How to Cite:
Kumari, P., Yadav, R., Pareet, R., & Meena, S. C. (2022). Pattern of clinical presentation, lab findings and mortality risk among patients of dengue fever admitted in pediatric intensive care unit in a tertiary care centre in South-east Rajasthan. *International Journal of Health Sciences*, *6*(S2), 12425–12435. https://doi.org/10.53730/ijhs.v6nS2.8300

Pattern of clinical presentation, lab findings and mortality risk among patients of dengue fever admitted in pediatric intensive care unit in a tertiary care centre in South-east Rajasthan

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***Abstract*---**Background: India is one of the 7 identified countries in south-east Asia region regularly reporting dengue fever outbreaks. Dengue can present with varying degrees of severity of illness in Indian children, present study is aimed at studying the clinical presentation lab findings and mortality risk among patients of dengue fever admitted in PICU in a tertiary care centre in South-east Rajasthan. Methods: It is a retrospective observational study. All dengue seropositive patients admitted in PICU from August 2021 to October 2021 were included in the study. Patients were classified based on National Vector Borne Disease Control Program (NVBDCP). Clinical presentation laboratory findings and mortality risk among patient were studied. esults: Out of 61 patients with dengue, 28(46%) were males and 33(54%) were females. Fever was present in 100% cases followed by GI symptoms vomiting(54.1%), pain abdomen(52.5%) and bleeding manifestations(26.2%) were common

Manuscript submitted: 09 March 2022, Manuscript revised: 18 April 2022, Accepted for publication: 27 May 2022

presenting complaints. On examination common findings were conjunctival congestion (57%) , hepatomegaly (44%) and flushing (26%). Among complications hypotension/shock (51%) was the commonest followed by hemorrhage (31%), pleural effusion and hepatitis each 21%. Most common bleeding manifestation was melena (19%). Most common affected age group was between10-15 years (42.6%). Significantly more number of children had liver failure and renal failure among who died compared to those who survived [p value- .0013 and .00001 respectively. Also more number of children had encephalitis and fluid refractory shock who died compared to those survived (.0015 and .00001 respectively). 67% of severe dengue patients required IV fluid bolus, 16.3% required inotropes 23.3% mechanical ventilation and 48,9% required blood component therapy. Significantly more number of dengue affected children who died needed mechanical ventilation and inotropes when compared to those who survived. Conclusion: Significantly more no. of children who died had liver failure, renal failure , encephalitis, fluid refractory shock and received ventilator support and inotropes. Commonest cause of death is encephalitis followed by DIC

***Keywords*---**dengue, conjunctival congestion, clinical presentation.

Introduction

Dengue fever is caused by arthropod-borne viruses transmitted by Aedes mosquitoes . Worldwide, around 2.5 billion people at a risk of infection and 50-100 million cases of dengue infections are reported annually.[1,2]Dengue viral infections ,caused by any of the four dengue serotype(DEN 1-4), are amongst the leading causes of the hospitalization and death amongst children in several tropical countries.[3]Initially dengue infection may be asymptomatic (50-90%)[4] , may result in a nonspecific febrile illness or may produce the symptom complex of classic dengue fever(DF). Classic dengue fever is marked by a rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation and a centrifugal maculopapular rash. The illness caused by DENV infection manifest either as classical dengue fever or severe dengue(Dengue Haemorrhagic fever/Dengue shock syndrome) which includes severe plasma leakage with severe haemorrhage and severe organ impairment.[1] It has been postulated that the viral non-structural protein ,NS1 activates the alternate compliment pathway and also interact with endothelial cells, ultimately resulting in increased vascular permeability and plasma leakage.[5] Dengue infection also activates clotting factors and fibrinolytic system. Mild disseminated intravascular coagulation, liver injury and thrombocytopenia act together and result in hemorrhagic manifestations. Thrombocytopenia, which often accompanies dengue infection may occur due to destruction of platelets by complement activation, cross-reaction of antibodies to viral proteins as well as bone marrow suppression by the virus.[6] At present very few studies have been conducted in this part of our country in children. The exact clinical and laboratory profile is important for early diagnosis and successful management thus crucial for saving life. Hence, this retrospective study was

undertaken with an aim to evaluate the clincal laboratory profile, complication, and the subsequent outcomes associated in serologically confirmed children with dengue fever admitted in pediatric intensive care unit tertiary care referral hospital.

Aims & Objectives

1. To estimate pattern of clinical features, laboratory parameters, in dengue fever patients admitted in PICU.
2. To estimate the complication and mortality risk in dengue fever patients admitted in PICU.

Material and Methods

a) Type of study: Hospital based retrospective Cross Sectional Study.
b) Study place: The study was conducted in Pediatric Intensive Care Unit, Department of Pediatric Medicine, Jhalawar Medical College and hospital, Jhalawar.
c) Study duration: 3 months from August 2021 to October 2021.
d) Sample size: All children admitted with dengue fever in PICU in the age group of 1 month to 18 years diagnosed by positive NS1 antigen/IgM antibody by ELISA.

Inclusion criteria

- All Children with age between 1 month to 18 years admitted in pediatric intensive care unit.
- Children who were positive for dengue NS1 antigen/IgM antibody by ELISA.

Exclusion criteria

- Children who were having other associated tropical infection (malaria ,scrub typhus etc.)
- Children who were negative for dengue fever.

Methodology

Medical records of children between 1 month to 18 years of age admitted in Pediatric Intensive Care Unit at Jhalawar medical college and hospital, a tertiary care referral teaching hospital situated in southeast of Rajasthan from August 2021 to Oct 2021, with a diagnosis of dengue fever using appropriate clinical features and a single positive serological test were retrospectively reviewed. The serological test performed was dengue fever NS1 antigen/IgM antibody by ELISA by In Bios International Inc, USA.

Dengue clinical classification was published in WHO guidelines in 1975 and updated in 1997 include dengue fever, dengue hemorrhagic fever(DHF)/dengue shock syndrome(DSS). Dengue fever was defined as a febrile illness with at least 2 clinical findings, including nausea vomiting, headache, arthralgia, retro-orbital pain, rash myalgia, haemorrhagic manifestations, and leukopenia. Dengue

hemorrhagic fever(DHF) was defined as an acute febrile illness with minor, major bleeding, thrombocytopenia (platelet count <1 lac /cmm), and evidence of plasma leakage documented by hemoconcentration (hematocrit increase by atleast1|5th or decreased by the same amount after intravenous fluid therapy), pleural or other effusion, hypoalbuminemia or hypoproteinaemia. Dengue shock syndrome(DSS) was defined as DHF with sign of circulatory failure, including narrow pulse pressure(20mmHg), hypotension, or frank shock.[3]The new WHO guidelines published in 2009 classifies dengue as dengue and severe dengue. Severe dengue (dengue hemorrhagic fever /dengue shock syndrome) which include severe plasma leakage, severe hemorrhage and severe organ impairment.[7] In this study cases were categorized based on NVBDP classification which include mild dengue, moderate dengue and severe dengue. Moderate dengue further include DF with high risk co-morbid conditions and DF with warning sign and symptoms.[8]

A proforma was used as a data collecting form to collect information on demographic profile, clinical and laboratory features. Complications of disease such as ARDS, encephalopathy, thrombocytopenia ,pleural effusion, ascites, acute kidney failure, respiratory failure, heart failure etc. inotropic support, and oxygen support, duration of PICU stay, hospital stay and mortality were noted in the proforma. Laboratory investigations such as complete blood count, Liver function test, kidney function test, serum electrolytes, rapid antigen test for malaria, scrub typhus serology, Widal test, blood and urine culture, chest X-ray, etc. were recorded.

Statistical analysis

The data were entered in Microsoft Excel worksheets and analyzed. Categorical variables are expressed as the number of patients and the percentage of patients; continuous variables are expressed as mean and standard deviation. An alpha level of 5% has been considered, i.e. if any p-value is less than 0.05, it has been considered as significant. SPSS version 23 has been used for the analysis.

Results

A total of 61 patients admitted in PICU from August 2021 to October 2021 were seropositive for dengue and satisfied the inclusion criteria. Out of 61 patients with dengue, 28(46%) were males and 33(54%) were females. Male: Female ratio was 1:1.18 in general. Fever was present in 100% cases followed by GI symptoms vomiting(54.1%), pain abdomen(52.5%) and bleeding manifestations(26.2%) were common presenting complaints (Table 1).

Table. 1. Presenting complaints of children with dengue fever

SYMPTOMS		NO. OF PATIENTS	PERCENTAGE
Fever		61	100%
	fever with chills	9	14.80%
	fever with rigor	2	3.30%
Vomiting		33	54.10%

abd. Pain		32	52.50%
bleeding manifestations		16	26.20%
reduced intake		15	24.50%
Edema		13	21.30%
Cough		13	21.30%
breathing difficulty		8	13.10%
altered sensorium		7	11.50%
Convulsions		7	11.50%
Rash		6	9.80%
Bodyache		5	8.20%
Headache		5	8.20%
loose stools		2	3.30%
chest pain		2	3.30%
reduced urine output		2	3.30%

On examination common findings were conjunctival congestion (57%), hepatomegaly (44%) and flushing (26%). Among complications hypotension/shock (51%) was the commonest followed by hemorrhage (31%), pleural effusion and hepatitis each 21% (Table 2).

Table.2. examination findings and complications

Signs		no. of patients	Percentage
conjunctival congestion		35	57.40%
Flushing		16	26.20%
Hepatomegaly		27	44.30%
	tender	12	44.30%
	non tender	15	55.70%
Splenomegaly		4	6.60%
pleural effusion		13	21.30%
	right Sided	10	77%
	left sided	1	7.70%
	bilateral	2	15.40%
Ascites		8	13.10%
hypotension/ shock		31	51%
Hemorrhage		19	31.10%
Encephalitis		11	18%
Hepatitis		13	21.30%
Pneumonia		7	11.50%
ARDS		3	5%

31.1% of the total patients were having bleeding manifestations(Table 3). Most common bleeding manifestation was melena (19%) followed by gum bleeding (16%) and menorrhagia (16%) in adolescent girls. Two patients had pulmonary bleed who died.

Table.3. Bleeding manifestations

type of bleeding	no. of patients	Percentage
Melena	4	19%
Gum bleeding	3	16%
Menorrhagia	3	16%
Hematemesis	3	16%
Haematuria	2	11%
Epistaxis	2	11%
pulmonary bleed	2	11%
TOTAL	19	100%

Thrombocytopenia (82%) was the most common association noted followed by deranged liver function (36%) and leukopenia (34.4%). The lowest platelet count was 8000/cumm and two patients were having thrombocytosis. The lowest leucocyte count was 1400/cumm (Table 4).

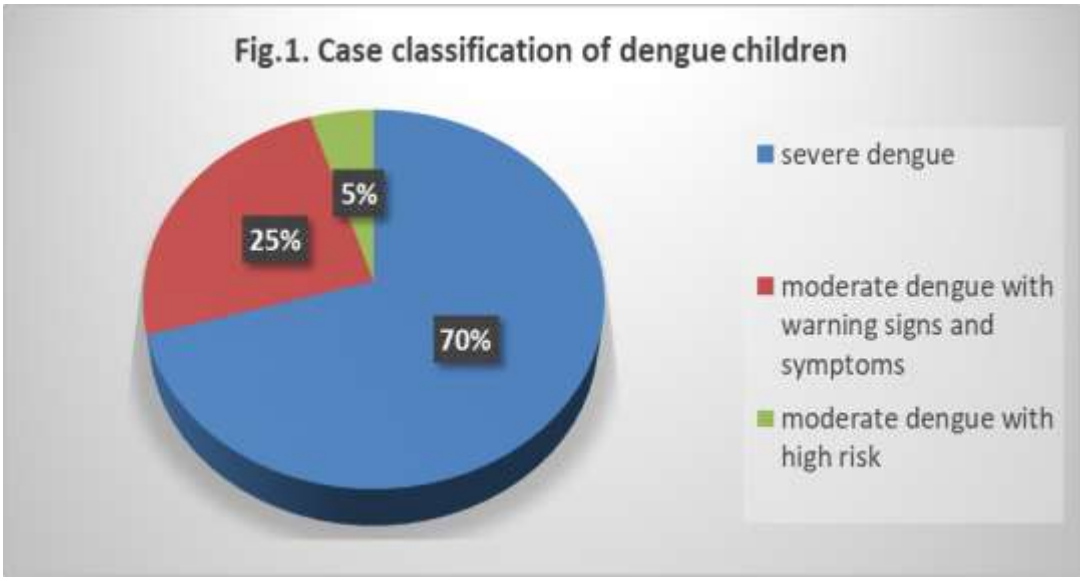
Table.4. Lab parameters

PARAMETERS	NO. OF PATIENTS	PERCENTAGE
LEUCOPENIA	21	34.40%
THROMBOCYTOPENIA (<1 LAKH/dL)	50	82.00%
ABNORMAL RENAL FUNCTION TEST	9	14.70%
ABNORMAL LIVER FUNCTION TEST	22	36.00%
HYPONATREMIA	2	3.30%

Most common affected age group was between10-15 years (42.6%) followed by 5-10 years (25%). Patient were classified based on severity (Table 5, Fig 1). Out of total 61, 18(29.5%) patients were of moderate dengue and 43(70.5%) were of severe dengue. Most cases of severe dengue were in the age group of 10-15 years of age. Among severe dengue cases male: female ratio was 1:1.39.

Table.5. Age wise distribution of study population

Categories	0-1 yr	1-5 yr	5-10 yr	10-15 yr	15-18 yr
moderate dengue with high risk	3 (33.3%)	0	0	0	0
moderate dengue with warning signs and symptoms	2 (22.2%)	1 (16.7%)	4 (26.7%)	6 (23.3%)	2 (40%)
severe dengue	4 (44.5%)	5 (83.3%)	11 (73.3%)	20 (76.7%)	3 (60%)



43 patients were having severe dengue among which 9 died and 34 survived at discharge. Overall case fatality rate was 14.8% while case fatality rate among severe dengue was 21%. Out of 9 deaths 4 were due to encephalitis, 3 were due to DIC, 1 each due to severe pneumonia and catecholamine resistant shock. Renal failure was present in 11(25.6%) out of 43 children with severe dengue. 8(88.9%) out of 9 patients who died had renal failure and 3(8.8%) out of 34 who recovered had renal failure. Liver failure was present in 18(41.9%) out of 43 children with severe dengue. 8(88.9%) out of 9 who died and 10(29.4%) out of 34 who recovered had liver failure. Significantly more number of children had liver failure and renal failure among who died compared to those who survived [p value- .0013 and .00001 respectively (table.)]. Hemorrhage was present in 19(44.2%) out of 43 children with severe dengue. 3(33.3%) out of 9 patients who died had hemorrhage and 16(47%) out of 34 who recovered had hemorrhage.

Fluid refractory shock was present in 7(16.3%) out of 43 children with severe dengue. 6(66.7%) out of 9 patients who died and 1(2.9%) out of 34 who recovered had fluid refractory shock. Significantly more number of children had fluid refractory shock among who died compared to those who survived [p value- .00001(Table 6)]. Severe capillary leak was present in 36(83.7%) out of 43 children with severe dengue. 6(66.7%) out of 9 patients who died and 30(88.2%) out of 34 who recovered had severe capillary leak.

Encephalitis was present in 11(25.6%) out of 43 children with severe dengue. 6(66.7%) out of 9 patients who died and 5(14.7%) out of 34 who recovered had encephalitis. Significantly more number of children had encephalitis among who died compared to those who survived [p value- .0015 (table.)].ARDS was present in 4(9.3%) out of 43 children with severe dengue. 1(11.1%) out of 9 patients who died and 3(8.8%) out of 34 who recovered had ARDS. 67% of severe dengue patients required IV fluid bolus, 16.3% required inotropes 23.3% mechanical ventilation and 48.9% required blood component therapy. Significantly more

number of dengue affected children who died needed mechanical ventilation and inotropes when compared to those who survived [p- .00001 (Table 7).

Table.6. complications and outcome among severe dengue

complications		death n (%)	discharge n (%)	Total	P value
capillary leak	Yes	6 (66.7)	30 (88.2)	36	0.12
	No	3 (33.3)	4 (11.8)	7	
	Total	9	34	43	
hemorrhage	Yes	3 (33.3)	16 (47)	19	0.46
	No	6 (66.7)	18 (53)	24	
	Total	9	34	43	
fluid refractory shock	Yes	6 (66.7)	1 (3)	7	0.00001
	No	3 (33.3)	33 (97)	36	
	Total	9	34	43	
liver failure	Yes	8 (88.9)	10 (29.4)	18	0.0013
	No	1 (11.1)	24 (70.6)	25	
	Total	9	34	43	
real failure	Yes	8 (88.9)	3 (8.8)	11	0.00001
	No	1 (11.1)	31 (91.2)	32	
	Total	9	34	43	
encephalitis	Yes	6 (66.7)	5 (14.7)	11	0.0015
	No	3 (33.3)	29 (85.3)	32	
	Total	9	34	43	
ARDS	Yes	1 (11.1)	3 (8.8)	4	0.83
	No	8 (88.9)	31 (91.2)	39	
	Total	9	34	43	

Table.7. treatment modalities and outcome among severe dengue

treatment modality		death n (%)	discharge n (%)	Total	P value
intravenous fluid bolus	Yes	5 (55.6)	24 (70.6)	29	0.12
	No	4 (44.4)	10 (29.4)	14	
	Total	9	34	43	
Inotropes	Yes	6 (66.7)	1 (3)	7	0.00001
	No	3 (33.3)	33 (97)	36	
	Total	9	34	43	
mechanical ventilation	Yes	9 (100)	1 (3)	10	0.00001
	No	0	33 (97)	33	
	Total	9	34	43	
blood components	Yes	4 (44.4)	17 (50)	21	0.76
	No	5 (55.6)	17 (50)	22	
	Total	9	34	43	

Discussion

Our study looked into clinical presentation, lab findings and mortality risk among patients of dengue fever in pediatric intensive care unit South-east Rajasthan. A total of 61 seropositive dengue patients admitted in PICU during the study period were analysed. 43 patients were having severe dengue (70%). Male to female ratio was 1:1.18 in general while among severe dengue cases male: female ratio was 1:1.39. In our study there was a female predominance, while study by Khan MAS et al[9], Rathod N P et al[10] and Mishra S et al[11] showed a male predominance with a M:F ratio of 1.22:1,1.43:1 and 3.4:1 respectively. Commonest age group in our study was 10-15 yrs. In Khan MAS et al[9] study majority (46.1%) of cases belonged to the age group of 10-14 yrs. Most common age group in Rathod N P[10] study and Mishra S et al[11] study was 6-12 yrs and >11 yrs respectively. Reason for dengue being common in older children may be due to their more involvement in outdoor activities.

Fever was the most common presenting complain seen in 100% cases which is comparable to earlier studies,[9,10,11] whereas Sriram P et al [12] reported fever in 94.6%, Aggarwal A et al[13] reported fever in 93% of patients. Second most common clinical feature vomiting(54.1%), followed by pain abdomen(52.5%) and bleeding manifestations(26.2%) which is similar to other studies.[9,10,13]While in study of Mishra S et al [11] myalgia and abdominal pain were common finding after fever, Sriram P et al [12] reported conjunctival congestion followed by myalgia as second most common findings. 31.1% of the total patients were having bleeding manifestations. Most common bleeding manifestation was melena (19%) followed by gum bleeding (16%) and menorrhagia (16%) in adolescent girls. Two patients had pulmonary bleed who died. In Khan MAS et al [9] study epistaxis(6.3%) and melena(5.8%) were the most frequent bleeding manifestations. Thrombocytopenia (82%) was the most common association noted followed by deranged liver function (36%) and leukopenia (34.4%), findings were similar to study by Khan MAS et al.[9] Significantly more no. of children who died had liver failure, renal failure , encephalitis, fluid refractory shock which is same as study by Chulananda DAG et al.[14]

Case fatality rate among severe dengue in this study was 21%, which was comparable to study by Sachdev A et al [15] 25.6%. Disease severity at admission, need for multiple vasoactive drugs and mechanical ventilation are predictor of mortality in sever dengue infection in children admitted in PICU.[15] In our study most common cause of death was encephalitis followed by DIC. One of the limitation of this study is, in view of small sample size due to limited data collection at a single centre only second , clinical classification of dengue was used for stratification of severity which might cause misclassification bias due to subjective nature of the assessment.

Conclusion

Dengue is a common disease in this part of world. It is one of the dreaded fevers for the pediatrics age. The disease has various presentations and features, but early diagnosis and management can decrease case fatality rate significantly. Fever with GI symptoms with conjunctival congestion and flushing are important

clinical feature to distinguish dengue from other acute febrile illnesses. In this study overall case fatality rate was 14.8% while case fatality rate among severe dengue was 21%. Most common cause of death was encephalitis followed by DIC. Significantly more no. of children who died had liver failure, renal failure, encephalitis, fluid refractory shock and received ventilator support and inotropes.

Conflict of interest: none
Source of funding: none

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