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Panacea Journal of Medical Sciences

Journal homepage: http://www.pjms.in/

Original Research Article

A profile of acute kidney injury in Eastern India: A cross sectional study

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ARTICLE INFO

Article history: Received 05-03-2021 Accepted 28-04-2021 Available online 24-11-2021

Keywords: AKI RIFLE AKIN KDIGO

ABSTRACT

Introduction: AKI is an important cause of morbidity and mortality with mortality remaining unchanged in the last decade inspite of advances in treatment. It is classified as pre renal, renal and post renal categories with overlap. The classification criterias are RIFLE, KDIGO and AKIN, based on which the present study has been conducted, as the new markers of AKI such as NGAL, IL 18 and KIM 1 are not sensitive and specific.

Aims and Objectives: The purpose of the study is to determine the aetiologies, clinical features, risk factors and comorbidities associated with AKI in a Tertiary Care Hospital.

Materials and Methods: This prospective observational study was conducted in RKMSP with 60 indoor patients after taking consent and applying the inclusion and exclusion criteria. After taking history and performing clinical examination, laboratory investigations were done and detailed statistical analysis was performed to obtain the results.

Results: Study showed that with rise of age, AKI increased. Females were more commonly affected with sepsis being the commonest cause and DM is the commonest associated co morbidity. Most of the patients were in RISK stage according to RIFLE criteria and incidence of AKI was more or less similar, according to different classification systems.

Conclusion: The importance of the study lies in the fact that study of risk factors, aetiology, clinical features and co morbities associated with AKI will pave the path for larger studies so that the mortality and morbidity from AKI may be modified.

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1. Introduction

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Acute kidney injury(AKI) is a heterogenous syndrome defined by a rapid decline in the GFR resulting in the retention of metabolic waste products and dysregulation of fluid, electrolytes, and acid base homeostasis.¹

AKI represents a broad constellation of pathophysiologic process of varied severity and etiology, These includes decrease in GFR, partial or complete obstruction to urinary flow, and a spectrum of processes with characteristic patterns of glomerular, interstitial, tubular, or vascular parenchymal injury.

Decreased urine output is often a cardinal manifestation of AKI, and patients are frequently classified based on urine flow rates as non oliguric (urine output

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>400ml/day), oliguric (urine output<400ml/day) or anuric (urine output<100ml/day).² Multiple mechanisms may contribute to this increased susceptibility, including diminished renal functional reserve, impaired salt and water conservation predisposing to intravascular volume contraction, decreased activity of detoxification mechanism increasing susceptibility to cytotoxic injury etc.

AKI usually divided into three broad patho- physiologic categories based on cause.

- 1. Prerenal Disease characterised by effective hypoperfusion of the kidneys in which there is no parenchymal damage to the kidney.
- 2. Intrinsic Disease involving the renal parenchyma.
- 3. Postrenal Disease associated with acute obstruction of the urinary tract.

Although these categories are useful and help to inform the initial clinical assessment of patients with AKI, there is often a degree of overlap among these categories.

AKI, previously called ARF, was first described by the term 'ischuria renalis' by William Herbeden in 1802.³ The term AKI was used for the first time by William Mac Naider in 1918 in a situation of mercury poisoning, but became the preferred term in 2004 when ARF was redefined as AKI by RIFLE criteria.⁴ The latest classification of AKI proposed by the Acute Kidney Injury Working Group of KDIGO definition and staging system is the most recent and preferred definition, is based on the previous two classification, and had the aim of unifying the definition of AKI.⁵ Despite significant advances in both critical care and nephrology, the mortality rate of hospitalized AKI cases has remained relatively unchanged at around 50% . Despite its widespread use, however, serum creatinine has significant limitations as a tool for assessing GFR as age. gender, muscle mass and diet, mostly protein intake, are determinants of creatinine production.⁶ Some equations for e GFR account for some of these variables (such as age and gender in the MDRD equation), muscle mass and nutritional considerations are not reflected by these equations. So need of some alternative diagnostic molecules was evident and here comes the new biomarkers for early detection and monitoring outcome and prediction of mortality and morbidity in AKI. The newer diagnostic biomarkers include NGAL, urinary Cystatin-C, Kidney Injury Molecule-1 (KIM-1) and IL 18. In case of early post ischemia, up regulation of NGAL transcription and translation, particularly in proximal tubular cells occurs. So, level of urinary as well as blood NGAL increases well before (within 2 hours of injury) than rise in serum creatinine (12-24 hours). During any form of ischemic renal injury, IL-18 increase well before rise of serum creatinine. Following ischemic injury, KIM-1 it is dramatically up regulated in regenerating proximal tubules. Cystatin C, is produced by all nucleated cells. Serum levels of cystatin

C have been established as a reliable correlate of GFR, superior to serum creatinine in that cystatin C production is not influenced by muscle mass; its level is not affected by age, race, or gender; and its urinary clearance does not involve tubular secretion. However, while serum cystatin C level can be used as a surrogate marker of GFR, it is not a true biomarker of AKI in that its levels are not a direct marker of renal injury. Elevation in urinary cystatin C, on the other hand, is closer to a true biomarker of AKI. Cystatin C is freely filtered at the glomerulus and then nearly completely reabsorbed by the proximal tubules. Recent human studies on urinary cystatin C have shown promise in using this measurement as a biomarker of AKI, with cystatin C levels assayed by ELISA.

These markers have been evaluated in various studies either alone or in combination but the sensitivity and specificity data is lacking, hence these have not been included still in the classification criterias, i.e. RIFLE, AKIN and KDIGO.

This study is based on the RIFLE, AKIN and KDIGO criterias. There are several studies all over the world and also in India but all of them points towards a particular etiology of acute kidney injury. So the main purpose of this study is to assess the etiology, clinical features, risk factors and co morbities associated with AKI and to reduce the overall morbidity and mortality.

2. Aims and Objectives

- 1. To evaluate the different etiologies (sepsis, like pneumosepsis, urosepsis, intraabdominal sepsis; drugs like diuretics, heart failure, acute gastroenteritis, pancreatitis etc, cancer) of AKI.
- 2. To study the different clinical presentation of AKI (like dyspnea, oliguria, anasarca, uremic features like encephalopathy and vomiting, infection, postoperative presentation).
- 3. To evaluate the risk factors of AKI (hypotension, dehydration).
- 4. To study the comorbid illness associated with AKI (DM, hypertension, anemia, chronic obstructive lung disease, CLD).

3. Materials and Methods

After taking Ethical consent, the study was conducted in RKMSP. It is a prospective, observational, cross sectional study with the patients admitted in Medicine Ward, ICU(Medicine) and post-operative HDU and the study was conducted for one and half years.

- 3.1. Variables
 - 1. Diseases causing AKI (sepsis, heart failure, over use of diuretics, acute gastroenteritis, acute pancreatitis).

- 2. Clinical presentation of AKI (dyspnea, fatigue, drowsiness, oliguria).
- 3. Risk factors of AKI (dehydration, postoperative, hypotension, dehydration).
- 4. Co-morbidities with AKI (diabetes mellitus, hypertension, chronic lung disease and CLD).

3.2. Inclusion criteria

- 1. Patients willing to participate in this study.
- 2. All patients admitted in Medical ward, Medicine ICU and Post-operative HDU.

3.3. Exclusion criteria

- 1. Patients with back ground CKD.
- 2. Patients on maintenance dialysis.
- 3. Patients admitted here from other hospital(s) without proper documents.
- 4. Age below 12 years.

3.4. Sample size

Patients from above mentioned units.

3.5. Nature of data collection

- 1. History
- 2. Examination
 - (a) General examination
 - (b) Gastro intestinal system
 - (c) Cardio vascular system
 - (d) Respiratory system
 - (e) Central nervous system
 - (f) Locomotor system
 - (g) Skin and appendages
- 3. Laboratory parameters CBC (hematology analyser and manual technique), CRP (latex agglutination test), RFT (automated analyser), LFT (automated analyser), Electrolytes (automated analyser), Chest X ray(digital), MP (thick and thin smear) and MP dual antigen test , Dengue IgM Ab (ELISA), Scrub Typhus IgM Ab (ELISA),ECG, Echocardiography, vasculitis and collagen vascular disease profile (Rheumatoid factor, ANF by HEP2, ANA profile, pANCA), Blood Culture and Sensitivity (aerobic and anaerobic), Urine RE/CS (aerobic and anaerobic), Test for other Tropical Illness, USG WA,KUB, CT KUB.

4. Results and Analysis

For statistical analysis .data were entered into a Microsoft excel spreadsheet and then analysed by SPSS (version 25.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data have been summarized as mean and standard deviation for Statistical Analysis: numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. p-value ≤ 0.05 was considered for statistically significant.

Table 1: Distribution of Age in Years

Age in Years	Frequency	Percent
≤30	3	5.0%
31-40	5	8.3%
41-50	4	6.7%
51-60	16	26.7%
61-70	10	16.7%
71-80	16	26.7%
81-90	6	10.0%
Total	60	100.0%

32 patients (53.4%), are of above 60 years. Out of them, 16 patients (26.7%) were between 71 years and 80 years.



Fig. 1: Showing sex distribution 40(66.7%) patients were female and 20(33.3%) patients were male.

Among total 60 patients 22(36.7%) patients had sepsis, 6(10.0%) patients had drugs, 2(3.3%) patients had obstructive uropathy, 8(13.3%) patients had heart failure, 4(6.7%) patients had surgery, 3(5.0%) patients had acute gastro enteritis/acute pancreatitis, 2(3.3%) patients had collagen vascular disease/vasculitis, one of systemic lupus erethymatosus and one of granulomatosis with polyangiitis; 4(6.7%) patients had malignancy, 1(1.7%) patient had LVF and 2(3.3%) patients had hepatic disease (CLD, others).URO sepsis followed by pneumosepsis (5 cases, 20%).

Here, 31(51.7%) patients had T2DM followed by hypertension of 16(26.7%). Among cardiac morbidities, 1(1.7%) patient had CAD and 6(10%) patients dilated cardiomyopathy.

BAR DIAGRAM 1

The mean hospital stay (mean \pm S.D.) of patients was 11.4237 \pm 5.4495 days

So, all the three criterias showed similar and comparable results. It is clear from the above tabulation regarding the grading as per RIFLE criteria on the basis of

Table 2: Distribution of Etiology-Sepsis, drugs, obstructive
uropathy, heart failure, surgery, acute gastro enteritis/ acute
pancreatitis, collagen vascular disease/vasculitis, malignancy and
hepatic (CLD)

		Frequency	Percent
Sancia	No	35	58.3%
Sepsis	Yes	25	41.7%
Denas	No	53	88.33%
Drugs	Yes	7	11.66%
Obstructive	No	57	95%
Uropathy	Yes	3	5%
Heart failure	No	51	85%
Heart failure	Yes	9	15%
D	No	56	93.3%
Post-operative cases	Yes	4	6.7%
Acute gastro	No	57	95.0%
enteritis/acute			
pancreatitis	Yes	3	5.0%
Collagen vascular	No	58	96.7%
disease/vasculitis	Yes	2	3.3%
Maliananau	No	55	91.66%
Malignancy	Yes	5	8.3%
Hepatic causes,	No	58	96.7%
chronic liver			
disease(CLD)			
	Yes	2	3.3%

Table 3: Distribution of sepsis cases among patients with sepsis causing acute kidney injury

SEPSIS	Frequency	Percentage
Urosepsis	18	72 %
Pneumosepsis	5	20 %
Intra-abdominal sepsis- appendicular abcess	1	4 %
Central nervous system infection- meningitis	1	4%
Skin and bone Infection- cellulitis and osteomyelitis	0	0%
Total	25	

Table 4:	Distribution	of co-r	norbidities	in	patients of	f AKI
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		Frequency	Percent
T2DM	No	29	48.3%
	Yes	31	51.7%
Hypertension	No	44	73.3%
	Yes	16	26.7%
Cardiac disease	CAD	1	1.7%
	DCM	6	11.66%
	No	52	86.7%



Fig. 2: Showing distribution of pre renal, renal, post renal causes of AKI among study population

		kdigo criteria

RIFLE	AKIN	KDIGO
28(46%)	28(46%)	28(46%)
21(35%)	21(35%)	21(35%)
10(16.6%)	11(19%)	11(19%)
1(1.66%)		
	28(46%)	28(46%) 28(46%) 21(35%) 21(35%) 10(16.6%) 11(19%)

serum creatinine level that patients having in RISK-28(46%), INJURY - 21(35%), FAILURE-10 (16.6%), LOSS-1(1.66%), no patient entered into the end stage renal disease. The patient who was in "LOSS", underwent maintenance dialysis.

As per AKIN and KDIGO criteria patients distribution are stage-1-28(46%), stage-2-21(35%), stage-3-11(19%) in total 60 patients.

Out of 60 patients 25 patients (41.66%) had sepsis, and among them 10 patients (16.66%) and 12 patients (20%) were in "INJURY" and "RISK" category respectively.

Among 60 patients, 7 patients (11.66%) received diuretics (frusemide and torsemide) and developed AKI and they were in "INJURY" and "RISK" category.

Out of 60 patients, 9 patients (15%) had heart failure and developed acute kidney injury. 28 patients (46.66%) were in RISK category and amongst them 8 patients (28.57%) had heart failure.

In the study, most of the patients (46%) were in Stage-1 as per AKIN criteria.

Out of 60 patients, 25 (41.66%) were in sepsis. Amongst them, 12 (20% of total) and 10 (16.66% of total) were in

Stage-1 and Stage-2 respectively.

In the present study, out of 60 patients, 9 patients (15%) had heart failure. Most (8) of them were in stage-1 as per AKIN criteria.

Out of 60 patients, 7 (11.66%) patients had undergone AKI due to diuretics use and most of them were is Stage-1 (3 no, 5% of total) and in Stage-2(4 no, 6.66% of total) respectively as per AKIN criteria.

Most of the patients (46%) were in Stage-1 as per KDIGO criteria.

5. Discussion

In the study, we found that AKI was more prevalent above age 50 years and it was 80%. In one study in 2007 by Ali Khan and Simpson et al,⁷ based on 223390 population median age group was found to be 76 years for AKI.

A study by Istifanus Bala Bosan, Abubakar Ibrahim, Sunday Musa Oguche et al⁸ which is a Nigerian study done in january 2016, shows 158 (49.4%) females out of 320 AKI patients whereas slightly male preponderance of 162 (50.6%) male patients. But those who were admitted due to sepsis (119), there were female preponderance as 70/119 (58.8%). Here also female preponderance was found.

Among 60 patients the etiological cause of AKI was evaluated and it was found that sepsis was the most common cause 25 (41.7%). S A multicentric study done by Sean M. Bagshaw, Shigehiko Uchino, Rinaldo Bellomo et al⁹ in 2007, sepsis was found to be the most common cause of oliguric renal failure among 1753 enrolled patients as 833 (47.5%) of patient developed acute kidney injury.

In background of heart failure, AKI is also an important predictors of adverse outcome. Here, 9 patients (15%) developed AKI who were cases of congestive heart failure. A study by Butler J, Wang Y, Abraham WT et al¹⁰ on worsening renal failure among 1007 enrolled heart failure cases, worsening of renal failure was found in 27% of cases with ARR 2.1; CI 1.5, 3.0 (significant). Moreover worsening of renal function occurred on the day of admission. Less number of patients with heart failure heres because of lower study population.

Among total sepsis patients (25, 41.7%) (Table 3), it is seen that 18 patients (72%) is due to urosepsis, followed by pneumosepsis (5 number, 20%). A study by Chih-Yen Hsiao, Huang-Yu Yang, Meng-Chang Hsiao, et al¹¹ showed 97 patients (12.3%) developing AKI after admission with 4 patients (0.5%) necessitating dialysis therapy among 790 enrolled UTI cases and upper UTI (46.4% versus 35.5%, P = 0.037) is the most common cause.

Drugs are important cause of AKI, while AKI is also associated with cancer and 6.7% cases among post surgery patients.

Here, two (3.33%) AGE and one (1.66%) acute pancreatitis patient was diagnosed as AKI. A study by Atim E. Pajai, Kalpana S. Mehta et al showed that Incidence of AKI due to diarrhea was 23%, and affecting males predominantly in 4th decade among 230 patients admitted with AKI. But in our study it is low because of the fact that most of the patients with acute gastroenteritis are admitted in other designated Centres.

None of the patients developed severe acute pancreatitis during study period and also, pancreatitis patients were well resuscitated with fluid and supportive measures, hence, number of cases due to pancreatitis is low. In my study prevalence of AKI in collagen vascular disease and vasculitis is 3.3%. In hepatic cause two (3.33%) CLD patient were diagnosed here.

It was seen here, that three co-morbidities, T2DM, hypertension, and cardiac disease are related with AKI. Among these T2DM is related in 51.7% cases and most of them had sepsis, and urosepsis was diagnosed mostly, that causes intrinsic AKI.

In this study 26.7% of cases were found to be hypertensive. The study by Chih-Yen Hsiao, Huang-Yu Yang et al¹¹ shows hypertension(54.6% versus 40.7%, P = 0.009) to be a significant comorbidity amongst AKI patients.

Here, 60% of cases were of renal etiology and 31.66% were of pre renal etiology. In one study by Santos WJ, Zanetta DM et al¹² 88% of cases (524 cases out of 593) developed intrinsic renal AKI. This data also corroborates with our study as the cases of renal causes of AKI was more than those of pre renal and post renal.

As per RIFLE classification risk-46%%, injury-35%, failure-16.6%, loss- 1.66%.

In this study it was found in AKIN classification of AKI, patients are in stage-1 46%, stage-2 35%, stage-3 19% with similar result and out come as in RIFLE classification.

5.1. Comparison between RIFLE and AKIN classification

From the analysis here, it is obvious that in spite of some theoretical benefit for diagnosis of AKI practically AKIN classification does not provide any extra benefit than RIFLE classification and as per KDIGO classification, it was found that the result was similar AKIN classification.

6. Conclusion

This study showed that increasing age increased the risk of AKI with higher incidence in the female population and sepsis is the commonest cause. The commonest comorbidity is T2 DM. Most of the patients as per RIFLE classification were in Risk stage (46%) followed by Injury stage (35%) followed by failure. Also the incidence of AKI as per different classification systems, i.e. RIFLE, AKIN, KDIGO showed no significant difference.

7. Limitations

However this study has its own limitations with low study population, lack of acute gastroenteritis cases(as they are admitted in Government and Infectious Disease Hospital) and no snake bite(admitted in Government set up)patients or HIV cases.

8. Abbreviations

AKI-acute kidney injury; RIFLE-Risk, Injury, Failure, Loss, End stage renal disease; AKIN- Acute Kidney Injury Network Criteria; KDIGO- Kidney Disease Improving Global Outcomes; GFR-Glomerular filtration Rate; NGAL-Neutrophil Gelatinase-Associated Lipocalin; KIM 1-Kidney Injury Molecule-1; CLD-chronic liver disease; CKD-chronic kidney disease; T2 DM/DM-Type 2 diabetes mellitus.

9. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

10. Source of Funding

None.

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Cite this article: Mazumdar A, Mazumdar S, Chakravarty UK, Pakira TK, Maitra S, Chatterjee SS. A profile of acute kidney injury in Eastern India: A cross sectional study. *Panacea J Med Sci* 2021;11(3):452-457.