International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

A Prospective Study on Clinical Profile & Mortality Determinants of Acute Kidney Injury in Patients Attending Tertiary Care Center in Southern Rajasthan

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Abstract: ***Introduction: Although the term acute renal failure was replaced by Acute Kidney Injury (AKI) recently, there is a paucity of data on clinical profile of AKI in hospitalized patient from the developing world. The aim of this study was to study clinical profile, mortality determinants and the treatment protocol of patients of AKI. Methodology: It was a hospital based prospective observational study conducted in R.N.T. Medical College, from May 2017 to April 2018. 250 patients admitted with AKI, defined according to the AKI Network criteria. The patients with AKI were followed-up until discharge/death. Their clinical and biochemical data were studied. Results: The common symptoms were fever (57.6%), oliguria (38.4%), GIT symptoms (38.0%). The common aetiologies were AFI (45.6%) followed by hypovolemia (22.4%), sepsis (8.8%). conservative treatment was done in 74.4% of patients, 56 (22.4%) were kept on hemodialysis and 7(2.8%) were kept on peritoneal dialysis. Overall mortality was 34.8%. Conclusion: Timely diagnosis and management of this disease condition confer a favorable prognosis to the patient. The progression of AKI leads to increased hospital mortality rates and increased length of stays that might proved overuse of limited resources in a setting like India, more specifically in tribal part of Rajasthan. Hence more number of studies has to be done to efficiently pinpoint the predictors of AKI and preventing its occurrence in the near future.***

Keywords: Acute kidney injury, symptoms, haemodialysis

1. Introduction

Acute kidney injury[1] depicts the abrupt decline in renal function that mostly occurs over the course (hours to days) and ends in retention of metabolic waste products and dysregulation of fluid, electrolytes, & acid base homeostasis.[1, 2]

Acute Kidney Injury (AKI) has now replaced the term Acute Renal Failure (ARF) and a universal definition and staging system has been proposed to allow earlier detection and management of AKI The new terminology enables health care professionals to consider the disease as a spectrum of injury. This spectrum extends from less severe forms of injury to more advanced injury when acute kidney failure may require Renal Replacement Therapy (RRT). Clinically, AKI is characterized by rapid reduction in kidney function resulting in a failure to maintain fluid, electrolyte, and acid base homeostasis.[3] AKI occurs in almost 7% of all hospitalized patient & up to 36% to 67% of critically ill patients. AKI is defined by any one of the following:

1. Increase in Serum Creatinine (Cr.) by more than or equal to 0.3mg /dl (>26.5 micromol/l) within 48 hours; or
2. Increase in Serum Creatinine to more than or equal to 1.5 times baseline, which is known or presumed to have occurred within prior 7 days.
3. Urine volume <0.5 ml/kg/hr for 6 hours.

AKI may complicates 5% of hospital admission & 30% of admission to ICU risk of AKI is contributed by the acute insult & background comorbidity. (Age, CKD, CHF, DM) (Sepsis, Hypoperfusion, Toxicity, Obstruction). Causes of AKI can be divided in to three categories:- Pre Renal, Renal & Post Renal. Rachoin et al[17] demonstrated the ICU patient with AKI & BUN: creatinine Ratio > 20:1 had high mortality than Prerenal azotemia.

2. Aims & Objectives

Aims & objective of on study was to study clinical profile various mortality determinants & treatment protocol of patients of AKI.

3. Material & Methods

This hospital based prospective observational study was conducted from May, 2017 to April, 2018 in RNT Medical College & attached group of hospital, Udaipur after having approval from ethical committee.

This study was conducted on 250 patients admitted to various wards of our hospitals & fulfilling definition of AKI & inclusion & exclusion criteria. Patients social, demographic, economic & Medical details were recorded in proforma sheet. Also the history regarding the symptoms of AKI like decease in urine output was recorded & duration of symptoms (in days) was also recorded. Diagnostic procedure if necessary kidney Biopsy, USG, Urine analysis or urine culture etc. was done. Requirement of RRT was assessed & patients were followed up for its outcome.

Inclusion Criteria:

1. Patients (>18 years) admitted in RNT Medical College and associated group of hospital fulfilling criteria of AKI

Exclusion Criteria:

1. Known case of CKD admitted for maintenance hemodialysis.
2. Patient <18 years of age.
3. Patient with history of Diabetes, Hypertension and chronic medical renal disease.
4. History of childhood renal disease.
5. History of familial renal disease.

4. Statistical Analysis

Outcome of each patient were classified as either discharged or expired. The collected data were entered in Microsoft Excel and then analyzed and statistically evaluated using SPSS-PC-17 version. Quantitative data were expressed by mean, standard deviation and difference between comparable groups were tested by student's t-test (unpaired) or Mann Whitney 'U' test, while from more than two groups 'ANNOVA' or Kruskal Wallis 'H' test was used followed by post-hoc test. Qualitative data were expressed in percentage and differences between the proportions were tested by chi square test or Fisher's exact test. 'P' value less than 0.05 was considered statistically significant.

5. Observation & Results

Table 1: General Parameter of Study Subjects

	Parameter	No. of patients (%)
1	**Sex:** Male:	153 (61.2%)
	Female	97 (38.8%)
2.	**Age Group (Yrs)**	
	18-25 yrs	52 (21.2%)
	26-35 yrs	40 (16.01%)
	36-45 yrs	48 (19.2%)
	46-55	28 (11.2%)
	56-65	48 (19.2%)
	>66	33 (13.2%)
3.	**Clinical features of study subjects-**	
	GI symptoms	95 (38.0%)
	Fever	144 (57.6%)
	Cough	3 (1.2%)
	SOB	84(33.6%)
	Pain abdomen	49(19.6%)
	Oedema	20(8.0%)
	Decrease urinary output	96(38.4%)
	LUTS	6(2.4%)
	Post delivery	15(6.0%)
	Post trauma	15(6.0%)
	Postoperative	10(4.0%)
	Abcess/ulcer	8(3.2%)
	Bleeding	14(5.6%)
	Seizure/altered sensorium	45(18.0%)
4.	**Type of AKI:**	
	Pre Renal	67 (26.8%)
	Renal	167 (66.8%)
	Post Renal	16 (6.4%)
5.	**Outcome:**	
	Death	87 (34.8%)
	Survived	163 (65.2%)

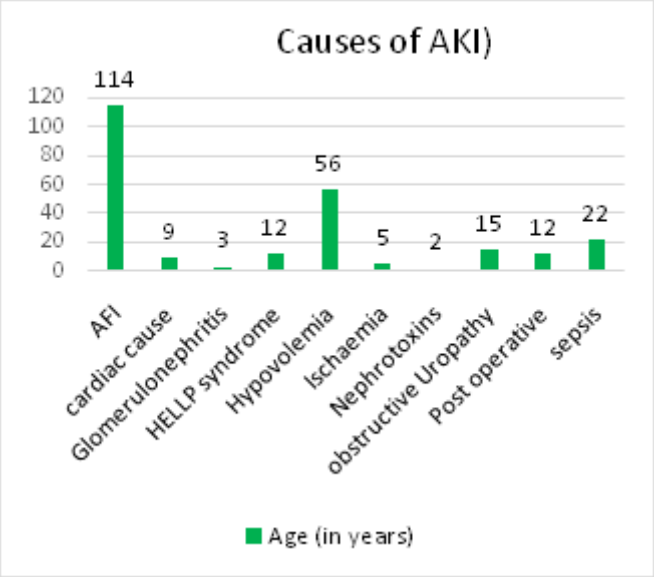


Figure 1: Cause of AKI in study subject

We studied 250 patient admitted in our hospital. General characteristics are summarized in table (1). Out of 250 patients, 153(61.2%) were male & 97(38.8%) patient were females. In our study majority of subjects fall within age limit of 18-25 yrs (21.2%). Mean age were 45.1±18.2 yrs. Most of study subject presented with fever (57.6%) followed by decreased urinary output (38.4%) & GI symptoms (38.0%). renal failure level was the most common type (66.8%) followed by prerenal (26.8%). In 16 study subject cause was at postrenal level. Out of 250 patients of AKI more than one third (34.8%) patient died, while rest survived. Most common cause of AKI was acute febrile illness (Tropical cause) followed by hypovolemia (22.4%), sepsis (8.8%) other causes were post operative, obstructive, cardiac cause etc. (figure 1).

Table 2: Microbiology of Study subject in Acute febrile illness group

Scrub Typhus	35(30.7%)
Typhoid	2 (1.7%)
Plasmodium vivax	6(5.2%)
Plasmodium falciparum	23(20.2%)
Dengue	1(0.8%)
PF+ Dengue IgM+	1(0.8%)
PF+PV+	1(0.8%)
PF+SCRUB+	1(0.8%)
Scrub &PF+PV+	1(0.8%)
Clinical AFI	43(37.7%)

In AFI with AKI patient, scrub types (30.7%) was the commonest pathogen followed byMalaria (30.7%). other were Dengue with multiple & mixed infection. 43% of AFI with AKI patients were categorized as clinical AFI as causative pathogen could not be diagnosed after preliminary battery of tests. (Table 2).

Table (3) showing correlation of various factor with prognosis. When urea level was >200 mg/dl, 37.3% patient died but this outcome was not found to be statistically significant (P value-0.80). Raised serum creatinine level was associated with poor prognosis but not statistically significant (Pvalue- 0.43). The severity of thrombocytopenia was significantly associated with mortality in AKI patient (P <0.05) When serum bilirubin was more > 3 mg/dl, Mortality increased significantly & this association was found to be statistically significant. When patient presented after 7 days of illness mortality was 42.2% while only 21.4% died if they presented within 3 days (Pvalue 0.09). Hypotension at admission was significantly associated with prognosis (P-value <0.01). Out of 250 patient 162 (84.8%) were oliguric & morality was 39.5% among them while morality was 51.5%, among anuric patient it is highly significant statistically. (P<0.001).

Table 3: Correlation of various factors with outcome

1. S. Urea Level (mg/dl)	N=250	Died	Survived	P Value
<100	44(17.6%)	15(34.1%	29(65.9%)	0.80
101-150	92(36.8%)	36(39.1%)	56(60.9%)	
151-200	55(22.01%)	14 (25.5%)	41 (74.5%)	
>200	59(23.6%)	22 (37.3%)	37(62.5%)	
2. S. Creatinine Level(mg/dl)				
<2	2(0.8%)	1(50%)	1(50%)	0.43
2-4	137(54.8%)	43(31.4%)	94(68.6%)	
>4	111(44.4%)	43 (38.7%)	68 (61.3%)	
3. Asso. Of platelet count (Lac/mm^3) with outcome				0.03
<0.2	31(12.4%)	15(48.4%)	16(51.4%)	
0.2-0.5	58(23.2%)	26(44.4%)	32(55.2%)	
0.5-1.0	55(22.9%)	18 (32.7%)	37 (67.3%)	
>.10	106(42.4%)	28 (26.4%)	78(73.6%)	
4. S.Bilirubin(mg/dl)				
<3	146(58.4%)	38(26.0%)	108(74.0%)	<0.01
3-6	56(22.4%)	29(51.8%)	27(48.2%)	
>6	48(19.2%)	20 (41.7%)	28(58.3%)	
5. BP on admission(mm of Hg)				
<90/60	85(34.0%)	53(72.4%)	32(37.6%)	<0.001
>90/60	165(66%)	34(20.6%)	131(79.4%)	
6.Urine output (ml/day):				
Anuria (<100)	35(14.0%)	18(51.4%)	17(48.6%)	<0.001
Oliguria (100-400)	162(64.8%)	64(39.5%)	98(60.5%)	
Non-oliguria (>400)	53(21.2%)	5 (9.4%)	48 (90.6%)	
7. Type of Renal Facture :				<0.01
Pre Renal	67(26.8%)	14(20.9%)	53(79.1%)	
Renal	167(66.4%)	71(42.5%)	96(57.5%)	
Post Renal	16(64%)	2 (12.5%)	14(87.5%)	
8. Causes of AKI				<0.01
Surgical	56(22.4%)	12(21.4%)	44(78.6%)	
Medical	177(70.8%)	72(40.7%)	105(59.3%)	
Obstetrical	17(6.8%)	3(17.6%)	14(82.4%)	
9. No. of Other Organ failure:				
1	101 (40.4%)	13 (12.9%)	88 (87.1%)	<0.01
2	75 (30%)	24 (32%)	51 (68%)	
3	62 (24.8%)	41 (66.1%)	21 (33.9%)	
4	12 (4.8%)	9 (75%)	3 (25%)	
10. Serum Sodium Level (mEq/l) :				
<120	22 (8.8%)	14 (63.6%)	8 (36.4%)	<0.01
120-134	122 (48.8%)	45 (36.9%)	77 (63.1%)	
135-145	91 (36.4%)	21 (23.1%)	70 (76.9%)	
>145	15 (6.0%)	7 (46.7%)	8 (53.3%)	
11. Management strategy :				
No RRT	186(74.4%)	59(31.7%)	127(68.3%)	<0.01
HD	56(22.4%)	20(35.7%)	36(64.3%)	
PD	7(2.8%)	7 (100%)	0 (0%)	
HD/PD	1(0.4%)	1 (100%)	0(0%)	

Table 4: Association of Type of Renal Failure with duration of hospital stay

		Mean	P value
Type of Renal Failure	Pre Renal	9.06 ± 6.46	0.41
	Renal	8.10 ± 5.32	
	Post renal	7.50 ± 4.22	
Cause of AKI	Surgical	11.86 ± 1.07	<0.001
	Medical	6.88 ± 3.75	
	Obstetrical	11.71 ± 5.52	

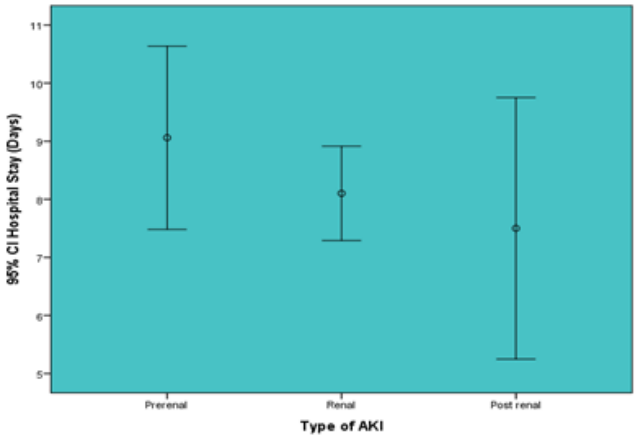
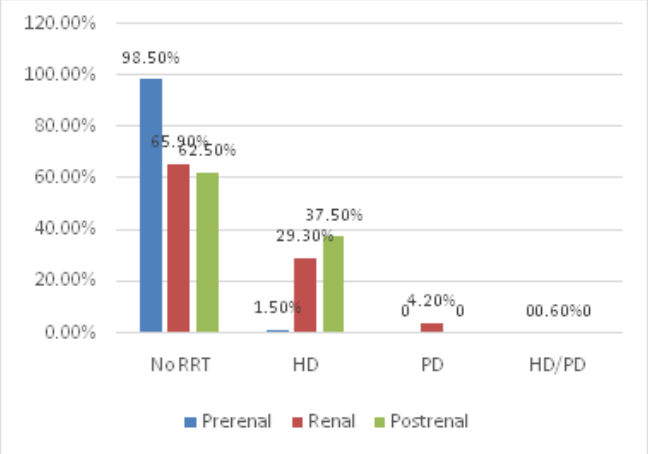


Table 5: Comparison of Mean Age, Urea Level and Serum Creatinine Level in Different Type of AKI

	Type of AKI			P value
	Prerenal	Renal	Postrenal	
Age (in years)	48.22±19.24	42.92±16.88	59.38±20.17	<0.01
Urea (mg/dl)	150.55±54.45	160.40±67.45	189.37±79.65	0.17
S. creatinine (mg/dl)	3.69±1.50	4.57±2.59	6.45±4.56	<0.01

Table 6: Management Strategy with type of Renal Failure



Highest significantly if there was other organs also involved i.e. if there was MODS present. In maximum cases (98.5%) of prerenal AKI, RRT was not required while for renal & post renal cause in around one-thirty of study subject RRT was given. This association was found statistically significant (P<0.001). Mean duration of hospital stay was significantly high for surgical and obstetrical causes of AKI. (P value <0.001)

6. Discussion

This study was conducted on patients of AKI admitted in various wards of R.N.T. Medical Collage, Udaipur & Attached hospitals. In the present study, age of the patients ranged from 18 to 90 years with a mean age of 45.1±18.2 years. There were 153 (61.2%) male and 97 (38.8%) females. Kandoth et al[5] conducted prospective study over two and a half years and analyzed 48 children of acute renal failure requiring dialysis therapy and reported that 67% of male & 23% of female patients are brought to the hospitals within 24 hours of oliguria. Berniech B[6] et al in their study of pattern of acute renal failure on 62 patients reported that 58% were males & 42%were females with mean age of 56.2 years. Similar to our study Ravindra L. Mehta et al[7] reported that out of 215 ICU patients with AKI, 59% males & 41% were females with mean age of 59.5 years, in our study mean age was lesser compared to other two studies. In a study by Yousuf Khan et al[12], out of 50 cases studied, 32(64%) patient were males and 18(36%) were females. Their age ranged from 20 to 65 years with mean age of 48.1years which was similar to our study. We concluded that Fever followed by oliguria, GI symptoms and shortness of breath were most common presenting symptoms comprising of 57.6%, 38.4%, 38% and 33.6% respectively. The incidence of pain abdomen (19.6%) and seizure and altered sensorium (18.0%) were also noticed. These findings were compared with other studies done by Singhal AS et al[9], which showed that oliguria and vomiting was seen in 85.2% and 80% of patients respectively. In the present study most common causes of AKI was medical (70.8%) followed by surgical (22.4%) & an obstetrical cause was responsible for 17 (6.8%). Medical AKI patients had high mortality with statistically significant association. Renal AKI were more associated with poor prognosis. This association was statistically

significant (P<0.01). prerenal AKI had best prognosis in our study. Out of 250 patient studied, 103 (41.2%) were in stage 1, while 90 (36%) were in stage 2. As stage of AKI increased mortality also increased significantly (P<0.001). In our study, dyselectrolytemia was also associated with poor prognosis. (P<0.01) Out of 250 patient 56 (22.4%) were kept on hemodialysis and 7 (2.8%) causes were dept on peritoneal dialysis while most of patient did not require any RRT. However mortality was highly in HD or PD group & this was statistically significant (P<0.001). Mortality was fever was seen in 57.6% of study subjects which was not observed in other studies. This could be explained by higher incidence of ARF associated with infections like scrub typhus, Dengue, Malaria in present study. Liano F et al, [10] in her conducted on 748 subjects of ARF found that hypotension was present in 32.8% of patients. 52% of patients had hypotension in Bernieh B et al[6] study and 20.6% of patients had hypotension in a study done by Singhal AS.[9]Similar to our study P Tabitha R J Chandrika et al[11] also observed in 100 patients admitted with AKI that oliguria or anuria (61%) and fever (55%) were most common sign & symptoms followed by diarrhea (34%), vomiting (32%), breathlessness (31%) and altered sensorium (20%). Yousuf Khan et al[12] also reported that Fever was observed in 35 (70%) cases and 16(32%) patient had loose stools, on general physical examination 15(30%) patients had hypotension, 14 (28%) patients had edema and 12 (24%) had icterus in AKI patients.

In present study, most common cause of AKI was Acute febrile illness (AFI) (45.6%) followed by hypovolemia (22.4%) and sepsis (8.8%). Other causes were postoperative uropathy (4.8%), obstructive uropathy (6.0%), cardiac causes (3.6%) etc. Renal level failure was the most common type (66.8%) followed by prerenal (26.8%). In 16 (6.4%) study subjects cause was observed at post renal level. This was compared with study done by Liano F et al[10], which has shown prerenal AKI was seen in 21% of patients. Similar findings were observed by Yousuf Khan et al[12] in which 10 (20%) patients had pre renal AKI, renal AKI was seen in 38(76%) patients, and 2(4%) had post renal AKI. Of the 10 patients who had prerenal AKI, 4 patients had acute GE, 5 patients had Malaria and one patient had AKI following septicemia and of the 38 patients who had renal AKI, malaria was the most common cause seen in 12 patients followed by drug induced AKI (6), septicemia (6) and acute gastroenteritis (5). Of 50 cases 2(4%) patients had AKI following bladder outlet obstruction. P. Vijai Ananth, et al[13] found acute diarrheal disease (ADD) as the most common cause in 44% of the cases, followed by multiple infections (leptospirosis+ malaria+ enteric fever) in 12% of the subjects and Sepsis in 10% of the subjects out of 100 cases studied. Yatendra Singh et al[14] from Uttarakhand also reported that out of 100 patients admitted with ARF, septicemia (32%) was most common cause of AKI followed by acutegastroenteritis (26%). Drug induced AKI was responsible in 8% of cases. Intrinsic renal ARF was seen in 52% patients. Forty percent patients had prerenal ARF and 8% had post renal ARF. In the present study out of 250 patients, 163 (65.2%) patients survived and about 87 (34.8%) patients expired. Out of 250 patients 56 (22.4%) were kept on hemodialysis and 7 (2.8%) were kept on peritoneal dialysis while most of the patients (74.4%) did not require RRT and were managed conservatively. However, mortality was higher in HD or PD group then conservative management and difference was found to be statistically significant. This was comparable to study done by Hakim al et al[15] in which 74% of patients were managed conservatively and 26% of patients underwent hemodialysis. However, in a study by Hakim al et al[15] about 58% of patients survived with conservative management and 48% survived among dialysis patients. In a study by Yatendra Singh et al[14] 64% patients were managed conservatively and 36% patients underwent hemodialysis. Among the patients managed conservatively, 23.43% patient died and among those who underwent hemodialysis 16.66% patients died. The difference in mortality was not statistically significant (P>0.05).The mortality in his study was 21%.In study by P Tabitha R J Chandrika et al[11] 48% patients of AKI required hemodialysis while 52% were treated conservatively. Out of 250 patients of AKI studied, 103 (41.2%) were in stage 1, while 90 (36%) were in stage 2.As stage of AKI increased mortality also increased significantly. Most common cause of AKI was medical (70.8%) followed by surgical (22.4%). Obstetrical cause was responsible for 17 (6.8%) cases. Medical causes were more associated with mortality in AKI patients and this association was found to be statistically significant (p =0.01).Similarly, P Tabitha R J Chandrika et al[11]also reported that out of 100 cases studied, 76% were due to medical causes, 16% were due to surgical causes and rest 8% were due to obstetric causes. In our study, we concluded that, higher level of serum urea level was associated with higher mortality but this relation was not statistically significant.(P-0.80) In study by P Tabitha R J Chandrika et al[11], more than one third (36.8%) of study subjects urea level was between 101-150mg/dl. In 23.6% subjects urea level was >200mg/dl. There were about 59 patients with blood urea of more than 200 mg/dl, out of which 22 (37.3%) died. The overall mortality had been increased in patients with blood urea more than 200mg/dl.

In present study 90 patients presented after 7 days of illness, in which mortality was 42.2% while only 21.4% died if they presented within 3 day of illness. Similar results were seen by Yatendra singh et al[14] in which they compared mean duration of symptoms before hospitalization and mortality, the patients who present late in their hospital (>3 days) the mortality was statistically significant (P<0.05).Guerin et al[16]., in his study found that incidence of AKI in hospitalized patients with serum creatinine more than 3.4meq/dl was 7.7% and need for renal replacement therapy is more. Overall hospital mortality due to AKI was 60% and 81% in patients developed AKI within one week of admission to ICU. In our study, there were about 111 (44.4%) patients with serum creatinine more than 4 meq/L, out of which 43 (38.7%) died. The overall mortality had been increased in patients with serum creatinine more than 4meq/l.In P Tabitha R J Chandrika et al[11] study mean serum creatinine levels were high in the acute kidney injury patients who only partially improved and in those who died when compared to those of improved and this difference was

statistically significant with low p-values (0.05%). In present study out of 250 patients, 162 (64.8%) were oliguric and mortality was 39.5% among them while mortality was 51.5% among anuric patients. This association with outcome was also found to be statistically significant. Similarly, in study of Yatendra Singh et al[14], 20 patients had non-oliguric AKI and mortality in non-oliguric AKI was 5% as compared to 40% in the oliguric patients (P<0.05).P Tabitha R J Chandrika et al[11] also found significant difference (30.7%-70.8%) in the pattern of outcome in acute kidney injury patients with normal urine output and those with oliguria and anuria and this difference was found to be statistically highly significant (p=0.002). And the risk of death among anuria patients was found to be 1.86 times when compared to those having normal urine output.

7. Conclusion

This study was conducted among 250 patients of AKI admitted in various wards of RNT MC, Udaipur & Attached hospitals. The findings of study were as follows: Mean age of study subjects were 45.1±18.2 years. The clinical features were studied; it was observed that Fever followed by decreased urinary output (38.4%), GI symptoms (38.0%) were the most common presenting symptoms. Most common cause of AKI was AFI (45.6%) followed by hypovolemia (22.4%), sepsis (8.8%). Other causes were postoperative, obstructive uropathy, cardiac cause etc. Renal level failure was the most common type (66.8%) followed by prerenal (26.8%). In 16 study subjects cause was at post renal level. Out of 250 patients of AKI more than one third (34.8%) patients died while rest survived. Most common cause of AKI was medical (70.8%) followed by surgical (22.4%). Obstetrical cause was responsible for 17 (6.8%) cases. Out of 250 patients 56 (22.4%) were kept on hemodialysis and 7 (2.8%) were kept on peritoneal dialysis while most of the patients (74.4%) does not required RRT. However, mortality was higher in HD or PD group then conservative management. Higher S. Bilirubin level, low platelets, low blood pressure, low urinary output, medical cause, higher stage of AKI, presence of ARDS, S. sodium level, requirement of mechanical ventilation & no. organs failed were found to be associated with higher mortality in AKI patients.

8. Recommendations & Limitations

Timely diagnosis and management of this disease condition confer a favorable prognosis to the patient. The progression of AKI leads to increased hospital mortality rates and increased length of stays that might prove a wastage of limited resources in a setting like India. Hence more number of studies has to be done to efficiently pinpoint the predictors of AKI and preventing its occurrence in the near future. This study was conducted at a tertiary care hospital in Udaipur Rajasthan. Facilities available at this centre are difficult to replicate at all hospitals across the country. Hence the results have limited generalizability. Furthermore, no outcome monitoring was performed beyond the period of hospitalization. Therefore, key data including the mortality rate, can be underrepresented.

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