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Original Research Article

Clinical profile and laboratory characteristics of dengue fever in children: analysis of 2019 outbreak from Bengaluru, Karnataka, India

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ABSTRACT

Background: Dengue, an endemic disease in most subtropical and tropical regions of the world is causing severe epidemics in India. An alarming rise of dengue has also been seen in India during the recent years. Majority of dengue viral infections are self-limiting, but complications may cause high morbidity and mortality. Present study was undertaken with an objective of describing various clinical presentations as noted in our cohort of dengue patients and to evaluate the outcome of dengue fever.
Methods: This retrospective study included all confirmed dengue cases below 18 years age admitted to Paediatric department of KIMS, Bengaluru over a period of 1 year in 2019. Medical records were reviewed and analysed. Those diagnosed to be positive for dengue serology (NS1 or IgM) were included in our study. Dengue was classified according to the WHO guidelines into 2 groups, Dengue fever (without/with warning signs) and Severe Dengue. Clinical features, haematological, biochemical, radiological parameters, management and the outcome were assessed.
Results: Out of 441 patients enrolled, 79% had non-severe dengue and 21% severe dengue. The commonest age of presentation was above 10 years with mean age of 8.68±5.25 years. Male to female ratio was 1.7:1. 60% presented within 4 to 7 days of illness (mean 4.26±1.72 days). Majority presented with fever (88%). 47% had vomiting and 31% abdominal pain. Bleeding manifestations were seen in 18%. Dengue serology was positive for NS1Ag (58%), IgM (21%), mixed (21%). Thrombocytopenia and leukopenia seen in 82% and 39.45% respectively. The association between dengue serology and platelet count was statistically significant (p value 0.001). 46% had raised SGPT. 31% had evidence of plasma leakage. The case fatality rate was 0.2%.
Conclusions: High grade fever, vomiting, abdominal pain and bleeding manifestations with normal or low platelet count were the presenting features. Early diagnosis, monitoring and prompt supportive management can reduce mortality.

Keywords: Dengue fever, Epidemic, Leukopenia, Thrombocytopenia

INTRODUCTION

Small bites, big threats.[1] Dengue fever has become one of the commonest endemic infectious disease in India that is responsible for causing a lot of morbidity and in a small percentage of the population even mortality.

Even though traction for prevention of dengue fever has gained large momentum in India, the number of cases continue to rise, increasing the economic burden to the country and its human resources.[2]

Before 1970, only 9 countries had experienced severe dengue epidemics. The disease is now endemic in more than 100 countries. The America, South-East Asia and Western Pacific regions are the most seriously affected, with Asia representing ~70% of the global burden of disease.[3] The number of dengue cases reported to WHO

has increased over 15fold over the last two decades. The largest number of dengue cases ever reported globally was in 2019.

According to data from the National Vector Borne Disease Control Programme (NVBDCP), Karnataka had reported 15,232 cases of dengue in 2019 from January till November, a more than four-fold rise over 2018 when 4,427 cases were reported in the entire year. Alarmingly, 61% of dengue cases were from Bengaluru city. Gujarat, Rajasthan Maharashtra, Telengana, Uttrakhand were among the other worst hit states in India in 2019.

Dengue virus is transmitted to humans through the bites of infected female mosquitoes, primarily the species Aedes aegypti and, to a lesser extent, Aedes albopictus. The incubation period is 4-7 days but range from 3 to 14 days.[4] Dengue is caused by a virus of the Flaviviridae family and there are four distinct, but closely related, serotypes of the virus that cause dengue (DENV-1, DENV-2, DENV-3 and DENV-4). Recovery from infection is believed to provide lifelong immunity against that serotype. However, cross-immunity to the other serotypes after recovery is only partial, and temporary. Subsequent infections by other serotypes increase the risk of developing severe dengue. Dengue is widespread throughout the tropics, with local variations in risk influenced by rainfall, temperature, relative humidity and unplanned rapid urbanization.

Expert consensus groups have suggested that dengue is a single entity with different clinical presentations and infected patients present with a range of clinical symptoms that vary according to severity and age.

Infection by any of the four dengue serotypes may be asymptomatic or lead to classic dengue fever (DF) or more severe forms of the disease, haemorrhagic fever (DHF) and dengue shock syndrome (DSS). Confirmation of dengue infection may be possible during the acute phase by testing the serum for presence of the non-structural protein NS1Antigen. Following an incubation period, the illness begins abruptly, going through three phases: febrile, critical and recovery. DF is observed more frequently in adults and adolescents, and can present with either mild fever only or a more incapacitating disease. This latter presentation is characterised by the sudden onset of high fever, severe headache, retro-orbital pain, myalgia, arthralgia and rash, symptoms occurring predominantly in the early febrile stage. In the critical phase, the skin is flushed with the appearance of a petechial rash. This usually occurs around the time of defervescence, typically on days 3–7, and is associated with capillary leakage and haemorrhage. DHF is characterised by a transient increase in vascular permeability resulting in plasma leakage, with high fever, bleeding, thrombocytopenia and haemoconcentration, which can lead to DSS. The 1997 WHO guidelines classified dengue into DF, DHF (Grades 1 and 2) and DSS (DHF Grades 3 and 4). The international DENCO study was designed to evaluate the perceived limitations of the 1997 criteria. Due to various limitations of the 1997 criteria, the international DENCO study was designed and in 2009 WHO criteria classified dengue according to levels of severity: dengue without warning signs; dengue with warning signs (abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, increasing haematocrit with decreasing platelets); and severe dengue (dengue with severe plasma leakage, severe bleeding, or organ failure). Severe Dengue includes the dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Patients who recover following defervescence are considered to have non-severe dengue, but those who deteriorate tend to manifest warning signs. These individuals are likely to recover with intravenous rehydration. However, further deterioration is classified as severe dengue, though recovery is possible if appropriate and timely treatment is given.

The exact clinical presentation in children is important for patient management and thereby saving lives. The objective of the present study is to study the clinical presentations and laboratory characteristics of dengue fever in children.

METHODS

This retrospective study was done over a period of 1 year from January 1st 2019 to December 31st 2019 in the Department of Paediatrics at KIMS, Bengaluru, India. Medical records were reviewed for all patients below 18 years of age with a clinical description of dengue fever and who were diagnosed as dengue NS1 antigen or IgM positive either by Dengue Spot test or by Dengue ELISA.

Patients with any other coinfections such as malaria, leptospirosis, enteric fever, rickettsial fever were excluded from the study as they are known to produce thrombocytopenia as well.

The data was collected by using a predesigned questionnaire which includes the following information like history of symptoms, findings on clinical examination, lab investigation values, treatment given and clinical outcome. The laboratory confirmed sero positive dengue cases were classified according to 2009 WHO Criteria in to non-severe dengue (dengue without/with warning signs) and severe dengue.

Manual checking and coding of data were undertaken before data entry commenced to clean the data and ensure consistency and entered. Once entered, data were checked for any errors; any necessary checks with the original questionnaires were undertaken and corrected before further analysis. All analyses were conducted using SPSS 23 Version; Texas, USA. A chi-square test was used to test association between the factors and outcome variables. A p value <0.05 was considered as statistically significant.

RESULTS

The total number of cases were 441, out of which 347 (79%) were non-severe dengue and 94 (21%) were severe dengue according to WHO guidelines (Figure 1).[4]

There were 269 (61%) males and 172 (39%) females in present study. Amongst the total number of cases, severe dengue was seen more in males (53%) than females (47%). But amongst all the females, 74% had non severe dengue and 26% had severe dengue and in males, 81% had non severe dengue and 19% had severe dengue. The maximum number of cases (177, 40%) were seen above 10 years of age group. The mean age of hospitalized patients was 8.68±5.25 years. The mean delay in admission after appearance of fever was 4.26±1.72 days. 80% of patients were hospitalized for 4-7 days. The mean tenure of hospitalization was 5.14±2.18 days (Table 1).

Table 1: Demographics of children hospitalized with dengue infection.

Parameters	Variables	Non severe dengue (n= 347)		Severe dengue (n= 94)		Total (n= 441)		Mean±SD
		N	%	N	%	N	%	
Age	<1 year	19	5.5	9	9.6	26	5.9	
	1-5 years	100	28.8	20	21.3	120	27.2	
	6-10 years	94	27.1	26	27.7	118	26.7	8.68±5.25
	>10 years	134	38.6	39	41.5	177	40	
Sex	Male	219	63.1	50	53.2	269	61	
	Female	128	36.9	44	46.8	172	39	
Day of admission after onset of fever	0-3 days	128	36.9	25	26.6	153	34.7	
	4-7 days	204	58.8	62	66	266	60.3	4.26±1.72
	>7 days	15	4.3	7	7.4	22	5	
Duration of hospital stay	0-3 days	50	14.4	2	2.1	52	11.8	
	4-7 days	280	80.7	73	77.7	353	80	5.14±2.18
	>7 days	17	4.9	19	20.2	36	8.2	
Outcome	Recovered	347	100	92	98	439	99.5	
	Complication	0	0	1	1.06	1	0.2	
	Death	0	0	1	1.06	1	0.2	

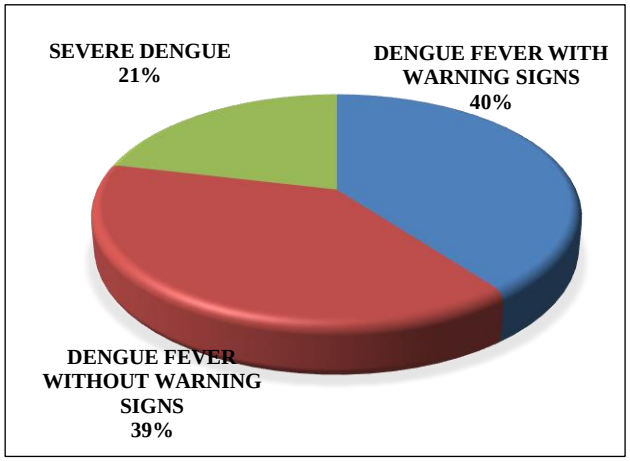

Figure 1: Frequency distribution of dengue fever.

The most common symptoms noticed were fever (88%) followed by vomiting (47%), pain abdomen (31%), myalgia (12%), diarrhoea (11%), headache (9%), petechiae (6%). 3% cases had seizures. Bleeding manifestations were seen in 18%. (Table 2).

Table 2: Clinical features of study population (multiple response).

Parameters	Number (n= 441)	%
Fever	387	88
Myalgia	51	12
Headache	38	9
Cough	22	5
Abdominal pain	136	31
Vomiting	208	47
Diarrhoe	47	11
Petechiae	26	6
Malaena	28	6
Epistaxis	6	1
Hematemesis	4	0.9
Hemoptysis	8	2
Hematuria	7	1.6
Seizures	12	3

Among 82% cases presented with thrombocytopenia. All severe dengue cases had thrombocytopenia whereas 77% of non-severe dengue cases had thrombocytopenia at

admission. 29% had platelets above 1 lakh cells/mm^3, 30% (50,000 - 1 lakh), 35% (20,000-50,000) and 6.6% cases had platelets <20,000. 17% of severe dengue had very low platelet count (<20,000 cells/mm^3) compared to only 4% of non-severe dengue.

Table 3: Laboratory parameters.

Parameters	Variables	Non severe dengue (n= 347)		Severe dengue (n= 94)		Total (n= 441)	
		N	%	N	%	N	%
Total count (cells/mm^3)	Normal (4000-11,000)	187	53.9	52	55.3	239	54.2
	Leukopenia (<4000)	144	41.5	30	31.9	174	39.5
	Leukocytosis (>11,000)	16	4.6	12	12.8	28	6.3
Platelet count (lakhs/mm^3)	≥1.5 lakhs	81	23	0	0	81	18.4
	>1 lakh- 1.49 lakhs	45	13	0	0	45	10.2
	1 lakh-51,000	118	34	15	16	133	30.1
	50,000 -20,000	90	26	63	67	153	34.7
	<20,000	13	3.7	16	17	29	6.6
Hematocrit (%)	≥36.3%	215	62	63	67	278	63
	<36.3%	132	38	31	33	163	37
SGPT (IU/L)	Normal (5-40)	206	59.4	34	36.2	240	54
	41-200	135	38.9	46	48.9	181	41
	201-1000	6	1.7	11	11.7	17	4
	>1000	0	0	3	3.2	3	1

Table 4: Clinical, radiological findings and dengue serology.

Parameters	Variables	Non severe dengue (n= 347)		Severe dengue (n= 94)		Total (n=441)	
		N	%	N	%	N	%
Hepatomegaly	Yes	219	63	94	100	313	71
	No	128	37	0	0	128	29
Pleural effusion	Yes	28	8	34	36	62	14
	No	319	92	60	64	379	86
Ascites	Yes	10	3	66	70	76	17
	No	337	97	28	30	365	83
Dengue serology	NS1Ag	211	61	47	50	258	58
	IgM	66	19	25	27	91	21
	NS1Ag and IgM	70	20	22	23	92	21

Among 39.45% of children had leucopenia and 6.3% had leucocytosis at admission. Raised hematocrit was seen in 63% of the cases.

Alanine aminotransferase (SGPT) was raised in 45.6% of all the dengue patients. 64% of all the severe dengue cases had raised SGPT and 3 patients had SGPT levels >1000 IU/L (Table 3).

In present study, the majority of the patients were positive for NS1 (58%) followed by IgM (21%) as a large number of patients presented within 4 days of fever. Majority (50%) of severe dengue cases was positive for NS1Ag+ve (Table 4). Among 14% of the cases were detected to have pleural effusion by chest X-ray. Hepatomegaly was seen in 71% of the cases and 17% had ascites (Table 4). The association between dengue serology and platelet count was statistically significant (p value 0.001) (Table 5).

Majority (88%) of the patients had fever and they were treated with antipyretics (paracetamol) in appropriate doses. Patients who presented with warning signs and stable vital signs were initially encouraged to take oral fluids; if they were not tolerated, intravenous fluids were started according to the WHO guidelines. Patients with persistent fever spikes were treated with antibiotics (13.4%). Blood products were transfused in 16.55% cases of which more than half were severe dengue cases (66%). Among 441 patients, 5.9% of the cases were started on vasopressors (Table 6).

In the present study, there was 1 death (0.2%) and 1 case developed dengue encephalitis.

Table 5: Association between dengue serology and platelet count.

Parameters	<20 thousand cells/mm^3	20-50 thousand cells/mm^3	51,000- 1 lakh cells/mm^3	>1 lakh/mm^3	Total N=441	p value
NS1Ag	13	85	72	88	258	
IgM	8	44	23	16	91	0.001445*
NS1 and IgM	8	24	38	22	92	

* Significant p value - <0.05

Table 6: Management.

Management	Non severe dengue (n= 347)		Severe dengue (n= 94)		Total (N= 441)	
	N	%	N	%	N	%
Antipyretics	331	95.4	56	59.6	387	87.75
Intravenous fluids	347	100	94	100	441	100
Blood products transfusion	25	7.2	48	51.1	73	16.55
Antibiotics	31	8.9	28	29.8	59	13.4
Vasopressors	0	0	26	27.65	26	5.9

DISCUSSION

Dengue is one of the most common arbo viral infection in tropical countries. A vast majority of cases are asymptomatic or mild and self-managed, and hence the actual number of dengue cases are under-reported. Many cases are also misdiagnosed as other febrile illnesses. Global incidence of dengue fever has increased significantly in the recent decades.[5] Dengue epidemic has increased in recent past probably due to unplanned urbanization with rapid construction activities, unhygienic condition and poor sanitation facilities contributing fertile breeding soil for mosquitoes. Moreover, there is increase in awareness in medical practitioners following the epidemics with availability of diagnostic tools in the hospitals have contributed to the increased detection of cases. Dengue has now become an expected post-monsoon phenomenon in many parts of India.[6,7] The hyper endemicity with two or more serotypes during the same time period have been widely recognised as important cause of disease severity in India.[8,9]

As per the WHO TDR 2009 dengue guidelines, dengue cases were analysed. In present study, 441 cases were analysed, out of which 347 (79%) were categorised as cases of non-severe dengue and 94 (21%) were cases of severe dengue. The maximum number of cases were seen in the above 10 years age group (39%) and the least affected age group was infants (6%) which was similar to other studies.[10] Male to female ratio in present study was 1.7:1 which was similar to a study by Dash PK et al, where male to female ratio was 1.28:1, and Neerja M et al it was 2:1.[11,12] This was probably due to covered dress used by females. This similar pattern of age and sex predilection was also seen in the retrospective analysis of the 2017 dengue outbreak from Central Kerala.[10] More than half (60%) of the children presented to us within 4 to 7 days of illness.

Patients were diagnosed as dengue fever based on detection of dengue non- structural protein (NS1Ag), anti-dengue IgM in the blood samples. Maximum cases showed serology test positivity for NS1Ag (58%), positivity for IgM in 21% patients and mixed positivity in 21% patients.

In this study, fever was present in most of the cases, followed by vomiting and abdominal pain similar to the study conducted in Karachi, Pakistan.[13] Other symptoms were myalgia, diarrhoea, headache, cough and seizures. Bleeding in dengue is multifactorial which was seen in 18% of all the dengue cases which was similar to a study by Laul et al.[14] The most common bleeding manifestations in dengue were petechiae, malaena, hemoptysis, epistaxis, hematuria, hematemesis. The various clinical findings like hypotension, pleural effusion, and respiratory distress were notable and were analogous to other studies.

In the present study leukopenia was seen in 39.5% which was similar to a study by Dhivya P et al, where leucopenia was seen in 36% cases.[15] In the study by Karoli R et al, and Singh N et al, leukopenia was noted in 86% and 68% of the population respectively. This outcome was significantly higher than noted in this study.[16,17] In this study, thrombocytopenia was seen to be more in those with severe dengue and 17% of severe dengue had platelets less than 20,000 cells/mm^3.[18] The

association between dengue serology and platelet count was statistically significant (p value 0.001).

Liver involvement in the form of hepatomegaly and increased transaminase was observed in this study. Hepatomegaly was seen in almost three-fourth of the study population. Alanine transaminase (SGPT) was increased in 45.6% of the subjects of which 3 patients had SGPT levels more than 1000 IU/L. These data were similar to the results described by Dhivya et al.[15]

Packed cell volume (PCV) is used regularly to evaluate plasma leakage in dengue infection. More than half (63%) of children and adolescents with dengue infection had initial hematocrit measurements above 36.3% at admission. It was also reported in previous studies that in some cases the fluid leakage does not achieve a high degree haemoconcentration even if the patient is in shock. In dengue patients the rise of PCV could have been due to dehydration as a result of poor intake and vomiting.[19] Evidence of plasma leakage in the form of pleural effusion was seen in 14% of study population and ascites in 17.2% which was similar to study by Dhivya P et al, where it was 16% and 19.2% respectively.[15]

The mean tenure of hospitalization was 5.14±2.18 days. Duration of hospitalization was more in severe dengue patients (20% cases hospitalized for more than 7 days). One patient had developed dengue encephalitis. The overall mortality in this study population was only 0.2% unlike a study conducted by Darshan Mehra et al, where the mortality rate was 1.55%.[20] This may be due to early identification and appropriate management as per the guidelines.

CONCLUSION

The study draws attention to susceptibility of the male and adolescent age group. Clinical assessment, serologically positive findings will help in early diagnosis and treatment. Dengue fever cannot just be simply considered as a viral infection, especially in a scenario where so many atypical presentations are seen.

There are so many aspects which are manifested differently which when noticed promptly can help in reducing complications of DHF and DSS. Lastly use of mosquito control measures should not be underestimated because it forms the baseline of the treatment in urban as well as rural population.

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REFERENCES

1. WHO. Small bite, big threat. WHO. Available at: http://www.who.int/campaigns/world-health-day/2014/posters/en/. Accessed on 23rd April 2019.
2. Chaudhuri M. What can India do about dengue fever? BMJ. 2013:346.
3. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL et al. The global distribution and burden of dengue. Nature. 2013;496(7446):504-7.
4. National Guidelines for Clinical Management of Dengue Fever. Available at: http://www.searo.who.int/india/publications/national_guidelines_clinical_management_dengue1.pdf?ua
5. Gupta P, Khare V, Tripathi S, Nag VL, Kumar R, Khan MY et al. Assessment of WHO definition of dengue hemorrhagic fever in North India. J Infect Dev Ctries. 2010;4:150-5.
6. Kumaria R, Chakravarti A. Molecular detection and serotypic characterization of dengue viruses by single tube multiplex RT-PCR. Diagn Microbiol Infect Dis. 2005;52(4):311-6.
7. Chakravarti A, Kumaria R. Eco-epidemiological analysis of dengue infection during an outbreak of dengue fever, India. Virology J. 2005;2:32;1-7.
8. Endy TP, Nisalak A, Chunsuttiwat S, Libraty DH, Green S, Rothman AL et al. Spatial and temporal circulation of dengue virus serotypes: a prospective study of primary school children in Kamphaeng Phet, Thailand. Am J Epidemiol. 2002;56:52-9.
9. Graham RR, Juffrie M, Tan R, Hayes CG, Laksono I, Ma'Roef C, et al. A prospective sero epidemiologic study on dengue in children four to nine years of age in Yogyakarta, Indonesia Studies in 1995-1996. Am J Trop MedHyg 1999;61:412-19.
10. Kumar SK, Rajendran NK, Brabhukumar AC. Clinical profile of dengue fever in children: analysis of 2017 outbreak from central Kerala. Int J Contemp Pediatr. 2018;5:2265-9.
11. Neeraja M, Lakshmi V, Teja VD, Umabala P, Subbalakshmi MV. Serodiagnosis of dengue virus infection in patients presenting to a tertiary care hospital. Indian J Med Microbio. 2006;24(4):280.
12. Dash PK, Parida MM, Saxena P, Kumar M, Rai A, Pasha ST et al. Emergence and continued circulation of dengue-2 (genotype IV) virus strains in northern India. J Med Virol. 2004;74(2):314-22.
13. Ahmed S, Arif F, Yahya Y. Dengue fever outbreak in Karachi 2006- a study of profile and outcome of children under 15 years of age. J Pak Med Assoc. 2008;58(1):4-8.
14. Laul A, Laul P, Merugumala V, Pathak R, Miglani U, Saxena P. Clinical profiles of dengue infection during an outbreak in Northern India. J Tropical Med. 2016;2016.
15. Dhivya P, Monika A, Jayaramachandran S. Clinical profile of Dengue fever in an urban tertiary care hospital in South India. Int J Adv Med. 2019 Jun;6(3):618-22.
16. Karoli R, Fatima J, Siddiqi Z, Kazmi KI, Sultania AR. Clinical profile of dengue infection at a teaching hospital in North India. J Infect Develop Countr. 2012;6(07):551-4.

17. Singh N, Jhamb R, Agarwal S, Gaiha M, Dewan R, Daga M, et al. The 2003 outbreak of dengue fever in delhi, india. Southeast Asian J Trop Med Public Health. 2005;36(5):5.
18. Ratageri VH, Shepur TA, Wari PK, Chavan SC, Mujahid IB, Yergolkar PN. Clinical profile and outcome of dengue fever cases. Indian J Pediatr. 2005;72(8):705-6.
19. Shah I, Katira B. Clinical and laboratory abnormalities due to dengue in hospitalized children in Mumbai in 2004. Dengue Bulletin. 2005;29:90-6.
20. Mehra D, Taori K, Agrawal S, Sharma M. Clinical Profile of Dengue Fever. JMSCR. 2019;7(7):249-53.

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