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A PROSPECTIVE STUDY ON PREVALENCE AND FACTORS ASSOCIATED WITH ACUTE KIDNEY INJURY-A SOUTH INDIAN PERSPECTIVE

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Abstract
Acute kidney injury (AKI) is not a disease in and of itself, but rather a silent and under recognized syndrome that develops as a result of other major aetiologies such as Heart failure and Sepsis/Shock. The pattern of AKI varies from region to region and even within the same region, the pattern of AKI varies over time. The main objective of the study was to determine the Prevalence and factors associated with AKI in patients. The study was a prospective observational study in the medical ward of a tertiary care hospital in south India over a period of 6 months. A total of 1500 patients were included in the study, of whom 12.53% patients had AKI according to the KDIGO criteria. Patients with AKI were older and had Hypertension (P = <0.01) as the major comorbidity. Sepsis (P = 0), UTI (P = <0.01), Acute gastroenteritis (P= < 0.05), Pyelonephritis (P = <0.05), and CKD (P = <0.05) were the main factors associated with AKI on logistic regression analysis. The study demonstrated the Prevalence and factors associated with AKI. Environmental and infectious causes which are largely preventable, are associated with significant morbidity of AKI. Larger prospective studies are required for a better understanding of the regional differences in the disease pattern, its management and prevention of its progression to CKD.

Keywords: Acute Kidney Injury, Prevalence, Sepsis, Urinary tract infection, Pyelonephritis

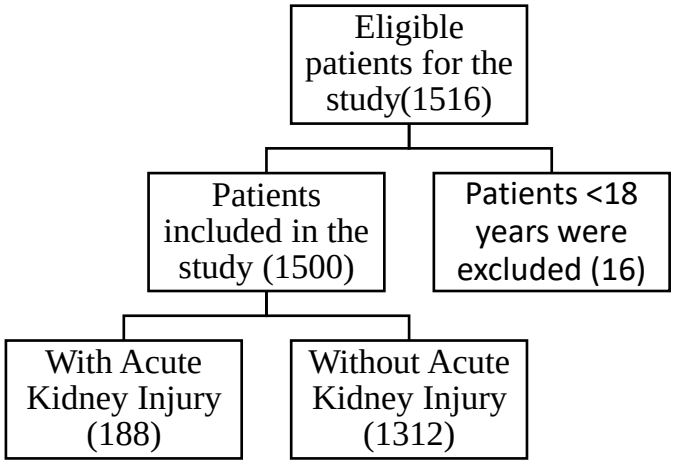
Introduction
Acute Kidney Injury (AKI) is a condition that causes a sudden rise in serum creatinine, a drop in urine output or both. AKI is not a disease in and of itself, but rather a silent and under recognized syndrome that develops as a result of other major aetiologies such as heart failure and sepsis/shock. More than a disease, AKI is a complication to other diseases and disorders. On developing AKI, a number of pathophysiological conditions occurs in the body that includes waste product accumulation, impaired electrolyte equilibrium, and a generalised inflammatory response that affects the various body organs [1]. AKI affects about 13.3 million people per year, with 85% of them are from the developing countries and it also contributes to about 1.7 million deaths every year. AKI is a common disorder that affects one in five adults and one in three children worldwide during a hospital admission. AKI develops primarily in hospitalised patients known as Hospital acquired acute kidney injury (HAAKI) in high-income countries. In low- and middle-income countries, AKI occurs primarily in the

community setting known as Community acquired acute kidney injury (CAAKI) which occurs during acute illnesses, usually in association with diarrhoea and dehydration, infections such as malaria, and toxins (venoms and poisons). Public health issues (such as contaminated water, poor sanitation, endemic infections such as malaria and dengue fever, venomous snakes, and toxic traditional medicines) and socioeconomic factors (such as the availability of health-care facilities) have an impact on the epidemiology of AKI worldwide [2]. The Kidney Disease Improving Global Outcomes (KDIGO) classification is an optimised description of two previous combined classifications (RIFLE and AKIN), which were proposed by international expert groups of nephrologists to demonstrate the severity of AKI [3]. The latest classification of AKI proposed by the Acute Kidney Injury Working Group of KDIGO, had the aim of unifying the definition of AKI. By the KDIGO definition, AKI is diagnosed by an absolute increase in Serum creatinine (SCr), at least 0.3 mg/dL (26.5 μmol/L) within 48 hours or by a 50% increase in SCr from baseline within 7 days, or a urine volume of less than 0.5 mL/kg/h for at least 6 hours [4]. The pattern of AKI and the factors varies from one country to other and even within the same country, it varies over time. There is a void on the information regarding the overall epidemiology of AKI due to the lack of central registry on AKI in India [5]. Due to the geographical and socioeconomic diversity in India, regional differences are expected in the factors associated with the development of AKI. A complete profile on various factors associated with the development of AKI helps in guiding to plan strategies to prevent AKI, prognosticate the patients, and prioritize the utilisation of sparse and expensive therapeutic modalities. Our study was a small initiative for this, with our study aim is to determine the prevalence and factors associated with the development of acute kidney injury in patients admitted in general medicine ward at a tertiary care teaching hospital.

Methods

We conducted a prospective study, which was carried out from September 2022 to February 2023 at Sri Venkateswara Ramnarain Ruia Government General Hospital (SVRRGGH), which was a tertiary care teaching hospital located in southern India. The study was approved by the Institutional ethics committee. Adult (>18years) patients of either gender admitted to general medicine ward with compliance to current KDIGO criteria for AKI diagnosis were included in our study. Patients with underlying chronic kidney disease (CKD) who experienced an episode of AKI during the study period were also included in the present study. Patients with underlying CKD with no evidence of AKI, patients on chronic haemodialysis, patients for whom it was not possible to ascertain a diagnosis (i.e., patients with one elevated serum creatinine result and no subsequent follow up), and patients hospitalized for less than 24 hours were excluded from the study. The patients with AKI were classified into Community acquired AKI and Hospital acquired AKI. We defined CAAKI as the development of AKI on admission or within 48 hours of admission. Patients developing AKI beyond 48 hours of admission were considered as HAAKI. The baseline serum creatinine was obtained from the patients previous hospitalization records. However all patients may not have the prehospitalization creatinine, making it to require an estimation of a reference baseline serum creatinine. In such condition baseline serum creatinine was calculated using the Modification of Diet in Renal Disease (MDRD) formula. Staging of AKI in patients was carried out according to the KDIGO criteria. The recruitment of patients is given in Figure 1.

Figure 1: Flowchart of patients included in the study



Statistical Analysis

To describe the data, descriptive statistics, frequency analysis, and percentage analysis were used for categorical variables (Type of AKI, Stage of AKI, Comorbidities, Social habits etc.) and mean with standard deviation were used for continuous variables (Age). Logistic regression analysis was done for factors associated with the development of AKI. A P- value of <0.05 was considered as statistically significant. All statistics were carried out using R programming statistics software version 4.2.1.

Results

During the six month study period, a total of 1500 patients were evaluated in the general medicine ward. Of these 188 (12.53%) patients had AKI. The mean age of the patients was 56.9 ± 14.4 years. The mean age of the AKI patients was higher than that of the non AKI patients (56.9 ± 14.4 vs. 51.2 ± 16.8, P < 0.0001). Out of 188 patients, 81 (43.08%) patients were aged between 60-79 years, 79 (42.02%) patients were 40-59 years, 20 (10.63%) patients were 20-39 years and 8 (4.25%) patients were ≥ 80 years. Majority of patients were Males n = 129 (68.62%) followed by Females n = 59 (31.38%).

Comorbidities in AKI patients

The main comorbidity in patients with AKI was found to be Hypertension seen in 96 (51.06%) patients which was statistically significant with a P value of <0.01. 75 (39.89%) patients had diabetes mellitus, whereas Bronchial asthma was seen in 14 (7.44%), old Pulmonary tuberculosis in (PTB) 13 (6.91%), coronary artery disease in 12 (6.38%), cerebrovascular accident in 12 (6.38%), chronic obstructive pulmonary disorder (COPD) in 7 (3.72%), Epilepsy in 5 (2.65%) patients etc.

Type and Stage of AKI

From the total 188 AKI patients, CAAKI was the leading cause of AKI contributing 172 (91.48%) patients, followed by HAAKI seen in 16 (8.51%) patients. The staging of AKI was done according to the KDIGO criteria. Out of total 188 AKI patients, majority of patients were at stage 3 AKI, 96 (51.06%) patients followed by stage 1, 51 (27.12%) patients and stage 2, 41 (21.8%) patients (Table 1).

Table 1: Demographics and baseline profile of study population	
Gender	
Male, n (%)	129 (68.62%)
Female, n (%)	59 (31.38%)
Age (Years)	
Mean±SD	56.9±14.4
Range	20-86
Comorbidities,	
Hypertension	96 (51.06%)

Diabetes mellitus	75 (39.89%)
Chronic kidney disease	34 (18.08%)
Bronchial asthma	14 (7.44%)
Old Pulmonary tuberculosis	13 (6.91%)
Coronary artery disease	12 (6.38%)
Cerebrovascular accidents	12 (6.38%)
Chronic obstructive pulmonary disorder	7 (3.72%)
Epilepsy	5 (2.65%)
Cardiomyopathy	4 (2.12%)
Chronic liver disease	4 (2.12%)
Hypothyroidism	4 (2.12%)
Others	4 (2.12%)
Type of AKI	
Community acquired AKI, n (%)	172 (91.48%)
Hospital acquired AKI, n (%)	16 (8.51%)
Staging of AKI	
Stage 1, n (%)	51 (27.12%)
Stage 2, n (%)	41 (21.80%)
Stage 3, n (%)	96 (51.06%)

Factors associated with AKI

In most of the cases, the factors were multifactorial. Chronic kidney disease was the most common factor seen in 40 (21.28%) patients. Next to Chronic kidney disease, sepsis contributed to AKI in 29 (15.43%) patients. These was followed by Congestive cardiac failure in 20 (10.64%), Acute gastroenteritis in 18 (9.57%), COPD in 15 (7.98%), Urinary tract infection (UTI) in 14 (7.45%) patients. Tropical fevers such as Dengue, Scrub typhus, and Chikungunya was seen in 9 (4.79%), 7 (3.72%), and 4 (2.13%) patients respectively. AKI due to toxins such as poisoning and snake bite was seen in 2 (1.06%) patients each (Table 2).

Table 2: Main factors associated with the development of AKI in patients:

Factors	**With AKI (n=188)**	**Without AKI (n=1312)**	**Total (n=1500)**
CKD	40 (21.28%)	149 (11.35%)	189 (12.6%)
Sepsis	29 (15.43%)	12 (0.91%)	41 (2.73%)
CCF	20 (10.64%)	125 (9.52%)	145 (9.67%)
Acute gastroenteritis	18 (9.57%)	59 (4.49%)	77 (5.13%)
COPD	15 (7.98%)	77 (5.86%)	92 (6.13%)
Urinary tract infection	14 (7.45%)	19 (1.44%)	33 (2.19%)
Dengue	9 (4.79%)	51 (3.88%)	60 (4%)
CLD	8 (4.26%)	99 (7.54%)	107 (7.13%)
Pneumonia	8 (4.26%)	18 (1.37%)	26 (1.73%)
Shock	8 (4.26%)	10 (0.76%)	18 (1.2%)
Scrub typhus	7 (3.72%)	33 (2.51%)	40 (2.67%)
Pyelonephritis	6 (3.19%)	6 (0.45%)	12 (0.8%)
Chikungunya	4 (2.13%)	6 (0.45%)	10 (0.67%)
Poisoning	2 (1.06%)	109 (8.3%)	111 (7.39%)
Snake bite	2 (1.06%)	31 (2.36%)	33 (2.19%)
ARDs	2 (1.06%)	6 (0.45%)	8 (0.53%)

The univariate logistic regression analysis revealed that advancing age, hypertension as comorbidity, and the factors such as sepsis, UTI, acute gastroenteritis, pyelonephritis and CKD were the independent factors associated with the development of AKI (Table 3).

Table 3: Logistic regression analysis of factors associated with the development of AKI

Factors	**With AKI 188 (12.53%)**	**Without AKI 1312 (87.46%)**	**P value**
Sepsis	29 (15.43%)	12 (0.91%)	$8.7e^{-11}$***
UTI	14 (7.45%)	19 (1.44%)	0.004097**
Acute gastroenteritis	18 (9.57%)	59 (4.49%)	0.010314*
Pyelonephritis	6 (3.19%)	6 (0.45%)	0.017621*
CKD	40 (21.28%)	149 (11.35%)	0.030825*
Pneumonia	8 (4.26%)	18 (1.37%)	0.844212
Shock	8 (4.26%)	10 (0.76%)	0.587675
Poisoning	2 (1.06%)	109 (8.3%)	0.067637

Discussion:

In this study from southern India looking prospectively at hospitalized patients in the General medicine ward of SVRRGGH Hospital, Tirupati, using KDIGO criteria, we found that the prevalence of AKI in patients was 12.53%. In the study by Vignesh Kumar Chandiraseharan et al. in the department of Internal Medicine, Christian Medical College, Vellore, India, showed a similar report of 19.13% of AKI in patients [6].

The mean age of patients with AKI in our study was found to be 56.9 ± 14.4 years. Most of the Indian studies had reported the mean age of patients varying from 35 to 50 years [7-10]. The mean age of our study population was significantly higher than the mean age described by other studies in India, probably due to the fact that unlike other studies which have concentrated on de novo AKI, our study has also included patients with pre-existing CKD. In our study, Male (68.62%) patients contributed the majority of AKI cases. The predominance of male gender in our study corresponds well with the majority of other studies [5] [11] [12]. The higher percentage of males can be due to occupational hazards in males that prone them to vector borne diseases and envenomation. In the present study Hypertension was present in 96 (51.06%) patients, which was statistically significant with a P value of < 0.01. Diabetes mellitus was present in 75 (39.89%) patients. Chronic kidney disease, Bronchial Asthma, and Old PTB were present in 34 (18.08%), 14 (7.44%), and 13 (6.91%) patients respectively. One of the factor associated with the development of AKI in these patients may be due to the use of Angiotensin converting enzyme inhibitors, Angiotensin receptor blockers, and Calcium channel blockers in hypertensive patients, use of Diuretics in case of CKD patients, and use of Anti tubercular therapy in case of Old PTB patients.

The factors associated with the development of AKI was multifactorial. The various factors in our study which were significant on logistic regression analysis were CKD, Sepsis, acute gastroenteritis, UTI, and Pyelonephritis. In our study the proportion of AKI patients with CKD was 21.28%. Very limited studies in India included CKD patients in their study on AKI [11][13]. Narinder Pal Singh et al. conducted a study on "Acute Kidney Injury in Intensive care Unit: A Clinical and Outcome Study" included patients with pre-existing CKD in the study and reported 78.8% patients of AKI with pre-existing CKD [14]. In our study, sepsis was present in 29 (15.43%) patients. In the epidemiological studies on AKI in our country, the major factor associated with the development of AKI was sepsis. In the study by Ramesh Kaaviya et al. sepsis was present in 12.9% of AKI patients [11]. In a similar study by Priyamvada et al. sepsis was the most important cause of AKI, accounting for 22% of AKI patients [13]. In our study AKI due to acute gastroenteritis was seen in 18 (9.57%) patients. In the studies conducted before 2015, there is a significant proportion of patients with AKI due to acute gastroenteritis [9, 10, 15]. Shraddha Goswami et al. reported that acute gastroenteritis was the major factor for the development of AKI contributing 62% of total AKI cases [15]. The proportion of AKI patients due to acute gastroenteritis was less in our study compared to other studies conducted before 2015. This may be probably because acute diarrheal diseases has been decreasing over the past few

years due to good hygiene, better facilities and effective management at the hospitals [16]. AKI due to UTI was seen in 14 (7.45%) patients. UTI may cause sudden deterioration of kidney functions. A similar study from Sanjay Vikrant et al. reported an incidence of AKI due to UTI as 14% [5]. This was followed by pyelonephritis with 6 (3.19%) patients. In a study of Ramesh Kaaviya et al. pyelonephritis was the second most common cause of AKI contributing 17.7% of total AKI patients [13].

In our study AKI due to Pneumonia was seen in 8 (4.26%) patients, which was similar to that reported by Ramesh Kaaviya et al. [11] (5.4%) and Sanjay vikrant et al. [5] (9.1%). Congestive cardiac failure and Chronic liver disease contributed 20 (10.64%) and 8 (4.26%) AKI patients respectively. Tropical infections such as Scrub typhus, Chikungunya, Dengue and Leptospirosis were also responsible for AKI cases in the present study. In the present study AKI due to Scrub typhus was seen in 7 (3.72%) patients which was similar to that reported by Prasanta Kumar Bhattacharya et al. [17] (8%). AKI due to Leptospirosis was seen in 1 (0.53%) patients similar to that reported by Sanjay Vikrant et al. [5] (1.6%). AKI due to Chikungunya and Dengue were present in 4 (2.13%) and 9 (4.79%) patients respectively. In the present study there were no AKI cases that was related to Malaria among the AKI patients. AKI due to Snake bite was seen in 2 (1.06%) patients which was similar to that reported by Prasanta Kumar Bhattacharya et al. [17] 1 (1.33%). Ramesh Kaaviya et al. reported Snakebite as the most common cause of AKI seen in 49 of 186 (26%) cases. This differences may be due to the geographical differences in snakes and the occupation of the patient population, where in the study of Ramesh Kaaviya et al. most of the patient population were underprivileged agricultural laborers and the Hospital also caters to the districts where agriculture was the main occupation. [11] In the present study AKI due to poisoning was seen in 2 (1.06%) patients which was similar to that reported by Sanjay Vikrant et al. [5](1.3%).

Majority of AKI cases in our study are Community acquired contributing 172 (91.48%) AKI patients which was similar to that reported by Sanjay vikrant et al. [5] (92.2%), and M. Jayakumar et al. [10] (92.08%). Staging of AKI was done according to the KDIGO criteria. Stage 1 AKI was present in 51 (27.12%) patients, Stage 2 in 41 (21.80%) patients and Stage 3 was contributed by 96 (51.06%) patients. Greater proportion of AKI patients in our study were at Stage 3, this may be due to delay in the timely diagnosis of AKI or due to the inclusion of CKD patients in our study, which may contribute to the major proportion of AKI patients at stage 3.

Conclusion

Our study describes the Prevalence and Factors associated with AKI among hospitalized adult patients at a tertiary care hospital in south India. CAAKI remains a common problem affecting 91.48% of AKI patients. We found that presence of Hypertension, Sepsis, UTI, Pyelonephritis, CKD, and acute gastroenteritis are contributing factors in these patients. Results from this study may help to clarify the factors associated with AKI and burden of AKI in India. Environmental and infectious causes which are largely preventable, are also associated with significant morbidity of AKI. We had attempted to use the KDIGO criteria to emphasize the patients with AKI. Larger prospective studies are required for a better understanding of the regional differences in the disease pattern, its management and prevention of its progression to CKD.

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