphide poisoning; these 4 patients had 100% in-hospital mortality as there is no specific antidote available. Patients with low CCI scores had lower mortality of 5.8%, with 95% CI of 3% to 9% due to a low baseline hazards compared with high CCI score's mortality 17.8% with 95% CI of 7% to 29%. By diagnostic category, patients with a primary diagnosis of sepsis in ND-AKI had 20% mortality with 95% CI of 9% to 31% compared D-AKI mortality of 9.8% with 95% CI of 4% to 15%. In D-AKI group lowest mortality was associated with tropical infections and highest mortality with GIT (including liver) diseases; 5% (95% CI 5-15%) and 16.7% (95% CI 2-32%) respectively. Interestingly in ND-AKI group also, tropical infections had lowest mortality (2.4%). The association between AKI and mortality was also evident in patients treated with mechanical ventilation 20% (95% CI 9% to 31%) and vasopressors 19.7% (95% CI 11% to 28%) in D-AKI patients but was more pronounced in ND-AKI patients with 63% (95% CI 44-84%) and 100% (95% CI 100%) respectively. The overall most common cause of death in AKI patients was ARDS/MODS (37.3%); followed by septic shock (29.4%) and cardiogenic shock (21.6%). Liver cirrhosis was responsible for the remaining 9.8%. One patient died due to sudden cardiac death. In cause of death category, maximum number was associated with ARDS/MODS among both D-AKI and ND-AKI group; 42% (95% CI 23-61%) and 32% (95% CI 14-50%) respectively. As compared to the survival group, the mean hemoglobin was significantly lower (<6.0 gm/dl) in patients who died. Hypoalbuminemia was also found to be an independent risk factor for AKI and for mortality in patients who developed AKI [37]. Overall mortality in D-AKI group was 8.6% (95% CI 5 % to 12 %) compared to the mortality in ND-AKI group 11.8% (95% CI 7 % to 16 %.

Table 6: In-hospital subgroup mortality comparison among ND-AKI and D-AKI deaths (N=51).
CCI Score: Charlson comorbidity index score,

Category	Patient Mortality Characteristics	ND_AKI(N=25)		D_AKI (N=26)		Correlation coefficient
		Total (death)	Cumulative mortality % (95% CI)	Total (death)	Cumulative mortality %(95% CI)	
Overall AKI	Overall	212(25)	11.79%(0.07-0.16)	304(26)	8.55%(0.05-0.12)	1
Age group, years	12-30	48(4)	8.33%(0.01-0.16)	24(2)	8.33%(-0.03-0.19)	1
Age group, years	31-50	46(5)	10.87%(0.02-0.20)	66(3)	4.55%(-0.00-0.10)	1
Age group, years	51-70	50(7)	14.00%(0.04-0.24)	97(5)	5.15%(0.01-0.10)	1
Age group, years	71-90	68(9)	13.24%(0.05-0.21)	117(16)	13.68%(0.07-0.20)	1
CCI Score, Low	Score 0	103(6)	5.83%(0.01-0.10)	205(12)	5.85%(0.03-0.09)	1
CCI Score, Medium	Score 1-2	58(9)	15.52%(0.06-0.25)	54(6)	11.11%(0.03-0.19)	1
CCI Score, High	Score >3	51(10)	19.61%(0.09-0.31)	45(8)	17.78%(0.07-0.29)	1
Primary Diagnosis, Total	A. Sepsis	50(10)	20.00%(0.09-0.31)	112(11)	9.82%(0.04-0.15)	1
Primary Diagnosis, Total	B.Tropical Infections	42(1)	2.38%(-0.02-0.07)	20(1)	5.00%(-0.05-0.15)	1
Primary Diagnosis, Total	C. GIT Diseases	17(1)	5.88%(-0.05-0.17)	24(4)	16.67%(0.02-0.32)	1
Primary Diagnosis, Total	D.Toxins(chemical, biological)	15(2)	13.33%(-0.04-0.31)	19(2)	10.53%(-0.03-0.24)	1
Primary Diagnosis, Total	E. CAP	10(1)	10.00%(-0.09-0.29)	11(1)	9.09%(-0.08-0.26)	1
Primary Diagnosis, Total	F. Acute MI	20(2)	10.00%(-0.03-0.23)	13(2)	15.38%(-0.04-0.35)	1
Primary Diagnosis, Total	G. Acute Stroke	14(2)	14.29%(-0.04-0.33)	26(2)	7.69%(-0.03-0.18)	1
Primary Diagnosis, Total	H. Postrenal Obstructive Urosepsis	39(5)	12.82%(0.02-0.23)	70(2)	2.86%(-0.01-0.07)	1
Primary Diagnosis, Total	I. Others	5(1)	20.00%(-0.15-0.55)	9(1)	11.11%(-0.09-0.32)	1
Critical care treatment	A. Mechanical Ventilator use	22(14)	63.64%(0.44-0.84)	50(10)	20.00%(0.09-0.31)	1
Critical care treatment	B.Vasopressures support	4(4)	100.00%(1.00-1.00)	81(16)	19.75%(0.11-0.28)	1
Cause of Death, Total	Cause of Death, Total	25(25)	100.00%(1.00-1.00)	26(26)	100.00%(1.00-1.00)	1
Cause of Death, Total	A. ARDS & MODS	25(8)	32.00%(0.14-0.50)	26(11)	42.31%(0.23-0.61)	1
Cause of Death, Total	B. Septic Shock	25(7)	28.00%(0.10-0.46)	26(8)	30.77%(0.13-0.49)	1
Cause of Death, Total	C. Cardiogenic Shock	25(7)	28.00%(0.10-0.46)	26(4)	15.38%(0.02-0.29)	1
Cause of Death, Total	D. Liver Cirrhosis	25(2)	8.00%(-0.03-0.19)	26(3)	11.54%(-0.01-0.24)	1
Cause of Death, Total	E. Sudden Cardiac Death	25(1)	4.00%(-0.04-0.12)	26(0)	0.00%(0.00-0.00)	1

Sensitivity analysis

The associations between AKI and mortality were 10.87% (95% CI 5% to 17%) for the AKI-stage1, 13.49% (95% CI 8% to 19%) for the AKI-stage2 and 8.05% (95% CI 5% to 11%) for the AKI-stage3. The associations between AKI and mortality was more pronounced in AKI stage2 patients; may be due to worsening of AKI during the MICU stay. The in-hospital overall mortality of AKI patients was 9.9%. Further, Mortality in D-AKI group was 8.6% as compared to ND-AKI mortality of 11.8%.

DISCUSSION

In this prospective study conducted within a hospital based medical ICU setting cohort, we found that 21.1% of MICU patients had AKI during the hospital admission. We have studied and analyzed AKI patients's detailed clinical characteristics including primary diagnosis, risk factors, indication for acute dialysis, treatment, complications and survival or death.

Our study extends current knowledge by providing information on clinical profile, outcome and mortality of AKI; and also by examining the differential impact of AKI on mortality in sub groups of the ICU population in a hospital-based setting in Rajasthan, India. The current study is the only study from this part of India to examine clinical characteristics along with in-hospital mortality in medical diseases associated AKI based on the KDIGO AKI severity criteria; and also, to

compare the mortality among subgroups; S1, S2 and S3 along with acute dialysis requiring AKI (D-AKI) and AKI without the requirement of acute dialysis (ND-AKI).

Existing studies

Previous studies reported a higher prevalence of RIFLE-defined AKI at the time of ICU admission (22% to 36%) compared to our findings[38]. This may stem from heterogeneity in study cohorts, difference in RIFLE versus KDIGO criteria and from estimation of baseline creatinine by assuming GFR of 75 ml/min in cohorts including patients with CKD, which may overestimate the prevalence of AKI [39-41]. In accordance with our findings of increased short term mortality, a study from north India using KDIGO criteria for AKI found that 23.3% of AKI patients required dialysis and AKI mortality was 8.7% [26]. Five recent large studies with between 5,000 and 120,000 ICU patients all reported increased in-hospital mortality among patients with RIFLE-defined AKI at ICU admission or during an ICU stay, compared with ICU patients without AKI [14,42]. In our study, all the patients were having AKI related to medical etiology only as per study inclusion criteria. Previous studies have shown that medical, surgical and obstetrical causes accounted for 77.5%–87.6%, 8.3%–8.9%, and 3.4%–14.2% cases, respectively [22,43].

Sepsis is the most common cause of AKI in critically ill patients [44,45]. In our study also it was a major (31.4%) cause of AKI. Malaria, dengue and scrub typhus are important causes of acute febrile illnesses in the Indian subcontinent, and these should be part of the differential diagnosis of acute febrile illness with AKI [46-48]. Scrub typhus leading to AKI is thought to be a consequence of multiorgan dysfunction secondary to sepsis.The AKI is frequent, ranging from 20% to up to 60% [49,50]. Scrub typhus was the cause of 9.9% sepsis-associated AKI in the sepsis subgroup AKI in the present study.

Acute gastroenteritis (AGE) and pancreatitis was the cause of AKI in 7.0% of the patients. Among subgroups half of the AGE patients were from S3 stage while only one tenth were from S1 stage. The difference in the incidence of AKI secondary to diarrheal illness could be due to social factors or improvement in nutrition or hygiene, patient education in oral re-hydration and health services. Similarly, a significant decline in diarrhea related AKI has been reported from India by Prakash et al. [23]. AKI is one of the most common complications in patients with severe acute pancreatitis. 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 pressure due to abdominal compartment syndrome, intraabdominal hypertension or hypovolemia [51].

Community acquired pneumonia (CAP) and acute exacerbation of chronic obstructive pulmonary disease (COPD) leading to AKI in our study was 4.1% only. Murugan et al reported AKI in 34% of patients with CAP; and AKI was found to be common in even non-severe categories of CAP [52]. This difference may be due to difference in comorbidities,geographical and socioeconomic factors. In previous studies, it was also found that AKI is common in CAP and was observed in one-quarter of patients who had an uncomplicated course of pneumonia [53]. Sarah Paterson et al found that there is correlation between severity of CAP and presence of AKI. Patients admitted with a greater severity of CAP are more likely to have concurrent AKI on presentation and are more likely to die from the combination. In their study the overall 30 day mortality was 38% and the mean length of stay (LOS) for surviving patients was 10.5 days. It was observed that CAP associated with AKI presents a higher risk of mortality and increased LOS, thus early recognition and optimal management of both should be emphasized in order to improve clinical outcomes [54].

Five (1%) patients developed AKI secondary to acute hepatic failure; among these 80% had severe AKI(S3) and none had mild AKI(S1). Out of these, one patient had acute fulminant hepatic failure with DIC due to aluminium phosphide poisoning; a thirteen year old girl. In one patient acute viral hepatitis B led to decompensation of his chronic alcoholic liver disease leading to AKI. In two patients, non fulminant form of viral hepatitis B and E each was associated with AKI. The patient with viral hepatitis E had intravascular hemolysis secondary to G6PD deficiency. G6PD deficiency should be suspected in patients with acute viral hepatitis E with marked bilirubinemia and anemia [55]. However, AKI in acute hepatitis E can occur even in the absence of G6PD deficiency due to hyper-bilirubinemia and retained biliary nephrotoxic substances along with a possible direct toxicity of the virus [56]. None of these patients survived.

Acute stroke and acute myocardial infarction (AMI) was the primary diagnosis in 8.8% and 6.8% respectively of AKI patients. After a stroke, neurological deficit leading to dysphasia and physical disability, physiological effects including changes in blood pressure and cerebral salt wasting, as well as radiological investigations and treatment; can all potentially contribute to the development of AKI. Furthermore, older, comorbid patients are at greatest risk of AKI. Mortality in stroke patients who develop acute kidney injury is significantly increased; strategies to prevent AKI in stroke patients could therefore be of great importance [57]. In a Chinese study approximately 26.0% of patients of AMI developed AKI, and the development of AKI was strongly correlated with in-hospital mortality. The risk factors for AKI in patients with AMI mainly were age, hypertension, Killip's class ≥3, extensive anterior myocardial infarction, use of furosemide and non-use of ACEI/ ARB [58].

In our study 59.1% patients with snake bite venom-induced AKI were KDIGO AKI stage3 and required dialysis (D-AKI). There was no mortality in this group. Snake bite is an important cause of community acquired AKI in tropical countries. About 12%– 30% of patients bitten by venomous snakes; primarily vipers develop AKI. Hemorrhage, hypotension, DIC, intravascular hemolysis, and rhabdomyolysis are main pathophysiology for the development of AKI. Enzymatic activities of snake venom account for direct nephrotoxicity. Immunologic mechanism plays a minor role. In other studies mortality in snake bite-induced AKI is 1%–20% [59]. 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 [60].

Obstructions distal to the collecting system, such as cervical cancer, nephrolithiasis, prostatic hypertrophy or operative injury, represent the most common post renal causes of AKI. Urosepsis was major cause of sepsis- associated AKI in our study accounting for 24.9% patients of which 3% was secondary to carcinoma of cervix. A study from India reported UTI to be the most common source of AKI associated sepsis in critically ill patients [61,62]. UTI may cause sudden deterioration in renal function. Further, hypovolemia, hypotension, sepsis, the use of nephrotoxic drugs, contrast media and other urinary obstruction are AKI risk factors in UTI patients [63,64].

As all the patients in our study were from acute medical diagnosis, doing renal biopsy may further risks AKI complications in critically ill patients, so we avoided renal biopsy; although the renal biopsy is the current gold standard for acute glomerulonephritis (AGN) to diagnose underlying medical disease. The spectrum of glomerulonephritis presenting as AKI also varies depending on many factors, such as age, sex, race and region of the world, as well as the biopsy policies. Although our understanding of the causes of AGN is still at a basic level, inflammation is thought to be autoimmune mediated and involve both cellular and humoral immune systems. Whatever the initial events, common inflammatory pathways follow with activation of the coagulation and complement cascades and production of proinflammatory cytokines.The treatment of AGN falls into two categories. Supportive treatment such as blood pressure control and dialysis is immediate and frequently life saving but does not attempt to reverse the underlying pathology [65]. Though difficult to accurately diagnose AGN through clinical means but it was found to be quite reasonable method. We diagnosed AGN clinically when there was an acute onset of oliguria followed by body swelling, with new onset hypertension, glomerular haematuria and some degree of proteinuria. In the current study AGN was a risk of AKI in only 2.3% of patients; as compared to 9.3% reported in a previous study from India [23].

In the current study, only two patients (0.4%) developed AKI secondary to drug associated hypersensitivity. Both the patient had Stevens- Johnson Syndrome (SJS). In one patient the cause was Amoxycillin Clavulanic acid combination (Augmentin) while in other it was diclofenac sodium (Voveran). Both the patient came to our hospital after development of skin necrosis and oliguria; they required dialysis and completely recovered with supportive treatment. AKI is a common complication in an SJS/TEN and is an independent risk factor for mortality in patients with SJS/TEN[66]. We did not had any patient of NSAIDs induced direct nephrotoxicity.

Risk, Complications and Outcome of AKI subgroups

In our study, life threatening risk factors warranted for acute dialysis were oliguria (75%), hyperkalemia (38.2%), multiorgan failure with sepsis(37.3%), fluid overload (36.2%) and metabolic acidosis (35.2%) (table 5). In the current study, we found that sepsis, acute hepatic failure, acute myocardial infarction, chemical-biological toxins and

acute stroke related etiologies of AKI were associated with significant high in-hospital mortality of 13.0%, 12.2%, 12.1%, 11.8% and 10.0% respectively. In acute dialysis requiring AKI (D-AKI) group highest mortality was associated with GIT diseases including acute hepatic failure (16.7%) and acute MI (15.4%); compared to dialysis not requiring AKI (ND-AKI) group 5.9% and 10.0% respectively. Notably in ND-AKI group, sepsis and acute stroke were associated with high mortality; 20.0% and 14.3% as compared to 13.0% and 10.0% respectively in D-AKI group. Similarly, the proportion of anemia (32.6%), need for ventilator support (26.4%) and the requirement of vasopressors (16.4%) was significantly higher in D-AKI group as compared to ND-AKI group (table 5). AKI at ICU admission was associated with a one and half fold increased in-hospital mortality for patients in the AKI-stage1 and the AKI-stage3 groups and two fold increased mortality in the AKI-stage2 group.The presence of anemia, use vasopressor drugs, and requirement of ventilator support were independent predictive factors for in-hospital mortality in both the groups. A similar association of increased mortality with above factors was also observed by Kaul et al.[22].

In the current study the relative impact of AKI on mortality was most pronounced among 71-90 years age group who had acute hepatic failure or acute cardiac failure. In contrast to the high mortality associated with AKI in developed nations, AKI mortality is lower (10%–40%) in developing countries because primarily AKI caused by a single disease rather than multiple etiology. In developing countries, 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 [67]. According to KDIGO online supplement (2012); in a meta-analysis of 48 studies, 12 incident all-cause mortality was 8.9 deaths per 100 patient-years following a single episode of AKI, compared to 4.3 deaths per 100 patient-years in controls (rate ratio 2.59; 95% CI 1.97 to 3.42). The AKI was associated independently with mortality risk in six of six studies that performed multivariate adjustment (adjusted rate ratio, 1.6-3.9) [68].

Early diagnosis and treatment of complications of AKI are of utmost importance The most dreadful complications of AKI which requires urgent critical, supportive treatment measures are hyperkalemia, volume overload, metabolic acidosis, encephalopathy, thrombocytopathy-DIC, severe anaemia (Hb <6.0 gm/dl), decreased immune response, myopathy and pleural effusion. Except anaemia all other complications requires RRT in the form of dialysis along with other supportive treatment measures [69]. Evaluation and treatment of the volume status by adequate history taking, clinical examination, and laboratory data interpretation is certainly the most important single measure to prevent the development of AKI complications and mortality.

In the current study ND-AKI group had significantly high mortality compared to D-AKI group. We found that it was primarily because in ND-AKI group proportions of stage2 AKI was more and these (stage2) patients had complications similar to stage3 AKI; but as per KDIGO criteria stage2 is not an indication for acute dialysis; although we had six patients who required dialysis. All of these six patients were survived. In our study, low threshold and early initiation of dialysis was found to be significantly effective in reversing life threatening complications and decreased in-hospital mortality of AKI. Larger studies are required to find the significance of these results, which may help in revising the criteria for dialysis in AKI patients.

We found that many causes of AKI and its complications are potentially preventable and reversible. Early use of anti snake venom at primary health centers, timely referral to a higher center having a standard ICU and dialysis facility; low threshold for initiation of dialysis and use of ventilator support may improve AKI outcomes. In conclusion, early fluid resuscitation, effective anti-infective treatment, appropriate antidotes, use of mechanical ventilator support, vasopressors and early dialysis are the pivotal treatments to improve AKI outcomes.

Summary, Strengths and limitations

Our study described the etiological, laboratory spectrum; and outcome of the medical diseases associated AKI; among hospitalized ICU adults at a tertiary care hospital in South Rajasthan. This unique spectrum represents the community acquired AKI from rural areas. Results from this study may help to clarify the epidemiology and outcome of AKI in India.

The main strengths of our study include its duration, well-defined study population, comprehensive clinical and laboratory data including baseline serum creatinine and complete follow-up till discharge or death; and outcome based comparison among dialysis requiring AKI and dialysis not requiring AKI groups. The impact of AKI on mortality was evident in subgroups of ICU patients treated with mechanical ventilation, vasopressors and acute dialysis, which may be indicators of more severe illness.

However, our study has certain limitations; and these should be considered when interpreting our results. First, we used clinical and lab data to assess only the medical etiology AKI patients; surgical AKI patients were excluded. Second, as our routine data did not include information about urine output we could not utilize urine criteria in the KDIGO classification of AKI. However, urine output criteria are affected by diuretics, which are commonly used in ICU patients. Third, despite adjustment for potential confounders, we cannot rule out unmeasured and residual confounding. Finally, long term outcome could not be studied in our patients due to no complete data was available, on post discharge follow up at the time of writing of this research manuscript.

Although, our study describes very relevant information on adult AKI in-hospital mortality at a tertiary care referral ICU in India; however larger studies are required to interpret the true incidence of in-hospital AKI mortality.

CONCLUSIONS

In this hospital based prospective study, clinical profile of AKI varied from different etiologies and risk factors pertaining to geographical and tropical differences. The in-hospital mortality of adult AKI was 9.9%. Any degree of AKI at medical ICU admission was associated with increased in-hospital mortality and the association was found in all the subgroups of AKI stages. The high mortality in KDIGO stage2 and ND-AKI subgroups was found to be associated with worsening of complications of AKI, which potentially could have been reversed with early initiation of dialysis; although larger studies are required to find the significance of these results; which may form the basis for the revision of dialysis criteria in adult AKI patients.

Key messages

The increased risk of development of community acquired AKI was evident in many acute medical diseases; mainly in sepsis, tropical infections, acute MI, acute stroke, acute hepatic failure, pneumonia and toxins.

The association was evident regardless of age, gender, acute risk factors, preexisting comorbidity, and diagnostic category.

The relative in-hospital AKI mortality was higher in sepsis, acute MI, advanced age (71-90 years), preexisting multiple comorbidities, chemical toxins, severe anaemia and liver diseases patients.

Abbreviations

AKI: acute kidney injury; AKD: acute kidney diseases and disorders; CKD: chronic kidney disease; SCr: serum creatinine; GFR: glomerular filtration rate; RIFLE: risk, injury, failure, loss of kidney function, and end stage kidney disease; AKIN: acute kidney network; KDIGO: kidney disease improving global outcomes; D-AKI: dialysis requiring AKI; ND-AKI: dialysis not requiring AKI; CCI: Charlson comorbidity index; CI: confidence interval; HR: hazard ratio; Hb: Haemoglobin; MI: myocardial infarction; LVF: left ventricular failure; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease,; ASV: anti snake venom.

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Declarations

Ethics approval and consent to participate

The study was approved by the institutional ethics committee and written informed consent was taken from the participants.

Consent for publication

All the authors gave consent for the publication.Availability of data and material

Authors' contributions

JV and PP conceived the study idea, designed the study and collected the data. JV, PP, KRS and SKV reviewed the literature and analyzed the data. All authors interpreted the findings. JV wrote the first draft, and all authors critically reviewed and edited the manuscript and approved the final version.

Data availability

Data and relevant materials are available with corresponding author and can be obtained anytime on request.

Competing interests

The authors declare that they have no competing interests.

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REFERENCES:

1. Tanner G. Kidney Function. In: Rodney R, Tanner G, eds. Medical Physiology. 1st ed. Little, Brown and Company, 1995:417-445.
2. Levey AS, Eckardt KU, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005; 67: 2089-2100.
3. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group; KDIGO Clinical Practice Guideline for Acute Kidney Injury.Kidney Int Suppl. 2012; 2: 1-138.
4. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P: Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004, 8:R204-R212.
5. Srisawat N, Hoste EE, Kellum JA: Modern classification of acute kidney injury. Blood Purif 2010, 29:300-307.
6. Kidney International Supplements (2012) 2, 6; doi:10.1038/kisup.2012.6.
7. Murray PT, Devarajan P, Levey AS, et al. A framework and key research questions in AKI diagnosis and staging in different environments. Clin J Am Soc Nephrol 2008; 3: 864-868.
8. Murray PT, Le Gall JR, Dos Reis Miranda D, et al. Physiologic endpoints (efficacy) for acute renal failure studies. Curr Opin Crit Care 2002; 8: 519-525.
9. Joannidis M, Metnitz B, Bauer P, et al. Acute kidney injury in critically ill patients classifified by AKIN versus RIFLE using the SAPS 3 database. Intensive Care Med 2009; 35: 1692–1702.
10. Kellum JA, Lameire N, KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: A KDIGO summary (Part 1). Crit Care 2013;17:204.
11. Hoste EA, Clermont G, Kersten A, et al. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Crit Care 2006; 10: R73.
12. Bagshaw SM, George C, Dinu I, et al. A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. Nephrol Dial Transplant 2008; 23: 1203–1210.
13. Thakar CV, Christianson A, Freyberg R, et al. Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration study. Crit Care Med 2009; 37: 2552–2558.
14. Ostermann M, Chang RW. Acute kidney injury in the intensive care unit according to RIFLE. Crit Care Med 2007; 35: 1837–1843.
15. Ali T, Khan I, Simpson W, et al. Incidence and outcomes in acute kidney injury: acomprehensive population-based study. J Am Soc Nephrol 2007; 18: 1292–1298.
16. Amdur RL, Chawla LS, Amodeo S, et al. Outcomes following diagnosis of acute renal failure in U.S. veterans: focus on acute tubular necrosis. Kidney Int 2009; 76: 1089–1097.
17. Coca SG, Yusuf B, Shlipak MG, et al. Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta analysis. Am J Kidney Dis 2009; 53:961–973.
18. Wald R, Quinn RR, Luo J, et al. Chronic dialysis and death among survivors of acute kidney injury requiring dialysis. JAMA 2009; 302: 1179–1185.
19. Susantitaphong P, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, Koulouridis J, et al. World incidence of AKI: a meta-analysis. Clin J Am Soc Nephro. 2013; l8(1):1482–93.
20. Bagshaw SM, Laupland KB, Doig CJ, et al. Prognosis for long-term survival and renal recovery in critically ill patients with severe acute renal failure: a population-based study. Crit Care 2005;9:R700-9.
21. Metnitz PG, Krenn CG, Steltzer H, et al. Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients. Crit Care Med 2002;30:2051-8.
22. Kaul A, Sharma RK, Tripathi R, et al. Spectrum of community-acquired acute kidney injury in India: A retrospective study. Saudi J Kidney Dis Transpl 2012;23:619-28.
23. Prakash J, Singh TB, Ghosh B, et al. Changing epidemiology of community-acquired acute kidney injury in developing countries: Analysis of 2405 cases in 26 years from eastern India. Clin Kidney J 2013;6:150-5.
24. Vikrant S, Gupta D. Epidemiology and Outcome of Acute Kidney Injury from a Tertiary Care Hospital in India; Saudi J Kidney Dis Transpl 2018;29(4):956-966.
25. Ibrahim et al; Clinical profile and outcome of patients with acute kidney injury requiring dialysis; an experience from a hemodialysis unit in a developing country. BMC Nephrology (2016) 17:91.
26. Hoste EA, Kellum JA. Acute renal failure in the critically ill: impact on morbidity and mortality. Contrib Nephrol 2004; 144: 1–11.
27. Bagshaw SM, George C, Dinu I, Bellomo R: A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. Nephrol Dial Transplant 2008, 23:1203-1210.
28. Joannidis M, Metnitz B, Bauer P, Schusterschitz N, Moreno R, Druml W, Metnitz PG: Acute kidney injury in critically ill patients classified by AKIN versus RIFLE using the SAPS 3 database. Intensive Care Med 2009, 35:1692-1702.
29. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, Kellum JA: RIFLE criteria for acute kidney injury are associated with hospital mortality in critically illpatients: a cohort analysis. Crit Care 2006, 10:R73.
30. Clec'h C, Gonzalez F, Lautrette A, Nguile-Makao M, Garrouste-Orgeas Maïté, Jamali S, Golgran-Toledano D, Descorps-Declere A, Chemouni F, HamidfarRoy R, Azoulay E, Timsit JF: Multiple-center evaluation of mortality associated with acute kidney injury in critically ill patients: a competing risks analysis. Crit Care 2011, 15:R128.
31. Zavada J, Hoste E, Cartin-Ceba R, et al. A comparison of three methods to estimate baseline creatinine for RIFLE classification. Nephrol Dial Transplant 2010; 25: 3911–3918.
32. Rothman KJ: Measuring Interactions. Epidemiology: an introduction New York: Oxford University Press Inc.; 2002, 169-180.
33. Needham DM, Scales DC, Laupacis A, Pronovost PJ: A systematic review of the Charlson comorbidity index using Canadian administrative databases: a perspective on risk adjustment in critical care research. J Crit Care 2005, 20:12-19.
34. Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987, 40:373-383.
35. Thygesen SK, Christiansen CF, Christensen S, Lash TL, Sorensen HT: The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. BMC Med Res Methodol 2011, 11:83.
36. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G: National Kidney Foundation practice guidelines for chronic kidney disease:evaluation, classification, and stratification. Ann Intern Med 2003, 139:137-147.
37. Wiedermann CJ, Wiedermann W, Joannidis M. Hypoalbuminemia and acute kidney injury: a meta-analysis of observational clinical studies. Intensive Care Med 2010; 36: 1657-1665.
38. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, Kellum JA: RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Crit Care 2006, 10:R73.
39. Bagshaw SM, George C, Dinu I, Bellomo R: A multicentre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. Nephrol Dial Transplant 2008, 23:1203-1210.
40. Joannidis M, Metnitz B, Bauer P, Schusterschitz N, Moreno R, Druml W, Metnitz PG: Acute kidney injury in critically ill patients classified by AKIN versus RIFLE using the SAPS 3 database. Intensive Care Med 2009, 35:1692-1702.
41. Bagshaw SM, Uchino S, Cruz D, Bellomo R, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Oudemans-van Straaten HM, Ronco C, Kellum JA, Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators: A comparison of observed versus estimated baseline creatinine for determination of RIFLE class in patients with acute kidney injury. Nephrol Dial Transplant 2009, 24:2739-2744.
42. Clec'h C, Gonzalez F, Lautrette A, Nguile-Makao M, Garrouste-Orgeas Maïté, Jamali S,Golgran-Toledano D, Descorps-Declere A, Chemouni F, HamidfarRoy R, Azoulay E, Timsit JF: Multiple-center evaluation of mortality associated with acute kidney injury in critically ill patients: a competing risks analysis. Crit Care 2011, 15:R128.
43. Jayakumar M, Prabahar MR, Fernando EM, et al. Epidemiologic trend changes in acute renal failure – A tertiary center experience from South India. Ren Fail 2006;28:405-10.
44. Bagshaw SM, Uchino S, Bellomo R, et al. Septic acute kidney injury in critically ill patients: Clinical characteristics and outcomes. Clin J Am Soc Nephrol 2007;2:431-9.
45. Zarbock A, Gomez H, Kellum JA. Sepsisinduced acute kidney injury revisited: Pathophysiology,prevention and future therapies. Curr Opin Crit Care 2014;20:588-95.
46. Abdul Manan J, Ali H, Lal M. Acute renal failure associated with malaria. J Ayub Med Coll Abbottabad 2006; 18: 47-52.
47. Ittyachen AM, Krishnapillai TV, Nair MC*, et al.* Retrospective study of severe cases of leptospirosis admitted in the intensive care unit. J Postgrad Med 2007; 53: 232-235.
48. Barsoum R, Sitprija V. Renal involvement in tropical diseases. In: Schrier RW (ed). Diseases of the Kidney and UrinaryTract, 8th edn. Lippincott Williams & Wilkins: Philadelphia, PA, 2007, pp 2013-2070.
49. Schrier RW, Wang W. Acute renal failure and sepsis. N Engl J Med 2004; 351: 159-169.
50. Burdmann EA, Jha V. Acute kidney injury due to tropical infectious diseases and animal venoms: A tale of 2 continents. Kidney Int 2017;91:1033-46.
51. Petejova N, Martinek A. Acute kidney injury following acute pancreatitis: A review. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2013;157:105-13.
52. Murugan R, Karajala-Subramanyam V, Lee M, et al. Acute kidney injury in non-severe pneumonia is associated with an increased immune response and lower survival. Kidney Int 2010;77:527-35.
53. Neil N. Turner, Norbert Lameire, David J. Goldsmith : Oxford Textbook of Clinical Nephrology, chapter 43, 4th Edition; 2018.
54. Sarah Paterson, Alexandra Bramley, Jennifer Thornley, Rajesh Yadavilli: Community acquired pneumonia and co-existing acute kidney injury have poor clinical outcomes; European Respiratory Journal, 2016,48; PA2587.
55. Abid S, Khan AH. Severe hemolysis and renal failure in glucose-6-phosphate dehydrogenase deficient patients with hepatitis E. Am J Gastroenterol 2002;97:1544-7.
56. Vikrant S, Kumar S. Severe hyper bilirubinemia and acute renal failure associated with hepatitis E in a patient whose glucose-6- phosphate dehydrogenase levels were normal. Clin Exp Nephrol 2013;17:596-7.
57. Arnold et al.Incidence and impact on outcomes of acute kidney injury after a stroke: a systematic review and meta-analysis. BMC Nephrology,2018; 19:283.
58. Wang C, Pei YY, Ma YH, et al. Risk factors for acute kidney injury in patients with acute myocardial infarction. Chin Med J (Engl). 2019;132(14):1660–1665.
59. Jha V, Chugh KS. Community-acquired acute kidney injury in Asia. Semin Nephrol 2008; 28:330-47.
60. Kanjanabuch T, Sitprija V. Snakebite nephrotoxicity in Asia. Semin Nephrol 2008;28:363-72.
61. Eswarappa M, Gireesh MS, Ravi V, Kumar D, Dev G. Spectrum of acute kidney injury in critically ill patients: A single center study from South India. Indian J Nephrol 2014;24: 280-5.
62. Soares M, Salluh JI, Carvalho MS, et al. Prognosis of critically ill patients with cancer and acute renal dysfunction. J Clin Oncol 2006; 24: 4003-4010.
63. Kooman JP, Barendregt JN, van der Sande FM, van Suylen RJ. Acute pyelonephritis: A cause of acute renal failure? Neth J Med 2000; 57:185-9.
64. Nahar A, Akom M, Hanes D, Briglia A, Drachenberg CB, Weinman EJ, et al. Pyelonephritis and acute renal failure. Am J Med Sci 2004;328:121-3.
65. Vinen CS, Oliveira DBG: Acute glomerulonephritis; Postgraduate Medical Journal 2003; 79:206-213.
66. Lee TH, Lee CC, Ng CY, Chang MY, Chang SW, et al. (2018) The influence of acute kidney injury on the outcome of Stevens–Johnson syndrome and toxic epidermal necrolysis: The prognostic value of KDIGO staging. PLOS ONE 13(9): e0203642.
67. Yang L. Acute kidney injury in Asia. Kidney Dis (Basel) 2016;2:95-102.
68. KDIGO Clinical Practice Guideline For Acute Kidney Injury. Online Appendices A-F; March 2012, page: 80-81.
69. White IR, Royston P: Imputing missing covariate values for the Cox model. Stat Med 2009, 28:1982-1998.