# Clinical profile of dengue fever in central India

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### Abstract

Introduction: Dengue fever is an arboviral infection that has been prevalent in India for more than two centuries. Epidemic dengue fever (DF) and dengue hemorrhagic fever (DHF) have emerged as a global public health problem in recent decades. Aims and objectives: To study various clinical presentations, complications and outcome in confirmed cases of dengue. Methodology: This prospective observational study was carried out after clearance from local ethical committee from December 2013 to November 2015 in tertiary care hospital. All eligible subjects of either sex according to inclusion/exclusion criteria who were admitted in the hospital due to acute febrile illness were evaluated for clinical and biochemical features of Dengue fever, dengue fever with warning signs and severe dengue. Continuous variables like age were presented as mean ± standard deviation while categorical variables like gender, symptoms and clinical signs were expressed as actual numbers and percentages. Categorical variables were compared across three groups by performing one-way ANOVA test. Pearson's chi square test was used to compare outcome with mortality. For small numbers Fischer exact test was applied. P value <0.05 was considered statistically significant. Statistical software STATA version 13.1 was used for statistical analysis. Result: Out of 200 dengue viral infection cases 117 were males and 83 were females. The male to female ratio was 1.4:1. Most cases were young and below age of 30 years. Fever was the most common clinical presentation seen in all subjects. This was followed by body ache (67%), headache (46.5%), oedema (39%), rash (36.5%), vomiting (28%) and abdominal pain (26%). An increased hematocrit percentage was seen with severity of dengue fever and a fall in platelet count was noted with severity of dengue. Cases having multiple systemic involvements such as acute renal failure, ARDS, hepatic and neurological involvement was significantly found to be associated with severity and mortality in dengue patients. Conclusion: It could be concluded from our study that, young adults are at risk of dengue the most. Dengue fever with warning signs and severe dengue is associated with more incidence of acute liver failure and hypoalbuminemia and is also statistically correlated with bleeding, AKI, ARDS and neurological manifestations in the study. Mortality in dengue is associated with multiple systemic complications. Key Words: dengue fever.

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## **INTRODUCTION**

Epidemic dengue fever and dengue hemorrhagic fever is a global health problem with over 16,000 cases reported every year in India<sup>1</sup>. Children below 15 years age account for up to 90% of patients with Dengue hemorrhagic fever<sup>2</sup>. In Asia, the dengue serotype of DEN-2 has been replaced by DEN-3<sup>3,4</sup>. The WHO 2009 classifies dengue fever into two groups: uncomplicated and severe<sup>5</sup>. The characteristic manifestations of dengue are: (i) continuous high grade fever for 2-7 days; (ii) hemorrhagic tendency-petechiae, epistaxis or positive tourniquet test; (iii) thrombocytopenia (platelet count < 100 x 10<sup>9</sup> /l) and (iv) evidence of plasma leakage manifested by hemoconcentration, pleural effusion and ascites etc.

#### **MATERIAL AND METHODS**

This prospective observational study was conducted on 200 serologically confirmed cases of dengue viral fever were observed and assessed for clinical and haematological and biochemical laboratory abnormalities using the WHO 2009 classification, and the outcome was measured in terms of discharge from hospital or death. Treatment was supportive and symptomatic according to

standard WHO treatment protocol. Continuous variables like age were presented as mean  $\pm$  standard deviation while categorical variables like gender, symptom and clinical signs were expressed as actual numbers and percentages. Categorical variables were compared across three groups by performing one-way ANOVA test. Pearson's chi square test was used to compare outcome with mortality. For small numbers Fischer exact test was applied. P value <0.05 was considered statistically significant. Statistical software STATA version 13.1 was used for statistical analysis.

## **OBSERVATIONS AND RESULTS**

The study population included 200 cases of dengue fever, of which 117 were males (58.5%) and 83 were females (41.5%). Severe dengue was observed in 48 cases (24%), dengue with warning signs was seen in 66 cases (33%) and dengue fever without warning signs was seen in 86 cases (43%).

 Table 1: Gender-wise distribution of dengue cases according to

		seventy		
	Dengue fever without warning sign	Dengue with warning signs	Severe dengue	Total
Male	49	46	22	117
Female	37	20	26	83
Total	86	66	48	200

Of the 200 cases, 44 subjects were in the age group of 12 to 20 years, 98 subjects were in 21 to 30 years group, 38 cases were in 31 to 40 years group, 18 cases were in 41 to

50 years group and 5 cases were above 50 years. Most cases were young and below 30 years age.

Table 2: Age- wise distribution of the study population

Age in yrs         Total cases         Male         Female           12-20         44         24         20           21-30         98         57         38           31-40         38         25         13           41-50         18         7         11           >50         5         4         1           Total         200         117         83				/ 1 1
12-20     44     24     20       21-30     98     57     38       31-40     38     25     13       41-50     18     7     11       >50     5     4     1       Total     200     117     83	Age in yrs	Total cases	Male	Female
21-30       98       57       38         31-40       38       25       13         41-50       18       7       11         >50       5       4       1         Total       200       117       83	12-20	44	24	20
31-40     38     25     13       41-50     18     7     11       >50     5     4     1       Total     200     117     83	21-30	98	57	38
41-50         18         7         11           >50         5         4         1           Total         200         117         83	31-40	38	25	13
>50 5 4 1 Total <b>200</b> 117 83	41-50	18	7	11
Total 200 117 83	>50	5	4	1
	Total	200	117	83

Fever was the most common clinical presentation seen in all subjects. This was followed by body ache (67%), headache (46.5%), oedema (39%), rash (36.5%), vomiting (28%) and abdominal pain (26%). Other complaints were mucosal bleed (24%), petechiae (20.5%), jaundice (8%), diarrhoea (4%), altered sensorium (4%) and convulsions (2%). The common clinical signs noted were rash (40.5%), oedema (39%), mucosal bleed (33%), petechia (20%), shock or hypotension (18%) and icterus (8%).

		0	
Parameter	Dengue fever without warning sign	Dengue with warning signs	Severe dengue
Mean hematocrit %	36.24	40.19	42.96
Mean Platelet count/mm <sup>3</sup>	91302.33	60872.73	44343.75

An increased hematocrit percentage was seen with severity of dengue fever and a fall in platelet count was noted with severity of dengue.

 Table 4: Thrombocytopenia and bleeding manifestation with severity of dengue cases

	Bleeding	Dengue fever without warning signs(n = 86)	Dengue with warning signs (n = 66)	Severe dengue (n = 48)	Total (n=200)
Thrombocytopenia	Present	10	48	38	96
(<100000/mm <sup>3</sup> )	Absent	51	14	7	72
P-value		<0.001,HS			
No thrombocytopenia	Present	3	2	-	5
(>100000/mm <sup>3</sup> )	Absent	22	2	3	27
P-value		0.119,NS			

Bleeding manifestations were more commonly seen in subjects with thrombocytopenia (platelet count<1lac/mm<sup>3</sup>)

Table 5: Hepatic parameters involvement with severity of dengue cases

P	arameters	Dengue fever without warning signs(n = 86)	Dengue with warning signs (n = 66)	Severe dengue (n = 48)	Total	P-value
Clinical	Jaundice and/or Hepatomegaly	6	18	13	37	0.001,HS
	Hyperbilirubinemia T. Bili >1.2	4	5	19	28	<0.001,HS
	Elevated ALT >35 u	54	57	40	151	0.001,HS
Biochemical	Elevated AST >40 u	66	58	42	166	0.123
	Elevated ALP > 300 u	1	1	20	22	<0.001,HS
	Hypoalbuminemia <3gm%	7	11	21	39	<0.001,HS
Coagulation profile	Prolonged PT and/or INR > 1	12	12	26	50	<0.001,HS

Clinical hepatomegaly and/ or jaundice with hyperbilirubinemia was seen more commonly in subjects with severe dengue. Similarly hypoalbuminemia, serum alanine transaminase and serum alkaline phosphatase were found significantly correlated with severe dengue fever. Deranged INR or prolonged prothrombin time were also found more commonly in subjects with severe dengue fever.

Table 6: Mortality in Subjects With Dengue Fever		
Parameters of mortality	NUMBER	
Gender of succumbed subjects	Male 9 female 2	
No. Of subjects having bleeding manifestation	11	
Class Of Dengue (Severe Dengue)	0/0/11	
Mean Platelet Count	19636.36	
Mean Haematocrit Value	43.95	
Acute Renal Failure	7	
Hepatic Involvement	10	
Acute Lung Injury/ARDS	6	
Neurological Involvement	7	

Out of all 200 subjects 11 succumbed of which 9 were males and 2 females. All 11 of them met criteria for severe dengue and had bleeding tendency with mean platelet count of 19636.36 / mm<sup>3</sup>. The mean hematocrit value was 43.95%. Of the 11, 10 had hepatic involvement, 7 suffered from acute renal failure, 7 had neurological involvement and 6 suffered from acute lung injury.

Table 7: Association of various parameters with mortality				
Parameters	Number of cases	Survival	Death	
Dengue fever without warning signs	86	86	0	
Dengue fever with warning signs	66	66	0	
Severe dengue	48	37	11	
Hepatic involvement	174	163	11	
Acute kidney injury	11	4	7	
ARDS	9	3	6	
Thrombocytopenia	160	159	11	
Bleeding	101	90	11	

Mortality was found exclusively in subjects categorized as severe dengue. Multiple organ systems were affected with subjects suffering from acute lung injury and acute renal failure showing maximum mortality.

#### **DISCUSSION**

In this study, out of 200 cases studied, 117(58.50%) were male and 83(41.50%) were female with ratio being 1.4:1. In the study conducted by Singh *et al* in 2003<sup>6</sup> in Delhi the ratio was approximately 3:1, while the study from Surat by Tank Arun G *et al*<sup>7</sup> had a sex ratio of 2.54:1 in favour of males thereby suggesting the predisposition of males to acquire disease. Also the average age of the subjects was 27+/-9 years. In a study conducted at Udupi Between 2002-08 by Ashwini Kumar et al<sup>8</sup> had most patients in the age group between 15-44 years. The reason for high prevalence in young males is probably due to involvement of young males in outdoor activity which exposes them to more chances of mosquito bites. The most common presented symptom was fever seen in all 200 cases. Myalgia was present in 134 subjects (67%) and headache in 93 subjects out of 200 (46.5%). Bleeding manifestations in the form of rash and mucosal bleeds were seen in 101(50.5%). In the 1996 outbreak in Delhi as reported by Sharma *et al*<sup>9</sup> most common presentation was fever and purpura was the most common bleeding manifestation seen in 33.8% of the subjects. Uncommon manifestations seen were jaundice (8%), diarrhoea (4%), altered sensorium (4%) and convulsions (2%). Even in the 2003 outbreak of dengue in Delhi<sup>6</sup>, altered sensorium, jaundice was seen as uncommon manifestations. Significant association between bleeding manifestations with severity of disease was found. This was like the study by R Karoli et al in 2012<sup>10</sup> from Lucknow wherein significant correlation was found between bleeding manifestations and DHF. On investigations, 160 subjects found to have thrombocytopenia (80%) were  $(<100,000/\text{mm}^3)$ . The mean platelet counts in subjects of dengue fever was 91,302.33/mm<sup>3</sup>, for dengue fever with warning signs was 60872.73/mm<sup>3</sup> and for severe dengue subjects it was 44,343/mm<sup>3</sup>. Relation between thrombocytopenia and dengue and its severity was found to be statistically significant. In the study from Delhi in 1996<sup>10</sup>, 94 out of 98 patients had thrombocytopenia with mean being 30000/mm<sup>3</sup>. Also in the study from Kolkata by Sanjay Kumar Mandal et al<sup>11</sup> in 2013 mean platelet counts were 99000/mm<sup>3</sup>. Bleeding diathesis is a known feature of dengue fever because of low platelet count and leakage from blood vessels. Bone marrow suppression, Immune mediated clearance, spontaneous aggregation of platelets to virus infected endothelium-all may be responsible for such thrombocytopenia<sup>11</sup>. The mean haematocrit in dengue fever subjects without warning signs was 36.24% in subjects of dengue with warning sign 40.19% and in severe dengue subjects 42.96% in this study. The mean haematocrit was 39.0% in the study from Delhi 1996<sup>9</sup>. Mean haematocrit was 40.9% in the 2013 study from Kolkata by Mandal *et al*<sup>11</sup>. There was statistical association between dengue positive cases and raised haematocrit in this study. The reason probably is due to haemoconcentration from increased vascular permeability<sup>11</sup>. In this study there were 174(87%) subjects who presented with some form of hepatic involvement in the form of clinical jaundice or deranged liver function tests or ultrasonography suggestive of hepatomegaly or gall bladder wall thickening. 28(14%) subjects had hyperbilirubinemia. Transmainase levels

were raised in 151(75.5%) and 166 (83%) subjects for ALT and AST respectively in this study. There was no correlation between elevation in levels of AST and dengue positive cases but a significant correlation was found between raised levels of ALT and dengue positive cases in our study. Serum AST and ALT were elevated in 88% and 76% patients respectively in the 1996 study from Delhi<sup>9</sup>. This could be probably due to increased occurrence of ischemic hepatitis as a complication of hypotension<sup>9</sup>. There were signs of coagulopathy in the form of raised INR or prolonged prothrombin time in 50(25%) subjects, all of whom had dengue fever, this correlation was found to be significant. Also hypoalbuminemia was noticed in 39(19.5%) subjects out of which 21 subjects had severe dengue and 11 had dengue fever with warning signs. These are consistent with results seen in the study by Karoli *et al*<sup>10</sup> from Lucknow. The clinical profile of patients who succumbed in this study suggested that the average age of these 11 subjects was 29 years with all 11 subjects falling under category of severe dengue. There was evidence of multiple systemic involvements, with 6 subjects having ARDS. 10 subjects had hepatic involvement. While 7 subjects had acute renal failure and 7 subjects had neurological involvement. Mean haematocrit amongst deaths in this study was 43.95%. On statistical analysis, significant correlation could be made between presence of AKI and ARDS with death. Bleeding manifestations were seen in all subjects who succumbed and were significantly associated with mortality. The mean platelet count of these subjects was 19636/mm<sup>3</sup>. The 2003 study in Delhi<sup>6</sup> witnessed 5 deaths. The mean platelet count in them was 64000/mm<sup>3</sup>. The presence of multiple systemic involvements was not described in the study. The mean haematocrit was significantly elevated to 64% in the study from Delhi in 2003<sup>6</sup> amongst patients who succumbed.

#### **CONCLUSION**

It could be concluded from our study that, young adults are at risk of dengue the most. Dengue fever with warning signs and severe dengue is associated with more incidence of acute liver failure and hypoalbuminemia and is also statistically correlated with bleeding, AKI, ARDS and neurological manifestations in the study. Mortality in dengue is associated with multiple systemic complications. Hence early attention to patients and intensive monitoring and care for these patients might change outcome.

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