

Original Research Article

The clinical profile of dengue infection cases presenting in a tertiary care institute: an observational study

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ABSTRACT

Background: Dengue is a mosquito-borne viral disease that has rapidly spread in all regions of WHO in recent years. It is an acute febrile illness, caused by infection with any of 4 related positive-sense, single-stranded RNA viruses of the genus Flavivirus, dengue viruses 1, 2, 3, or 4. Objective of study was to study the clinical profile of dengue viral infection in the paediatric age group.

Methods: This observational study was conducted in a tertiary referral centre in Central India. Cases were classified based on the WHO 2009 Dengue guidelines for diagnosis, treatment, prevention and control and the clinical and laboratory parameters were analyzed for demographic and other correlates.

Results: 75 patients met all the inclusion criteria and were analyzed. Most children were in age group 6-10 years. Fever, bleeding, rash, abdominal pain and vomiting were the common symptoms. We noted some atypical symptoms also.

Conclusions: When infected, early recognition and prompt supportive treatment in dengue infection can substantially lower the risk of medical complications and death.

Keywords: Children, Dengue fever

INTRODUCTION

Dengue is fast emerging pandemic-prone viral disease in many parts of the world. A viral disease, it has evolved with the globalisation of the modern world. The WHO in 2006 highlighted dengue as an emerging disease and in 2014, reported 40% of world population at risk of exposure, with 2.5% mortality amongst those needing hospitalisation.¹ Mortality and morbidity are often higher in regions where dengue has been endemic for decades.² For a disease that is so complex in its manifestations, management is relatively simple, inexpensive, and very effective in saving lives so long as timely interventions are instituted. Dengue has the unique capacity to attack more viciously on secondary infection. This coupled with

its ally in a tenacious vector makes prevention the best strategy to curb Dengue.³ There is a lack of data from the central part of India, where this study has been conducted regarding the clinical profile of Dengue infections, especially in the vulnerable paediatric age group. Atypical manifestations of Dengue though widely reported in adults and children, are still not delineated as regards to incidence, pathogenesis, and appropriate management. This study hopes to add to the growing literature on dengue in children.

METHODS

This study aimed to study the clinical profile of dengue viral infection in the paediatric age group. It was

conducted over a duration of 13 months (June 2015 - August 2016) in the Department of Paediatrics, Gandhi Medical College (GMC), Bhopal, which serves as a main referral centre for the district of Bhopal and its adjoining districts of Vidisha, Sehore, Ashoknagar, Sagar, Rajgarh, etc.

This was a hospital-based observational study in which the cases included were studied as per a proforma, classified based on the WHO 2009 *Dengue guidelines* for diagnosis, treatment, prevention and control and the clinical and laboratory parameters were analysed for demographic and other correlates.³

Patients meeting following criteria that were admitted in the hospital were included:

- Age 1 month to 12 years (144 months)
- Dengue NS1 antigen/ IgM positive

The patients with any co-existing infection along with Dengue were excluded from the study. All patients admitted in the Paediatric Department that presented with clinical features of dengue-like illness were initially investigated for evidence of dengue. Dengue was suspected if the child had any of the following features³

- Live in /travel to dengue endemic area.
- Fever and 2 of the following criteria:
 - a) Nausea, vomiting
 - b) Rash
 - c) Aches and pains
 - d) Tourniquet test positive
 - e) Leukopenia
- Any warning sign (Abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy, restlessness, liver enlargement >2 cm, Laboratory: increase in Haematocrit concurrent with rapid decrease in platelet count)

On the basis of above features, 206 patients were suspected to have dengue like illness. 128 patients tested negative for dengue NS1 antigen/ IgM and were therefore excluded. 3 patients that tested positive for dengue had to be excluded as 1 had coexisting tubercular infection, and 2 had previous neurological disorder. 75 patients met all the inclusion criteria and were analysed.

The cases were classified and treated as per WHO 2009 and 2012 protocols.^{3,4} They were followed and observed throughout the duration of their treatment and stay in the hospital. At admission a detailed history was taken from the patients' parents/ guardians of the patients as per a proforma.

Detailed examination was done, looking especially for multi-system involvement of the disease. Baseline laboratory investigations were initiated. Cases were

classified according to dengue severity based on WHO 2009 guidelines.³

The patients were observed throughout their stay in the hospital for development of any new signs and/or symptoms. Data analysis was done at the end of data collection using Minitab Version 17. Patients were analysed on the basis of demographic factors like age, sex, and area of residence.

The common presenting signs and symptoms were then studied, and laboratory markers were analysed. The following investigations were done in all cases - complete blood count, haematocrit, rapid diagnostic test and peripheral smear examination of thick and thin blood films with Giemsa stain to rule out malaria, random blood sugar, liver function tests, renal function tests, dengue ns1 antigen rapid card test, dengue IgM: (cases that presented with fever of more than 5 days duration were tested for dengue IgM).

RESULTS

This study was conducted at a tertiary care institute located in an urban area in the capital city of Bhopal, which caters to the largely rural populace hailing from the surrounding districts.

75 children were analysed, 1 month to 12 years of age with serologically confirmed dengue infection over a period of 13 months, and further reviewed for clinical findings in cases that had cardiac and neurological manifestations. In this study the maximally affected children (38.6%) were 6-10 years, followed by those more than 10 years (22.6 %) of age. 18.6% of cases were infants (<1 year). The youngest was 3 months old (Figure 1).

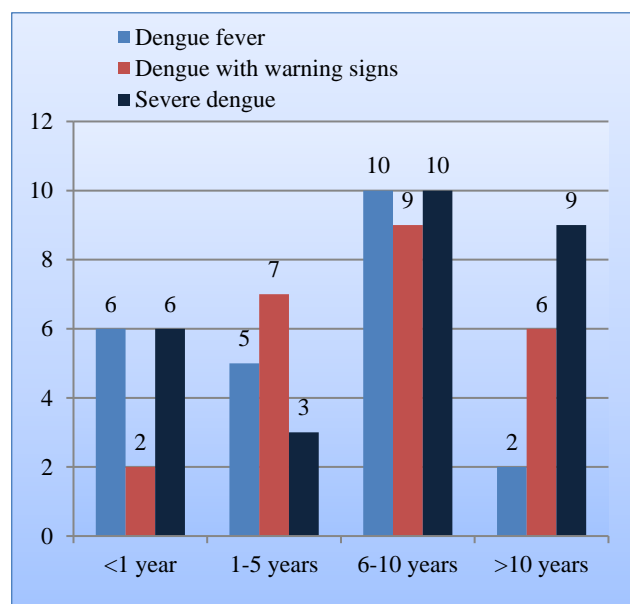


Figure 1: Age wise profile of severity.

Male preponderance with 65.3% males and 34.6% females was noted (Male:Female=1.8:1) (Figure 2). Males were affected more (24%) than females (13.3%) in severe dengue cases also. 30.6% subjects hailed from urban Bhopal, with the rest residing in adjoining rural regions. Clustering of cases was seen in the monsoon

months of July to October (Figure 3). Severe Dengue was seen in 37.3% cases, with 67.8% of these patients being >6 years of age. A mortality of 1.3% (1 in 75) was noted. 68% of the confirmed cases were positive for IgM, 61.3% were positive for NS1 antigen and 30.6% were positive for both.

Table 1: Clinical symptoms as per severity.

Symptom	Dengue fever	Dengue with warning signs	Severe dengue	Total
Fever	23 (30.7%)	24 (32%)	28 (37.3%)	75 (100%)
Rash	11 (14.7%)	11 (14.7%)	14 (18.7%)	36 (48%)
Abdominal pain	6 (8%)	9 (12%)	13 (17.3%)	28 (37.3%)
Vomiting/nausea	10 (13.3%)	8 (10.6%)	14 (18.75%)	32 (42.7%)
Headache	6 (8%)	9 (12%)	6 (8%)	21 (28%)
Cough	2 (2.7%)	3 (4.2%)	4 (5.3%)	9 (12%)
Diarrhoea	6 (8%)	6 (8%)	7 (9.3%)	19 (25.3%)
Major bleed*	11 (14.7%)	12 (16%)	17 (22.6%)	40 (53.3%)
Seizures	0	0	5 (6.7%)	5 (6.7%)

*Major bleeds include gastrointestinal bleed, epistaxis, IVH

Table 2: Comparison of significant clinical features between severe and non-severe dengue cases.

Variables	Severe dengue (n=28), No. or mean±SD	Non-severe dengue (n=47), No. or mean±SD	P value
Duration of fever	6.29±2.54	5.64±1.97	0.2212
Abdominal pain	12	15	0.1795
Vomiting	14	14	0.0800
Rash	12	24	0.4914
Headache	6	15	0.3279
Cough	4	5	0.6382
Diarrhoea	7	12	0.9591
Bleeding	15	23	0.6977
Third space loss	16	33	0.2500
Hemoglobin (gm dl)	11.5±1.33	10.53±1.84	* 0.0174
Haematocrit	37.18±4.36	36.28±5.09	0.4369
TLC (>11,000 cells/Cumm)	2	7	0.3177
TLC (< 5,000 cells/cumm)	6	6	0.3223
Thrombocytopenia (<1 Lakh/mm ³)	14	19	0.6240
SGOT (>200u/l)	7	14	0.6552
SGPT (>200 u/l)	5	7	0.7349
Renal function test	31.57±10.77	29.6±12.93	0.4988
APTT (abnormal)	5	6	0.5220
INR (abnormal)	5	9	0.8900
Serum sodium (meq/L)	140.29±6.04	139.28±8.5	0.5839
Serum potassium (meq/L)	4.18±0.75	4.26±0.76	0.6794
Hepatomegaly	8	12	0.7734
Splenomegaly	5	11	0.5706
Tourniquet test	11	20	0.8791

Fever, rash, vomiting, and haemorrhage were the most common complaints noted. 100% of patients had fever, with 56% patients presenting with fever of 4-7 days. 48% presented with a rash, 37.3% cases presented with abdominal pain, 42.7% had nausea/vomiting, and 25.3% had diarrhoea.

Headache was present in 28% of all cases and in 42% of cases with warning signs. 12% cases presented with cough and no association with severity was noted. 53.3% patients reported major bleeding, with melena occurring most frequently followed by haematemesis, epistaxis and one case of intraventricular haemorrhage. Seizures were

noted in 6.7% of cases (Table 1). 16% of patients presented with hypotension of which 9 were managed as Dengue Shock.

Bradycardia was observed in 6.7 % with complete normalisation of heart rate on recovery. 36% patients had pleural effusion while 34.7% were found to have ascites. Hepatomegaly was seen in 25.3% and 28.7% had with splenomegaly.

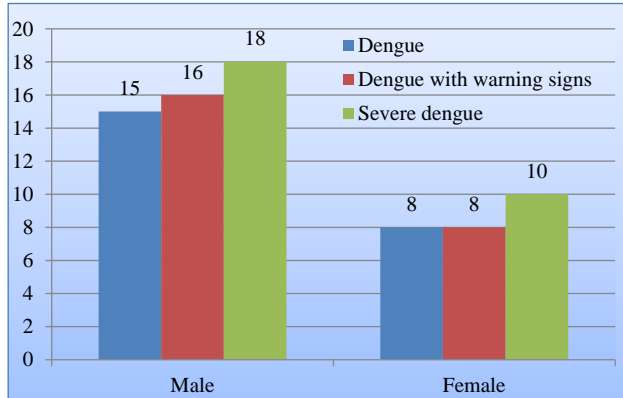


Figure 2: Gender profile of severity.

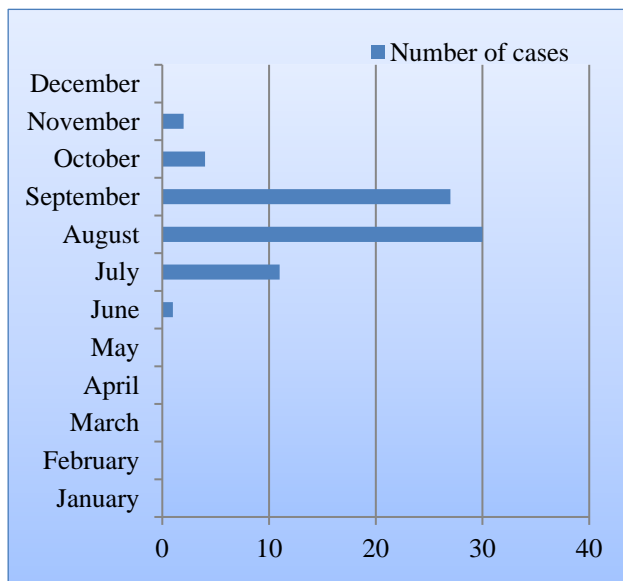


Figure 3: Seasonal variation of cases.

Lab Investigations

Mean Haemoglobin was 10.89 ± 1.73 gm/dl, and mean haematocrit was 36.61 ± 4.82 . Comparison of mean haemoglobin in severe dengue (11.5 ± 1.33) and non-severe cases (10.53 ± 1.84) revealed significant difference ($p < 0.05$) (Table 2). Dengue, especially severe dengue has been known to be more common on secondary infection and less in conditions of malnourishment and immune weakness. This possible correlation has not been reported extensively in children. Haematocrit could not be monitored as frequently as advised by the WHO

guidelines, and was not used as an indicator of shock severity.

DISCUSSION

In this study the maximally affected children (38.6%) were 6-10 years. This correlates with WHO data that reports the modal age of 6-8 years for low-endemic areas.³ Eregowda A et al also noted mean age of presentation to be 7.5 ± 4.7 years, while Chaudhary V et al⁶ reported mean age in their study as 5.68 ± 1.59 years.^{5,6} Pothapregada S et al and Sahana KS and Sujatha R reported similar results.^{7,8} Kamath S et al on the other hand reported that children less than 5 years were most commonly afflicted with severe disease, with infants forming the largest sub-group in their study.⁹

Pothapregada S et al reported a 1.2:1 male: female ratio, while Sahana KS and Sujatha R similar to this study reported 67.9% incidence in boys and 32.1% in girls with a ratio of 2:1.^{7,8} They also reported a higher percentage (65%) of boys with severe dengue. Other workers like Anders KL et al have reported a significant association between being female and severe dengue while Capeding M et al reported no gender difference.^{10,11} Wichmann D et al, in a study in adults found 52% females affected similar to Kularatne S et al.^{12,13}

30.6% of our subjects hailed from urban Bhopal, with the rest resided in adjoining rural regions. Industrialisation, increased movement of people from urban to rural areas, and environmental changes have all favoured the spread of dengue in rural as well as urban areas. Other studies also observed the same.^{14,15} No significant difference in incidence between rural and urban areas was reported by Tripathi P et al.¹⁶ This study found clustering of cases in the monsoon months of July to October, similar to the epidemiology noted in this part of Asia.¹⁶

Jakribettu R et al have reported 100% fever with 42% myalgia, and various others studies have reported varying incidence of presenting complaints.^{17,18} This difference in the clinical manifestation is possibly due to difference in the strain of the virus and its virulence factor. Gastrointestinal symptoms like abdominal pain and persistent vomiting are considered warning signs in dengue and have been reported in many studies.^{19,20}

Kumar A et al reported gastrointestinal manifestations more in cases of severe dengue, with equal distribution across all age groups.²¹

Sirivichayakul S et al proposed that diarrhea may be a predictor for DHF. They found highest prevalence just before the stage of shock suggesting that it may be related to plasma leakage that may cause malabsorption.²²

16% of patients presented with hypotension of which 9 were managed as Dengue Shock. Nair B et al reported 38.9% cases of shock in their study.²³ 45.3% patients had

a positive tourniquet test which was more than the 24% reported by Sahana K and Sujatha R.⁸

Kulkarni M et al found that abdominal pain and tender hepatomegaly may predict DHF in children and that these patients should be closely monitored for DSS.²⁴ Although hepatomegaly is among the WHO clinical criteria for dengue fever, splenomegaly is not generally held to be a feature of dengue infection. 30.7% of the study population had dengue fever (without warning signs), 32% had dengue with warning signs, and 37.3% were treated as severe dengue. This proportion of severe dengue cases was higher than those reported by Kumar A et al and Hammond SN et al in studies done in Central America, and lower than that reported in other regions of South Asia.^{21,25,11}

Unlike regions like Delhi and South India which have regularly reported increased hospitalisation of patients with severe dengue along with high mortality, the state of Madhya Pradesh has been relatively spared by the morbidity of dengue. This incidence of mild dengue forms in this region could be due to serotype prevalence. Certain studies have also reported milder incidence of dengue symptoms in certain races.¹⁷ This serves to reiterate the varying presentations of dengue incumbent on virus serotype and patient genetic make-up and immunity.

Nausea/vomiting, abdominal pain, rash, diarrhea and petechiae have been reported more commonly in DHF by Sirivichayakul C et al, while Nair B et al found fever with rash and abdominal pain most commonly.^{22,23} Sirivichayakul C et al found rhinorrhoea to be commonly associated in the clinical profile of dengue and Halstead SB et al suggested including dengue in the differential diagnosis of all acute respiratory tract infection in children.^{22,26}

Nair B et al reported 25% frank bleeding with epistaxis being most common. Melena and epistaxis were commonest bleeding manifestations noted which is similar to observation made in the study by Ahmed et al.^{23,27} In this study, children with bleeding tendencies were not necessarily those having low platelet count, indicating a combination of causes such as thrombocytopenia, coagulopathy, and vasculopathy leading to bleeding manifestations.

6.7% of cases had seizures which was similar to 6.8% seizures presentation noted by Nair B et al.²³ As observed in the study done by Wang C et al arthralgia and myalgia were relatively less common complaints in children compared to adults whereas pain abdomen (32.5%) and vomiting (60.5%) constituted the more common presenting symptoms and were seen more commonly in severe dengue patients.²⁸ Various studies have reported that Indian children with DHF have a lower than expected rise in hematocrit during the plasma leakage

period due to the high prevalence of iron deficiency anemia.²⁹

Liver enzymes were significantly altered in patients with mean SGOT 136.69 ± 126.38 and mean SGPT 105.77 ± 103.81 . Deranged liver function in dengue infection can be a result of the direct effect of the virus on liver cells or the unregulated host immune response against the virus. This study reported a mortality of 1.3% (1 in 75) which is lesser than those reported by other Indian authors.⁶ This can be attributed to a greater suspicion of dengue cases in febrile illnesses, effective fluid management in confirmed cases and the largely self-limiting nature of the infection).

The sample size for a comprehensive study of this kind should be larger than that we could include, and a multi-centric study including various ages across the country should be conducted. The cases of dengue that we studied could not be assessed for primary and secondary infections or for infecting serotypes which given the immune-modulatory capacity of dengue should be analysed in each case

CONCLUSION

We attempted to study the features of Dengue infection in Paediatric population in an area recently becoming endemic for the disease. Dengue has a self-limiting course in majority of the cases, but in the acute phase, it can present with multi-organ involvement. Along with other common causes of fever, Dengue must also be suspected, and its warning signs watched for in children in endemic areas.

The WHO guidelines on management of Dengue cases are useful but more information regarding management of cases with neurological and cardiac manifestations are needed. It becomes essential on the part of treating paediatrician to suspect and have knowledge of the atypical manifestations of dengue for the early diagnosis and proper management of the patient. In a country like India with limited healthcare resources, a large part of the population is at risk of dengue due to prevalent conducive conditions for the survival of its vector. Widespread community awareness, early healthcare intervention, and a strong and effective vector control program are urgently required to curb the growing menace of Dengue.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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