Original Article

Acute Kidney Injury Management — 15 Year Experience at A Tertiary Care Teaching Hospital in South India

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Abstract

Background: There is paucity of published data from Andhra Pradesh, India regarding aetiology, clinical presentation, outcome and temporal trends in patients presenting with Acute Kidney Injury (AKI) requiring hospitalisation. Hence, this study is submitted.

Materials and Methods: We retrospectively reviewed the case records of 1734 AKI patients managed at Sri Venkateswara Institute of Medical Sciences (SVIMS), a tertiary care teaching hospital in Tirupati, Andhra Pradesh State, South-India from the year 2002 to 2016, a fifteen year study.

Results: There were 1734 patients of AKI included in this study (0.62%) from among total hospital admissions (n=2,81,805) during the study period; 1710 (98.6%) were having community acquired AKI (CAKI) and 24(1.4%) were having Hospital Acquired AKI (HAKI). Infectious etiology (77.9%, n=1351) was the most common cause of AKI. Their mean age was 49.92 ± 16.03 years; males were 1127 (65%). Majority of the cases of AKI occurred in monsoon season (38.5%, n=668). Oliguria at the time of hospitalization was present in 756 (43.6%) patients. Hemodialysis was required in 639 (36.9%) and peritoneal dialysis in 24 (1.4%) patients. Of the 1734 patients, 361 (20.8%) died, which accounted for 2.07% of total hospital deaths (n=17, 439) during study period. The survived patients were 1373 out of 1734 AKI patients (79.18%). Of the survived patients progression to Chronic Kidney Disease (CKD) was observed in 133 patients (9.6%). The AKI to CKD progression was noted in most of the patients who required dialysis (p value < 0.001), those with diabetes mellitus (p value < 0.001) and hypertension (p value < 0.001).

Conclusions: This study highlights the presentation of AKI as CAKI, HAKI and their outcomes, temporal and seasonal trends of AKI emphasizing the importance of infection as cause of AKI in monsoon and also the progression of AKI to CKD in the survived patients on follow up (9.6%).

Key words: Acute Kidney Injury, Management, South-India.

cute Kidney Injury (AKI), which was previously called as Acute Renal Failure (ARF), has been a problem of global concern affecting around 13.3 million subjects annually with mostly being reported from developing countries. AKI is defined as any of the following: Increase in serum creatinine by ≥ 0.3 mg/dl (≥ 26.5 imol/I) within 48 hours; or increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or Urine volume <0.5 ml/kg/h for 6 hours¹.

Received on : 06/01/2023 Accepted on : 23/07/2023

Editor's Comment :

- AKI continues to be a challenging problem in tropics.
- Infections especially during monsoon period present as tropical AKI is a significant burden.
- Timely referral to advanced centers with critical care supports help in reducing the morbidity, progression to CKD and mortality in these patients.

Even in terms of mortality, low and middle income countries has the highest burden with 1.4 million deaths out of 1.7 million deaths annually². In view of the alarming numbers of AKI, International Society of Nephrology (ISN) launched "0by25" initiative in 2013 with aim of eliminating preventable deaths from AKI by 2025³.

AKI in most parts of developing world remains under diagnosed. Aetiology, presentation, complications, management and outcome are quite different in developing countries as compared to developed world and it is particularly challenging to rely on global data regarding them. As the diagnosis of AKI depends on laboratory parameters rather than clinical symptoms,

How to cite this article: Acute Kidney Injury Management — 15 Year Experience at A Tertiary Care Teaching Hospital in South India. Vakkakula DR, Pradeep V, Mohan A, Vishnubhotla S. J Indian Med Assoc 2025; 123(8): 23-8.

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such that the spectrum of disease ranges from asymptomatic elevation of serum creatinine to oliguria which often occurs at a much later stage of disease. It is of special concern as major portion of cases remains undiagnosed at community level, which is much evident in low and middle income countries.

Aetiology of AKI varies by geography as well as with socioeconomic differences between different parts of world. In high income countries, acute tubular necrosis resulting from one or more insults such as sepsis, renal ischemia from shock, bleeding, toxic effects of drugs, radio-contrast agents and pigment injury from haemoglobin or myoglobin are predominant causes of AKI, mostly affecting elderly age population^{4,5}. In middle and low income countries, among rural areas aetiology of AKI is much different as infectious causes like acute gastroenteritis or tropical infections like malaria, dengue fever, leptospirosis, respiratory tract infections, native medication intake were most common, predominantly affecting young population. Venomous snake bite and traditional medication intake are among other causes in African and southeast Asian regions. Obstetric related renal injury although declining, contributes to AKI in low income countries. Other causes of pregnancy related AKI include postpartum haemorrhage and puerperal sepsis⁵⁻⁷.

Multiple factors leads to progression of AKI to Chronic Kidney Disease (CKD), which include presence of comorbidities, nature of the aetiology leading to AKI, ineffective timely management of the initial event leading to AKI, severity of the disease at the time of presentation to hospital and requirement of dialysis and elderly age⁸. Even with trivial causes like acute gastroenteritis without timely intervention, can lead to greater morbidity as well as mortality^{9,10}.

Sparse published data are available regarding aetiology, clinical presentation, outcome and temporal trends in patients presenting with AKI from the state of Andhra Pradesh. Hence the present study was done retrospectively to find aetiology, comorbidities, seasonal and temporal changes in the incidence of AKI, outcomes and factors leading to progression to Chronic Kidney Disease (CKD) for one and half decades in patients presenting with AKI at our tertiary care teaching hospital.

MATERIAL AND METHODS

We retrospectively reviewed the case records of

patients presenting with AKI to Sri Venkateswara Institute of Medical Sciences (SVIMS), a tertiary care teaching hospital in Tirupati, Andhra Pradesh State, Southern India from the year 2002 to 2016. The SVIMS caters to the a population of around seven hundred and fifty thousands¹¹ not only from Andhra Pradesh State, but also from the border areas of neighbouring four states of Tamil Nadu, Karnataka, Telangana and Orissa. The study was approved by the Institutional Ethics Committee. Hospitalised patients diagnosed to have AKI according to Risk, Injury, Failure, Loss of kidney function and End stage kidney disease (RIFLE), Acute Kidney Injury Network (AKIN) and Kidney Disease Improving Global Outcomes (KDIGO) criteria had been included in this study keeping in view of the study population belonging to a period of one and half decades during which time the diagnostic and the staging of AKI changed from RIFLE criteria to AKIN criteria to KDIGO criteria^{1,12,13}. Patients with known CKD prior to admission and patient records not containing required information were excluded.

Demographic, clinical and laboratory data for all participants were collected at the time of study inclusion. Demographic data included age, gender, seasons, date of admission and discharge. Clinical data included aetiology of AKI, presence of oliguria, comorbid diseases, use of nephrotoxic agents, treatment, complications due to AKI and outcome. Laboratory data included urine routine-microscopy, serumcreatinine level and ultrasonography of renal system.

The primary outcome studied was morbidity and mortality of AKI during the course of illness. Secondary outcome studied was progression to CKD. Further the study also included details related to type of AKI (Community or hospital acquired AKI), oliguric or non oliguric AKI patients and management based on dialysis requirement. During study evaluation, important entities such as seasonal variation, temporal trends, elderly age group, pregnancy related AKI were also considered.

Definition:

AKI definition and staging has been changing from time to time in the literature over the study period of 15 years. Initially it was RIFLE criteria (2004), followed by AKIN (2007) and latest being KDIGO (2012) and our patient population were staged accordingly appropriate to the time^{1,12,13}.

Patients with AKI at the time of admission were considered to have community acquired AKI (CAKI). Patients without AKI on admission who subsequently developed AKI during the hospitalization (≥48 hours after admission) were considered to have hospital acquired AKI (HAKI)¹⁴.

De novo CKD was defined per the KDIGO guidelines as the persistence of eGFR< 60 mL/min per 1.73 m² for atleast 3 months¹ from the time of AKI event or from the time of admission (in those without AKI). Oliguria is defined as reduction in urine output of <400 ml/24 hours¹⁵. Elderly people were taken as population ≥60 years of age¹⁶. As per India meteriological department - climate profile of India, four seasons were considered, ie, winter (January, February), Summer (March, April, May), Monsoon (June, July, August, September) and Postmonsoon (October, November, December)¹⁷. Urine was considered abnormal in our study if there is any presence of proteinuria, hematuria or presence of casts.

Comorbidities noted in the study were diabetes mellitus, hypertension, ischemic heart disease, heart failure, vascular disease, malignancy, cerebrovascular accident, liver disease and respiratory diseases.

Statistical Analysis:

Data were recorded on a pre-designed proforma and managed using Microsoft Excel worksheet (Microsoft Corp., Redmond, WA). All the entries were double checked for any possible error. Descriptive statistics for categorical variables were performed by computing the frequencies (percentages) in each category. For the quantitative variables, approximate normality of distribution was assessed. Variables following normal distribution were summarised by mean ± standard deviation; the remaining variables were summarised as median [interquartile range (IQR)]. Categorical variables were reported as percentages.

The association between two categorical variables were evaluated by Chi-square (χ^2) test or Fisher's exact test as appropriate. Student's 't'-test or Mann-Whitney U test, as appropriate, was used to compare continuous variables between the groups. Correlation was done between outcome (alive or dead)/CKD as the dependent parameters with other patient parameters like age, gender, aetiology, presence or absence of oliguria, urinalysis, USG abdomen and

treatment. "Worst case-scenario" analysis 18 was done wherein, the Discharged Against Medical Advice (DAMA) patients were considered to have died. Age was categorised as <60 years and ≥60 years. A two-tailed P-value of <0.05 was considered statistically significant.

The statistical software IBM Statistical Package for Social Sciences (Version 20, IBM Corp., Somers NY, USA); and MedCalc Version 19.1(MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org;2016) were used for statistical calculations.

RESULTS

In the duration of 15 years spanning from January, 2002 to June, 2016, 1734 patients satisfying inclusion criteria were considered for analysis. During this time the patients of AKI studied were 1734 among the total hospital admissions of 2,81,805, amounting to AKI incidence of 0.62%. Their mean age was 49.92 ± 16.03 years. There were 1127 (65%) males and 607 (35%) females. Of 1734 patients studied, 1710 (98.6%) were having Community Acquired AKI (CAKI) and 24(1.4%) were having hospital acquired AKI (HAKI). Gender predilection for females was observed in HAKI patients and this was statistically significant (n=14, 2.3%, p value= 0.02). Over the past one and half decade number of admissions in SVIMS with AKI is increasing with peak cases observed in 2010 (n=218) and 2014(n=207). Majority of the cases of AKI occurred in monsoon season (38.5%, n=668) followed by post monsoon (25.5%,n=442), summer (22.1%,n=384) and winter(13.8%,n=240) respectively. CAKI was more common in monsoon season (n=660) followed by post monsoon (n=432), summer (n=380) and winter (n=238). Almost similar trend was observed in HAKI ie, it was more common in post monsoon (n=10) followed by monsoon (n=8), summer (n=4) and winter (n=2).

Out of 1734 studied 756 (43.6%) patients presented with oliguria, out of which 482 (63.8%) were males and 274(36.2%) were females. 43.7% CAKI patients and 37.5% HAKI patients presented with oliguria. Of the 756 patients who presented with oliguria, 448 (59.26%) showed urine abnormality (p value< 0.001). Requirement of dialysis was significant in patients presented with oliguria (n=404, 60.9%, p value <0.001).

Infectious aetiology (77.9%, n=1351) was the most

common cause of AKI. 46 (2.7%) patients were using nephrotoxic agents such as NSAIDS (n=31,1.8%), native medication (n=12,0.7%), amphotericin B(n=1,0.1%), aminoglycosides (n=2,0.1%). Most common cause of AKI in oliguric patients were infectious diseases (75.3%, n=570) followed by toxic nephropathy (10.3%, n=78). Similarly in patients with AKI requiring dialysis infectious diseases (n=482, 72.7%) followed by toxic nephropathy (n=96, 14.4%) were found to be the most common causes. Aetiological details of AKI in the present study were shown in Table 1.

Comorbidities like diabetes mellitus and hypertension were present in 284 (16.4%) and 247(14.2%) patients

Table 1 — Aetiology of patients presenting with AKI				
Aetiology	No	(%)		
Infectious causes	1351	77.9		
Acute gastroenteritis	506	29.2		
UTI	129	7.4		
Leptospira	128	7.4		
Malaria	120	6.9		
Sepsis with MODS	111	6.4		
LRTI	94	5.4		
Pyelonephritis	89	5.1		
Cellulitis	69	4		
Pancreatitis	21	1.2		
Viral fever	21	1.2		
Cholecystitis	12	0.7		
Scrub typhus	7	0.4		
Spleenicabcess	6	0.3		
Liver abcess	6	0.3		
Filaria	2	0.1		
HIV(AN)	1	0.1		
Hydatid cyst	1	0.1		
Chest wall abcess	3	0.2		
Meningitis	2	0.1		
Peritonitis	7	0.4		
Gluteal abcess	5	0.3		
Scrotal abcess	4	0.2		
Renal related	153	8.8		
(A) Glomerulonephritic	24	1.4		
(B) Toxic nephropathy	129	7.4		
Snake bite	93	5.4		
Rhabdomyolysis	12	0.7		
Contrast induced nephropathy	5	0.3		
Scorpion sting	1	0.1		
Poisoning	10	0.6		
Transfusion related AKI	8	0.5		
Pregnancy related	50	2.9		
Puerpueral sepsis	36	2.1		
PPH	2	0.1		
Eclampsia	12	0.7		
Surgical causes	60	3.5		
Obstructive uropathy	34	2		
Prostectomy	7	0.4		
Femur fracture	4	0.2		
Obstructive jaundice	1	0.1		
GE bleed	2	0.1		
Unknown	120	6.9		

respectively. Among patients presenting with comorbidities CAKI was more significant than HAKI (n=532, 99.6%, p value =0.01). Among oliguric patients 101 (13.3%) had hypertension and 115(15.2%) had diabetes mellitus. Other comorbidities noted in this study were Chronic Liver Disease (CLD) in 27 patients, hypothyroidism in 23 patients, chronic obstructive pulmonary disease in 30 patients, old pulmonary tuberculosis in 10 patients, coronary artery disease in 47 patients, cerebrovascular accident in 31 patients, carcinoma in 21 patients, congestive heart failure in 17 patients, Systemic Lupus Erythematosis (SLE) in 2 patients and HIV in 2 patients.

Among AKI patients 639(36.9%) patients required hemodialysis, 24(1.4%) patients treated with peritoneal dialysis and 30(1.7 %) patients underwent urological interventions like Double J (DJ) stenting for obstructive uropathy. Of the 1734 patients studied, 663(38.2%) required dialysis out of this 424(64%) were males and 239(36%) were females. Among females requiring dialysis 37% (n=88) were in middle age group. In this study, it was observed that 38.3% (655 out of 1710) of CAKI and 33.3 % (8 out of 24) of HAKI patients required dialysis. Of the 1734 patients 1373 (79.2%) survived and 361(20.8%) died, which accounted for 2.07% of total hospital deaths (n=17,439) during study period. Mean age of patients in death group was 51.85±16.61. Death was more significant in HAKI (p value=0.001), in elderly people of age \geq 60 years (p value=0.009), in patients presented with oliguria (p value<0.001), in patients having hypertension(p value=0.01). Details were tabulated (Table 2).

Upon discharge patients were followed for 3 months. We noticed progression to CKD in 133(9.7%) subjects out of 1373 survived AKI patients. Eight patients (6%) progressed from AKI to CKD directly without a period of recovery in between (representing category E in RIFLE). Patients of AKI secondary to renal related diseases showed predilection to progression to CKD (p value=0.03).Progression to CKD from AKI was noted in elderly (p value<0.001), in oligurics (p value<0.001), those patients who required dialysis (15.7%, p value<0.001), those with diabetes mellitus (16.4%, p value<0.001) and hypertension (19%, p value <0.001). We also found a correlation between the presence of urinary abnormality with requirement of dialysis (n= 393, p value <0.001), progression to CKD (n= 97, p value< 0.001) and death (n= 194, p value < 0.001).

Table 2 — Comparison of characteristics between CAKI and HAKI **CAKI** HAKI P-value Age in years (Mean) 50.01±15.94 43.20±20.68 Gender: Male 1117 10 Female 0.029 593 14 Definition: Oliguria 747 9 Non-oliquria 963 15 0.680 Diabetes Mellitus: Present 284 0 0.023 Absent 24 1426 Hypertension: 247 O Present Absent 1463 24 0.039 Urine analysis: 10 Normal 941 Abnormal 769 14 0.218 Renal Ultrasonography: Normal 993 14 Abnormal 717 10 1.000 Treatment: Dialysis 655 8

CAKI = Community Acquired Acute Kidney Injury, HAKI = Hospital Acquired Acute Kidney Injury

1055

1361

349

16

12

12

0.678

0.001

Comparison of the results of the present study with previously published studies from other developed and developing countries is shown in Table 3¹⁹⁻²².

DISCUSSION

Nondialysis

Outcome:

Alive

Dead

AKI is a clinical syndrome denoted by an abrupt

decline in Glomerular Filtration Rate (GFR) sufficient decrease in the elimination of nitrogenous waste products (urea and creatinine) and other uremic toxins. AKI is an important cause of morbidity and mortality in patients requiring hospitalization especially in the developing nations. Inspite of fact that AKI is one of the leading cause of morbidity and mortality, it largely remains underdiagnosed and under reported in the developing nations. Our study is one such attempt to know the demographic details, type (CAKI, HAKI), presentation (oliguric or non-oliguric), etiology, dialysis requirement, progression to CKD and mortality at a tertiary care centre in southern part of India, which can serve as a platform for future studies.

Most of the patients in the present study belong to fifth decade, men outnumbered women, is similar to the other studies from developed and developing countries. The putative reasons for male predominance could be that as men tend to stay outdoors and they are at a higher risk of exposure to a wide variety of infectious agents and men seeking medical attention earlier. Infectious causes emerged as most common etiology in the present study in comparision to developed countries where renal vascular related conditions such as diabetes and hypertension leading to AKI and further progression to CKD is much common (Table 3)¹⁹⁻²². In the present study AKI is more common in monsoon season, reflecting the increased incidence of infectious aetiology in monsoon season, where as in developed nations it is due to high incidence of cardiovascular and pulmonary diseases in winter seasons²³. Mortality

Variable			Study (reference)		
	Wang 2012 ¹⁹	Challiner R 2014 ²⁰	Yousif 2018 ²¹	Arshad 2020 ²²	Present study
Period of study	2009-2010	2013	2013-2014	2017	2002-2016
Place of study	Birmingham, USA	England, UK	Soba Uni-versity Hospital (SUH), Khartoum state, Sudan	Aga Khan University Hospital, Karachi, Pakistan	SVIMS, Tirupati, Andhra Pradesh, India
Study setting	Tertiary care centre	Tertiary care teaching hospital	Tertiary care teaching hospital	Tertiary care centre	Tertiary care teaching hospital
Study design	Retrospective	Retrospective	Prospective	Retrospective	Retrospective
Study subjects	4,365	745	71	134	1734
Age (years)	56.8±16.9	ND	54.0	60 ± 11.7	49.92 ± 16
Gender distribution (male:female)	51.9:40.1	54.6:44.4	66:64	55.2:44.8	65:35
Aetiology	Circulatory diseases (25.4%) and infection (16.4%)	ND	Intrinsic renal disease (25.34%)	Sepsis (45%)	Infectious causes (77.9%)
Progression to CKD	ND ` ´	ND	27 (38%)	ND	133 (9.6%)
Mortality	10.8%	11.4%	10 (14.1%)	ND	361 (20.8%)

was higher in patients with HAKI as well as those who presented with oliguria in the present study; similar trends were observed in the studies from other parts of the world^{24,25}. Progression to CKD is much less when compared to other studies from the world¹⁹⁻²².

CONCLUSION

This study represents a fairly good data of AKI patients from southern-India from 2002 to 2016 emphasizing it's incidence as 0.62%, types including CAKI and HAKI, presentation as oliguric and non-oliguric, infections as leading etiology in patient population predominantly in the fifth decade, with hypertension and diabetes mellitus as co-morbidities and in men. Mortality due to AKI was 2.07% among hospital deaths between 2002 to 2016. The progression of AKI to CKD was 9.6% of the survived AKI patients in the follow up reiterating the importance of periodic follow-up after the discharge to enable early detection and to implement effective measures to retard progression to CKD. "A STITCH IN TIME SAVES NINE".

Conflict of Interest: NIL.

Funding: NIL.

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