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STUDY OF CLINICAL PROFILE AND OUTCOME OF DENGUE FEVER WITH RENAL INVOLVEMENT

Medicine

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ABSTRACT

Dengue is a growing public health problem in India and acute kidney injury (AKI) is one of the least studied complications[1]. Dengue virus infection can exhibit a wide spectrum of renal dysfunction including tubular dysfunction (dyskalemia, dysnatremia, and acute tubular necrosis), and less commonly glomerular injury (*ie* microscopic hematuria or proteinuriain and acute kidney injury (AKI)[3]. Data from previous reports have shown that the incidence could be up to 80%.This study is undertaken to evaluate common modes of clinical presentation and renal complications in our hospital and correlate these features with lab findings which may help us in early diagnosis and better case management to reduce mortality.

1.The Aim of this study

a.To study Incidence ,Prevalence and Outcome of Renal Involvement in Dengue Fever

b. To study the impact of AKI on the length of hospital stay and mortality.

2.Materials and methods: It is prospective observational study carried out in a Tertiary Care Hospital. The study population consisted 50 patients of age group above 18 years .

Inclusion criteria: All the adult patients were admitted in General Medicine ward in NAIR Hospital with Dengue NS1/IgM/IgG/RT-PCR test positive were included in study.

Exclusion criteria: Mixed infections and also Patients with pre-existing Renal Diseases were excluded from the study.

Statistical analysis: Data was collected using a predesigned pretested questionnaire, data was entered in Microsoft Excel and was analysed using SPSS version 20 and EpiInfo version 7.2.1.. Significance level was set at $P < 0.05$.

Results: were analysed and discussed.

Conclusion: Out of all 50 cases, 10 patients had Acute kidney injury(20%).There was no any significant association between the gender and presence of AKI ($p = 0.89$).Highly significant association was seen between the diagnosis of dengue type and presence of AKI ($p < 0.001$).Our study observed significant association between the duration of hospital stay and presence of AKI ($p = 0.013$),These parameters conclude that though dengue associated AKI is aseverecondition, if managed properly it resolves after a period of time.

KEYWORDS

dengue infection, renal dysfunction, glomerular injury

1. INTRODUCTION

Dengue fever has a wide geographical distribution, and can present with a diverse clinical spectrum.Renal involvement is one of the most significant target organ involvements in dengue infection[4]. Acute kidney injury (AKI) has been increasingly recognized in dengue virus infection. The incidence of AKI was once as low as 1.6% among 617 Colombian children with dengue virus infection (Mendez and Gonzalez, 2003)[5], but in the recent report, the incidence of AKI had risen to as high as 35.7% in adults infected by dengue virus admitted to the tertiary hospital in India (Basu et al, 2011).

2. MATERIAL AND METHOD:

The study population consisted 50 patients of age group above 18 years those who were admitted with Dengue infection with Dengue NS1/IgM/IgG/RT-PCR test positive.

2. a} Aim and objectives of the study were as follow

1. To study Incidence ,Prevalence and Outcome of Renal Involvement in Dengue Fever
2 To study the impact of AKI on the length of hospital stay and mortality.

2. B} MATERIALS AND METHODS:

It is prospective observational study carried out in a Tertiary Care Hospital. Inclusion / Exclusioncriteria: All the adult patients with Dengue NS1/IgM/IgG/RT-PCR test positive were included in study.Mixed infection and Patients with preexisting Renal Diseases were excluded from thestudy.

2(c).Classification: Definition of AKI

Based on the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, AKI can be defined by either an increase in serum creatinine (S.Cr) by >0.3 mg/dL, an increase in S.Cr by >1.5-times baseline, or a reduction in urine volume <0.5 mL/kg/hour for 6 hours. It can be further subdivided into Acute Kidney Injury Network (**AKIN)** stages based on change in S.Cr level. **RIFLE** criteria are also used in the classification of AKI. A systematic review conducted by Mallhi et al.[7]found that the AKIN criteria was more sensitive as it picked up a higher incidence of AKI (3.3–13.3%).

2.d}Ethics:

The study initiated after obtaining necessary permission from the institutional ethics committee. They are further investigated with other biochemical, microbiological, hematological investigations mentioned in study protocol. For Renal assessment serum Creatinine, eGFR and kidney sizes will be taken and these parameters will be monitored throughout clinical course of disease till discharge or death of the patient.

2. e} Sample size calculation

The sample size was taken as a round figure of 50 patients.

2.f}Statistical analysis:

Data was collected using a predesigned pretested questionnaire, data was entered in Microsoft Excel and was analysed using SPSS version 20 and EpiInfo version 7.2.1. Continuous data will be compared using Student t test. Categorical variables were analyzed using $\chi 2$ or Fisher exact tests. Significance level was set at $P < 0.05$

2(g) Test parameters: The test for dengue was done using a rapid solid phase immune-chromatographic test for the qualitative detection of NS1 antigen and differential detection of IgM and IgG antibodies to dengue virus in human serum. The haematological investigations included a complete hemogram and peripheral smear. The blood counts were performed on the fully automated haematologyand biochemistry analyzer

3 RESULTS

The majority of our patients were diagnosed with dengue in the post monsoon months of September and October. Most of the patients presented with clinical symptoms of fever, myalgia and headache for 3 to 5 days. On examination, a rash was observed in very few cases. Only those patients tested positive for dengue were considered for the present study. Such patients were further tested for liver and renal involvement **Table 1** & **Table 2**

In our study, there were 29 (58%) males and 21 (42%) females. Males

were in majority in our study, with a male: female ratio of 1.38: 1.The majority of the study patients (98%) complained of fever with chills. Many had generalised body ache (62%), some patients had nausea (46%). history of rash (42%), headaches (38%) and bleeding manifestations (34%). Few patients also had oliguria (8%) and anemia (6%).Rash was the sign that was majorly observed in many patients (60%), other signs observed were Petechiae (24%), icterus (14%), pallor (6%) and pedal edema (4%).

On examination some patients showed tenderness per abdomen (18%), few showed bilateral chest Crepitations (12%), while 2 patients (4%) had altered sensorium. The blood urea and serum creatinine levels were raised in 23% of the patients and were normal in the rest of the patients. The average blood urea level was 40.2 mg/dl and that of serum creatinine was 1.5 mg/ dl.

Table 1: Investigations: Means of labparameters

Parameter	Mean	SD
Hemoglobin (g%)	12.35	2.01
TLC (mm3/ dl)	6305.60	3058.76
Platelet count	99325.00	79807.67
SGOT	80.76	82.74
SGPT	104.72	128.20
S. Creatinine	0.82	0.70
BUN	16.74	14.21
eGFR	115.94	49.27
Sodium	139.04	6.44
Potassium	4.22	0.75

Mean hemoglobin of the study patients was 12.35 ± 2.01 g%, mean platelet count was 99325.0 ± 79807.67. Mean Serum creatinine was 0.82 ± 0.70. Other means of different laboratory tests are as shown in the table.

Table 2:Dengue specific investigations

Investigation	Positive N (%)	Negative N (%)	Total N (%)
Dengue NS1	36 (72%)	14 (28%)	50 (100%)
Dengue IgM	9 (18%)	41 (82%)	50 (100%)
Dengue IgG	8 (16%)	42 (84%)	50 (100%)
Dengue PCR*	6 (60%)	4 (40%)	10* (100%)

Our study observed that majority of the patients (72%) had Dengue NS1 antigen test positive, few were positive for Dengue IgM (18%) and IgG (16%). Dengue PCR was done in 10 suspected cases which were showing signs of dengue but were tested negative by other tests, in those cases 6 were positive (60%) while rest 4 were negative (40%).

Table 3: Other Investigation findings

Investigation Findings	Present N(%)	Absent N(%)	Total N(%)
Hematuria on Urine Routine	10 (20%)	40 (80%)	50 (100%)
B/L Heterogeneous opacity on X ray Chest	5 (10%)	45 (90%)	50 (100%)
ECG Abnormalities	41 (82%)	9 (18%)	50 (100%)
Corticomedullary differentiation lost on USG	7 (14%)	43 (86%)	50 (100%)
Raised Cortical echogenicity on USG	11 (22%)	39 (78%)	50 (100%)

On further investigations, hematuria was seen in some cases (20%), X ray showed bilateral heterogeneous opacity in few cases (10%), while Ultrasonography showed raised cortical echogenicity in some (22%) cases and Corticomedullary differentiation was lost in few cases (14%). Table 3

ECG was abnormal in many patients (82%), of which 35 cases showed sinus tachycardia (70% of the total cases), 3 had sinus bradycardia (6% of the total cases) while rest 3 showed low voltage complex (6% of the total cases). Table 4

Table 4: Complications

Complications	Number	Percentage
Hepatic Involvement	11	22%
Isolated AKI	4	8%
Hepatorenal involvement	3	6%
AKI with ARDS	2	4%
Isolated ARDS	1	2%
Hepatic Involvement with ARDS	1	2%
Hepatorenal involvement with ARDS	1	2%
No any complication	27	54%
Total	50	100%

Out of all 50 patients, 23 had some or the other complication (46%) while majority (54%) did not have any complication. The most common complication seen was hepatic involvement (22%) followed by acute kidney injury (8%) and Hepatorenal involvement (6%) in few patients. Table 5

Table 5: Presence of AKI

AKI	Number	Percentage
Present	10	20%
Absent	40	80%
Total	50	100%

Out of all 50 cases, 10 patients had Acute kidney injury (20%).

Table 6: Management of AKI patients

Management	Number	Percentage
Conservative	8	80%
Haemodialysis	2*	20%
Total	10	100%

*Each patient underwent 3 sessions of haemodialysis each.

Majority of the patients who had AKI were managed conservatively (80%), while two of them had to undergo haemodialysis (20%) 3 cycles each. One of the patients on haemodialysis had died while the other recovered subsequently. Table 6 & 7

Table 7. Outcome of Patients with AKI

Outcome	Number	Percentage
Recovery and Discharge	9	90%
Death	1	10%
Total	10	100%

Our study observed that out of all 50 patients, there were two deaths (4%), one of them was a patient on haemodialysis due to AKI, thus concluding a mortality of 10% in patients with dengue related AKI. And the other one was having dengue related ARDS.

DISCUSSION

The mean age in our study was 28.36 ± 10.31 years .In a study by Naqvi.R et al,[4] had higher mean age of 34.65 ± 14.50. years.. Males were in majority in our study, with a male: female ratio of 1.38: 1. The study by Muhammad.A.M[6] et al,had majority males similar to the current study, there were 70.9% males. The majority of the study patients (98%) complained of fever with chills. Many had generalized body ache (62%), some patients had nausea (46%), vomiting (44%), history of rash (42%), headaches (38%) and bleeding manifestations (34%). Few patients also had oliguria (8%) and anemia(6%). Rash was the sign that was majorly observed in many patients (60%), other signs observed were Petechiae (24%), icterus (14%), pallor (6%) and pedal edema (4%).

On examination some patients showed tenderness per abdomen (18%), few showed bilateral chest Crepitations (12%), while 2 patients (4%) had altered sensorium.The study by Karlo et al, had 74% patients with proteinuria and 2.5%with haematuria and fever was seen in 50% of the infected individuals.

Mean heart rate of our study patients was 99.68 ± 17.49 beats per minute, mean systolic and diastolic BP were 106.56 ± 16.45 and 66.64 ± 10.62 mmHg and mean respiratory rate was 17.56 ± 3.90 cycles per minute. ECG was abnormal in many patients (82%), of which 35 cases showed sinus tachycardia (70% of the total cases), 3 had sinus bradycardia (6% of the total cases) while rest 3 showed low voltage complex (6% of the total cases).

Mean hemoglobin of the study patients was 12.35 ± 2.01 g%, mean platelet count was 99325.0 ± 79807.67. Mean Serum creatinine was 0.82 ±0.70.The study by Naqvi.R et al,[4]had mean haemoglobin level of 10.29 which was less than the current study. The mean platelet count was found to be 52.65 ± 41.77 which was well lower than the current study.The study by Cader et al, had creatinine level of 78.9

micromol/L. (median) which is higher than the current study.

Our study observed that majority of the patients (72%) had Dengue NS1 antigen test positive, few were positive for Dengue IgM (18%) and IgG (16%). Dengue PCR was done in 10 suspected cases which were showing signs of dengue but were tested negative by other tests, in those cases 6 were positive (60%) while rest 4 were negative (40%). On further investigations, hematuria was seen in some cases (20%), X ray showed bilateral heterogeneous opacity in few cases (10%), while Ultrasonography showed raised cortical echogenicity in some (22%) cases and Corticomedullary differentiation was lost in few cases (14%).Majority of the patients were diagnosed as having dengue fever (68%), some were diagnosed as dengue hemorrhagic fever (26%), while few were diagnosed as dengue shock syndrome (6%). The study by M.A.M. Khalil et al[8]. had 84.4% dengue fever and 14.3% DHF and 1.3% DSS which were less than the current study.

Out of all 50 patients, 23 had some or the other complication (46%) while majority (54%) did not have any complication. The most common complication seen was hepatic involvement (22%) followed by acute kidney injury (8%) and Hepatorenal involvement (6%) in fewpatients[2].

Out of all 50 cases, 10 patients had Acute kidney injury (20%).The study by Muhammad.A.M

et al , had similar percent of AKI patients , there were13.3% cases in the study. Bilirubin and Sodium levels of the study participants having AKI and patients without AKI (all $p > 0.05$).

Significant difference was seen between the two groups of patients in platelet count ($p = 0.003$) , serum creatinine ($p = 0.002$), BUN ($p= 0.001$), eGFR ($p = 0.02$) and Potassium levels ($p = 0.03$).

Highly significant association was seen between the diagnosis of dengue type and presence of AKI ($p < 0.001$). Majority of the patients (97.06%) with the diagnosis of dengue fever did not have AKI, while all of the patients with diagnosis of dengue shock syndrome and almost half (46.15%) of the patients having dengue hemorrhagic fever had AKI.

Our study observed significant association between the duration of hospital stay and presence of AKI ($p = 0.013$).Patients having the hospital stay of more than 7 days showed higher percentage (43.75%) of AKI cases.The study by Muhammad.A.M et al[6], also had similar findings.

Majority of the patients who had AKI were managed conservatively (80%), while two of them had to undergo haemodialysis (20%) 3 cycles each. One of the patients on haemodialysis had died while the other recovered subsequently.Our study observed that out of all 50 patients, there were two deaths (4%), one of them was a patient on haemodialysis due to AKI, thus concluding a mortality of 10% in patients with dengue related AKI. And the other one was having dengue related ARDS.The study by Naqvi R [4]saw 14% deaths while in the current study it was only 4%.

Highly significant difference was seen between the renal parameters of the patients with AKI when we compared them at the time of onset of AKI and after the recovery from AKI ($p < 0.001$). With mean values of S. Creatinine, BUN and EGFR changing from 3.31 ± 0.64, 68.10 ± 15.02, 27.40 ± 6.00 to 0.99 ± 0.19, 25.30 ± 6.02 and$\pm$ 25.32 respectively. Thus concluding that though dengue associated AKI is a severe condition, if managed properly it resolves after a period oftime.

CONCLUSION

This study concludes that the Dengue infection is an alarming sign for AKI, it should be suspected and evaluated at the earliest to start the necessary treatment which might include haemodialysis This study helps in making policies of hospital / physicians to prevent dengue fever related AKI, to halt the ongoing process and prevent permanent damage to the kidneys. Finally, further studies should focus on clarifying the pathogenesis of AKI in dengue and using novel biomarkers to assist in improving clinical outcomes.

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