IJBPAS, February, Special Issue, 2022, 11(2): 364-376
ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)
'A Bridge Between Laboratory and Reader'

www.ijbpas.com

STUDY OF CLINICAL PROFILE OF ACUTE KIDNEY INJURY IN DENGUE

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Received 15th July 2021; Revised 18th Aug. 2021; Accepted 29th Oct. 2021; Available online 15th Feb. 2022

https://doi.org/10.31032/IJBPAS/2022/11.2.1045

ABSTRACT

Introduction

Acute kidney injury presents as major complication of infective and non-infective aetiology. Acute febrile illness is a major cause of mortality.Our study aims to study incidence and spectrum of acute kidney injury in dengue.

Material and Methods

The cross sectional observational study was conducted in The Department of General Medicine at Dr D.Y. Patil Medical College, Hospital & Research Centre, situated in Pimpri, Pune. Approval was taken from Institutional Ethical Committee. All patients admitted to medical wards and MICU in Dr D.Y Patil Hospital, during September 2018 – August 2020, diagnosed with acute febrile illness were subjected to the study as per study design. A total of 100 patients of acute febrile illness admitted in all medical wards and MICU were selected for the study. The diagnosis was made as per the standard diagnostic criteria. All patients aged more than 12 yearsand all patients who present with symptoms of acute febrile illness were included in our study. Patients with age less than 12 years, pregnant females, chronic kidney disease patients, immunocompromised patients were excluded.

Results

Mean age of the participants in our study was 36.8 ±15.1 years. Out of 100 patients, 86 (86.0) participants were male and 14 (14.0) participants were female. According to RIFLE criteria, it was observed that 60 (60.0) participants were in Normal Grade, 17 (17.0) participants were in Risk Grade, 9 (9.0) participants were in Injury Grade and 14 (14.0) participants were in Failure grade. According to AKIN grading, it was observed that 61 (61.0) participants were in Normal Grade, 21 (21.0) participants were in Grade 1, 11 (11.0) participants were in Grade 2 and 7 (7.0) participants were in Grade 3. According to RIFLE criteria, It was observed that among the 74 Dengue NS1 positive participants, 52 participants were in Normal Grade,10 participants were in Risk Grade, 5 participants were in Injury Grade and 7 participants were in Failure grade and as per AKIN grading 52 participants were in Normal Grade, 12 participants were in Grade 1, 7 participants were in Grade 2 and 3 participants were in Grade 3.

Conclusion

Dengue is most common cause of AFI and AKI in this study. Acute Kidney Injury is major risk factor for morbidity with patients requiring Renal Replacement therapy in few patients in this study.

Keywords: Dengue, acute febrile illness, acute kidney injury, AKIN, RIFLE

INTRODUCTION

Acute Febrile Illness (AFI) is defined as all acute febrile syndromes with oral temperature more than 37.5°C which last from 24 hours to less than two weeks, including nonspecific symptoms that are not helpful for us to localize to a particular system. Acute Febrile Illness can present with fever, generalized body pain, vomiting, generalized swelling of the body, loose stools, decreased urine output, swelling of legs, breathlessness, headache, cough, chest pain, altered sensorium and signs like fever, rashes, tachycardia, myalgia, conjunctival congestion and others.[1–7] Acute kidney injury (AKI) is defined as heterogenous syndrome characterised by sudden decline in glomerular filtration rate (GFR) culminating into retention of metabolic waste products like urea and creatinine along with dysregulation of electrolytes and fluid and changes in acid base homeostasis.[8]

Acute kidney injury can manifest as a life threatening complication of infective and non-infective aetiology. Acute febrile illness is a major cause of mortality.[4,6] The

relevance of this quest is to minimise mortality and renal morbidity which is amplified by the fact that among all critically ill patients, the mortality is around 60% during hospitalization and dialysis dependency is 13% in survived patients.[9] In patients who recovered from acute renal failure after different periods of renal replacement therapy, 41% had a deterioration in renal function and five-year survival was present in 50% patients.[10] This puts an additional burden on health care system and economy.[11] Infectious disease resulting from established as well as novel bacterial and viral diseases are increasing with 13 million fatalities annually.

In developing nations infectious diseases account for about 50% deaths, as a consequence of increase in incidence of these diseases and poor health care infrastructure.[4] Majority of these diseases are sub optimally managed in the community, and they frequently present with complications that require referral to higher centres. Alternatively long hours spent in travel to health care centres contribute to deterioration in organ function and reserve. Our study aims to study incidence and spectrum of acute kidney injury in acute febrile illness.

MATERIAL AND METHODS

Approval was taken from the Institutional Ethical Committee before commencing the study. Consent (informed and written) was taken from all patients included in the study. The patients were informed about the study in their own comprehensible language.The study was conducted on 100 patients admitted in DR. D Y Patil medical college and hospital, pimpri, Pune with acute febrile illness symptoms. All patients with age more than 12 years were enrolled in the study. Detailed history of all participants was taken which included past, personal, medication and addiction history. Detail evaluation of all symptoms like fever, body ache, rash and other non-specific symptoms.

The data was analysed using social science statistics software web version. The graphs and tables were prepared using Microsoft Word and Excel (2010). The one-way analysis of variance was used for any statistically significant differences in independent groups. Chi-square test And Student's t test were used to test whether distributions of categorical variable differ from each another. P value was considered as significant if lesser than 0.05 at 95% confidence interval.

RESULTS

Mean age of the participants in this study was 36.8 ±15.1 years **(Table 1)**. Out of 100 participants, 86 (86.0) were male and 14

(14.0) were female It was observed that all the participants showed improved prognosis.

According to RIFLE criteria, it was observed that 60 (60.0) participants were in Normal Grade, 17 (17.0) participants were in Risk Grade, 9 (9.0) participants were in Injury Grade and 14 (14.0) participants were in Failure grade. According to RIFLE criteria, It was observed that among the 74 Dengue NS1 positive participants, 52 participants were in Normal Grade, 10 participants were in Risk Grade, 5 participants were in Injury Grade and 7 participants were in Failure grade. In the present study, according to RIFLE grade, it was observed that haemodialysis was required in 1 participant in injury group and 6 participants in failure group **(Table 2, Figure 1)**.

According to AKIN grading, it was observed that 61 (61.0) participants were in Normal Grade, 21 (21.0) participants were in Grade 1, 11 (11.0) participants were in Grade 2 and 7 (7.0) participants were in Grade 3. According to AKIN grade, it was observed that haemodialysis was required in 4 normal participants, 1 participant in Grade 2 group and 2 participants in Grade 3 group **(Table 3, Figure 2)**. In AKIN grading Dengue NS1 positive 52 participants were in Normal Grade, 10 participants were in Grade 1, 7 participants were in Grade 2 and 3 participants were in Grade 3.

The above **Table 5** shows comparison of Renal function test with RIFLE grading. It was observed that there was statistically significant difference observed in Urea and Creatinine level at day 0, day 2 and day 5 level between Normal participants and RIFLE grading with p value less than 0.05.

The above **Table 6** shows comparison of Glomerular filtration rate on day 0, day 2 and day 5 level with RIFLE grading. It was observed that there was statistically significant difference observed in Glomerular filtration rate on day 0, day 2 and day 5 level between Normal participants and RIFLE grading with p value less than 0.05.

The above **Table 7** shows comparison of Glomerular filtration rate on day 0, day 2 and day 5 with AKIN grading. It was observed that there was no statistically significant difference observed in Glomerular filtration rate on day 0, day 2 and day 5 between Normal participants and AKIN grading with p value more than 0.05.

Table 1: Distribution of study variables among the study participants (N=100)

S. No.	Variable	Frequency	Percentage
1	Age		
	<20	13	13
	21-30	31	31
	31-40	20	20
	41-50	18	18
	51-60	10	10
	61-70	5	5
	71-80	3	3
2	Gender		
	Male	86	86
	Female	14	14
3	USG findings		
	Mild Hepatomegaly	2	2
	Mild Splenomegaly	6	6
	Mild Hepatosplenomegaly	6	6
	Normal	86	86
4	RIFLE Grade		
	Normal	60	60
	Risk	17	17
	Injury	9	9
	Failure	14	14
5	AKIN Grade		
	Normal	61	61
	Grade 1	21	21
	Grade 2	11	11
	Grade 3	7	7
6	KDIGO Grade		
	Normal	60	60
	Grade 1	17	17
	Grade 2	9	9
	Grade 3	14	14

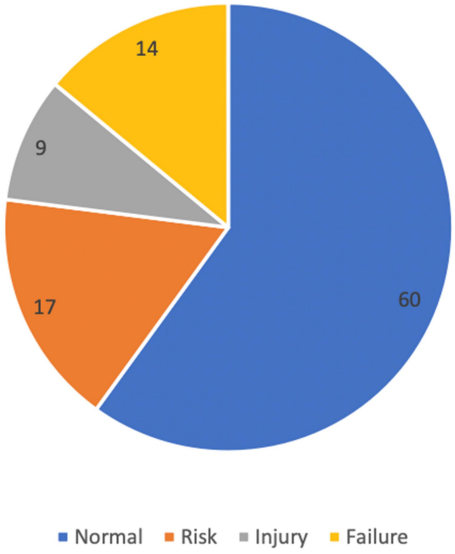

Figure 1: Distribution of participants according to RIFLE Grade (N=100)

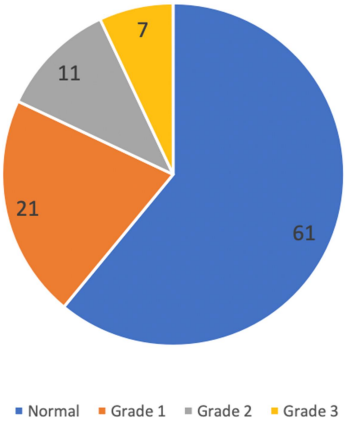

Figure 2: Distribution of participants according to AKIN grade (N=100)

Table 2: Comparison of study variables with RIFLE grading (N=100)

S. No.	Variable	Normal	Risk	Injury	Failure
1	Age				
	<20	8	2	2	1
	21-30	19	3	3	6
	31-40	14	2	2	2
	41-50	11	4	1	2
	51-60	6	2	0	2
	61-70	2	2	0	1
	71-80	0	2	1	0
2	Gender				
	Male	52	14	7	13
	Female	8	3	2	1
3	Dengue				
	NS1	52	10	5	7
	IgM	52	10	5	7
	IgG	0	0	0	0
4	Haemodialysis				
	Yes	0	0	1	6
	No	60	17	8	8
5	Prognosis				
	Improved	60	17	9	14

Table 3: Comparison of study variables with AKIN grading (N=100)

S. No.	Variable	Normal	Grade 1	Grade 2	Grade 3
1	Age				
	<20	8	2	2	1
	21-30	18	6	4	3
	31-40	15	2	3	0
	41-50	12	5	1	0
	51-60	6	2	0	2
	61-70	2	2	0	1
	71-80	0	2	1	0
2	Gender				
	Male	56	17	7	6
	Female	5	4	4	1
3	Dengue				
	NS1	52	10	5	7
	IgM	52	10	5	7
	IgG	0	0	0	0
4	Haemodialysis				
	Yes	4	0	1	2
	No	57	21	10	5
5	Prognosis				
	Improved	61	21	11	7

Table 5: Comparison of Renal function test with RIFLE grading (N=100)

RIFLE Grade		Urea Day 0	Creatinine Day 0	Urea Day 2	Creatinine Day 2	Urea Day 5	Creatinine Day 5
Normal	Mean	40.90	0.97	49.30	1.42	59.10	1.62
	N	60	60	60	60	60	60
	SD	19.06	0.20	28.26	0.75	42.05	0.68
Risk	Mean	42.06	0.94	54.88	2.52	66.29	2.52
	N	17	17	17	17	17	17
	SD	17.23	0.16	29.43	0.38	41.19	0.46
Injury	Mean	65.11	1.24	106.22	3.90	160.11	4.14
	N	9	9	9	9	9	9
	SD	18.29	0.19	17.36	0.59	27.08	0.69
Failure	Mean	73.71	1.25	121.79	3.89	184.64	5.34
	N	14	14	14	14	14	14
	SD	16.34	0.14	22.17	1.22	31.81	0.48
Total	Mean	47.87	1.03	65.52	2.17	86.99	2.52
	N	100	100	100	100	100	100
	SD	21.99	0.22	38.50	1.28	62.45	1.50
P value		0.001	0.001	0.001	0.001	0.001	0.001

Table 6: Comparison of Glomerular filtration rate on day 0, day 2 and day 5 with RIFLE grading (N=100)

RIFLE Grade		GFR Day 0	GFR Day 2	GFR Day 5
Normal	Mean	103.51	83.51	69.48
	N	60	60	60
	SD	35.62	25.53	19.64
Risk	Mean	98.56	78.31	64.51
	N	17	17	17
	SD	33.17	22.19	16.45
Injury	Mean	85.59	63.19	50.87
	N	9.00	9.00	9.00
	SD	48.32	29.09	20.01
Failure	Mean	66.36	53.21	44.94
	N	14	14	14
	SD	43.33	31.18	27.40
Total	Mean	95.86	76.55	63.53
	N	100	100	100
	SD	39.23	28.06	22.13
P value		0.001	0.001	0.001

Table 7: Comparison of Glomerular filtration rate on day 0, day 2 and day 5 with RIFLE grading (N=100)

AKIN Grade		GFR Day 0	GFR Day 2	GFR Day 5
Normal	Mean	99.14	80.24	66.97
	N	61	61	61
	SD	37.94	27.55	21.41
Grade 1	Mean	97.15	77.01	63.01
	N	21	21	21
	SD	35.77	24.75	18.94
Grade 2	Mean	78.75	58.80	47.66
	N	11	11	11
	SD	46.27	28.35	19.81
Grade 3	Mean	90.24	70.90	60.01
	N	7	7	7
	SD	49.76	35.55	32.33
Total	Mean	95.86	76.55	63.53
	N	100	100	100
	SD	39.23	28.06	22.13
P value		0.44	0.12	0.06

DISCUSSION

Distribution of participants according to age group

In the present study, it was observed that 13 (13.0) participants were less than 20 years, 31 (31.0) participants were between 21-30 years, 20 (20.0) participants were between 31- 40 years, 18 (18.0) participants were between 41-50 years, 10 (10.0) participants were between 51-60 years, 5 (5.0) participants were between 61-70 years and 3 (3.0) participants were between 71-80 years. In the present study, it was observed that mean age of the study participants was 36.8 ±15.1 years. In the study conducted by C.M.Atkar *et al*.,[12] it was observed that mean age of the study participants was 41.76±12.51 years. In the study conducted by JayalalJayapalan Nair *et al*.,[13] it was observed that mean age of the study participants was 40.34±15.42 years. In the study conducted by Gopal Basu *et al*., [3] it was observed that mean age of the study participants was 39.7±16.9 years. In the present study, according to RIFLE grading, it was observed that in 21 -30 years age group, 19 participants were in Normal Grade, 3 participants were in Risk Grade, 3 participants were in Injury Grade and 6 participants were in Failure grade. While among the 71 – 80 years age group, 2 participants were in the risk group and 1 participant was in the injury group. In the present study, according to AKIN grading, it was observed that in 21 -30 years age group, 18 participants were in Normal Grade, 6 participants were in Grade 1, 4 participants were in Grade 2 and 3 participants were in Grade 3 while among the 31 – 40 years age group, 15 participants were in Normal Grade, 2 participants were in Grade 1, 3 participants were in Grade 2 and 0 participants were in Grade 3.

Distribution of participants according to Gender

In the present study, it was observed that 86 (86.0) participants were male and 14 (14.0) participants were female. The male to female ratio is 6.1:1. In the study conducted by C.M.Atkar *et al*.,[12] it was observed that 93 (66.4) participants were male and 47 (33.6) participants were female. The male to female ratio is 2:1. In the study conducted by Kallol Bhattacharjee *et al*., [14] it was observed that 132 (66.0) participants were male and 68 (34.0) participants were female. The male to female ratio is 2:1. In the study conducted by JayalalJayapalan Nair *et al*.,[13] it was observed more than ¾th of the participants were males. The male to female ratio is 3:1. In the study conducted by Gopal Basu *et al*., [3] it was observed that 219 (59.7) participants were male and 148 (40.3) participants were female. The male to female ratio is 1.5:1. In the present study, according to RIFLE

grading, it was observed that among the male participants 52 participants were in Normal Grade, 14 participants were in Risk Grade, 7 participants were in Injury Grade and 13 participants were in Failure grade while among the female participants 8 participants were in Normal Grade, 3 participants were in Risk Grade, 2 participants were in Injury Grade and 1 participant was in Failure grade. In the present study, according to RIFLE grading, it was observed that among the male participants 56 participants were in Normal Grade, 17 participants were in Grade 1, 7 participants were in Grade 2 and 6 participants were in Grade 3 while among the female participants 5 participants were in Normal Grade, 4 participants were in Grade 1, 4 participants were in Grade 2 and 1 participant was in Grade 3. In the study conducted by Kallol Bhattacharjee *et al*.,[14] it was observed that among the male participants 32 (24.2) had AKIN while among the female participants 20 (29.4) participants had AKIN. In the study conducted by Kanodia *et al*.,[15] it was observed that 63% participants were male and 37% participants were female. These findings are similar to our study.

Distribution of participants according to RIFLE Grade

In the present study, it was observed that 60 (60.0) participants were in Normal Grade, 17 (17.0) participants were in Risk Grade, 9 (9.0) participants were in Injury Grade and 14 (14.0) participants were in Failure grade. In the study conducted by C.M.Atkar *et al*.,[12] it was observed that 101 (72.1) participants were in Normal Grade, 13 (9.3) participants were in Risk Grade, 10 (7.1) participants were in Injury Grade and 16 (11.4) participants were in Failure grade.

Distribution of participants according to AKIN grade

In the present study, it was observed that 61 (61.0) participants were in Normal Grade, 21 (21.0) participants were in Grade 1, 11 (11.0) participants were in Grade 2 and 7 (7.0) participants were in Grade 3. In the study conducted by JayalalJayapalan Nair *et al*.,[13] it was observed that 152 (46.9) participants were in Grade 1, 101 (31.2) participants were in Grade 2 and 71 (21.9) participants were in Grade 3.

Comparison of RIFLE grading among Dengue Patients

It was observed that among the 74 Dengue NS1 positive participants,52 participants were in Normal Grade,10 participants were in Risk Grade, 5 participants were in Injury Grade and 7 participants were in Failure grade.

In the study conducted by Gopal Basu *et al*., [3] according to RIFLE category, among the Dengue participants, 4 (14.3) participants had Risk grade, 1 (3.6)

participant had Injury grade and 5 (17.9) participants had Failure grade.

Comparison ofAKIN grading in Dengue

In the present study, it was observed that among the 74 Dengue NS1 positive participants, 52 participants were in Normal Grade, 12 participants were in Grade 1, 7 participants were in Grade 2 and 3 participants were in Grade 3.

In the study conducted by C.M.Atkar *et al*., [12] among the Dengue participants, in 10 (27.0) participants AKI was present while in 27 (73.0) participants AKI was absent.

In the study conducted by Kallol Bhattacharjee *et al*.,[14] among the Dengue participants, in 1 (12.5) participants AKI was present.

Comparison of creatinine and GFR level

In the present study, it was observed that there was statistically significant difference observed in Creatinine level and GFR at day 0, day 2 and day 5 level between Normal participants and RIFLE grading with p value less than 0.05. The mean creatinine level at Day 5 in risk group was 2.52 ± 0.46 mg/dL, in injury group was 4.14 ± 0.69 mg/dL and in failure group was 5.34 ± 0.48 mg/dL. The mean GFR level at Day 5 in risk group was 64.51 ± 16.45 mg/dL, in injury group was 50.87 ± 20.01 mg/dL and in failure group was 44.94 ± 27.40 mg/dL, In the study conducted by Gopal Basu *et al*., [3] the mean creatinine level in the Risk grade is 1.2 ± 0.3 mg/dL, in the injury grade is 1.8 ± 0.6 mg/dL and in the failure grade is 4.0 ± 2.7 mg/dL, In the study conducted by Gopal Basu *et al*., [3] the mean GFR in the Risk grade is 62.6 ± 13.6 mL/min/1.73 m2, in the injury grade is 46.2 ± 21.0 mL/min/1.73 m2 and in the failure grade is 25.5 ± 21.6 mL/min/1.73 m2. In the present study, it was observed that there was no statistically significant difference observed in Glomerular filtration rate on day 0, day 2 and day 5 in normal participants and with p value more than 0.05. In the study conducted by Gopal Basu *et al*., [3] 69 (45.7%) had a GFRdis<60 mL/min/1.73 m2, compared with none in the non-AKI group. Two of the three patients with pre-existing CKD had a GFRdis<60 mL/min/1.73 m2. In the study conducted by Gopal Basu *et al*.,[3] the mean creatinine level in the Risk grade is 1.2 ± 0.3 mg/dL, in the injury grade is 1.8 ± 0.6 mg/dL and in the failure grade is 4.0 ± 2.7 mg/dL. In the study conducted by Gopal Basu *et al*., [3] the mean GFR in the Risk grade is 62.6 ± 13.6 mL/min/1.73 m2, in the injury grade is 46.2 ± 21.0 mL/min/1.73 m2 and in the failure grade is 25.5 ± 21.6 mL/min/1.73 m2.

Comparison of haemodialysis as per Rifle Grade

In the present study, according to RIFLE grade, it was observed that haemodialysis

was required in 1 participant in injury group and 6 participants in failure group. In the study conducted by Gopal Basu *et al*.,[3] it was observed that 29 (7.9) participants required hemo-dialysis.

Comparison of haemodialysis as per AKIN Grade

In the present study, according to AKIN grade, it was observed that haemodialysis was required in 4 normal participants, 1 participant in Grade 2 group and 2 participants in Grade 3 group. In the study conducted by Kallol Bhattacharjee *et al*., [14] hemodialysis was required each in leptospirosis, enteric fever, dengue fever, falciparum malaria and mixed malaria. Total 5 participants required hemodialysis.

Comparison of Prognosis as per AKIN Grade

In the present study, it was observed that all the participants showed improved prognosis. In the study conducted by Kallol Bhattacharjee *et al*., [14] out of 52 participants who developed AKIN, 5 participants required Renal replacement therapy. Mortality was observed in 1 participants. Among this 1 was having dengue fever which complicated to Dengue shock syndrome.

The number of patients admitted during study with Acute Febrile illness was mostly of male gender. As there was no serum creatinine values prior to admission in hospital, possibility of acute on chronic failure cannot be denied. The study was conducted in tertiary care hospital, so referral bias arising from severely ill patients reaching a tertiary care centre, may overestimate the incidence of Acute Kidney Injury.

CONCLUSION

Acute Kidney injury in Acute Febrile Illness is common in tertiary care hospital and is assosciated with adverse events including high mortality and need for dialysis Adults are at more risk for Acute Kidney injury. The incidence of AKI among these patients is 40%

Acute Kidney Injury is a major risk factor for morbidity requiring Renal Replacement therapy in few patients in this study. So a high degree of suspicion should be kept for Early detection of AKI and aggressive management to reduce incidence of mortality in AFI presented with AKI. No mortality seen in this present study. Awareness about the potential renal complication and its treatment is a lifesaving measure.

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