Clinical and Laboratory Profile of Dengue Fever in the Paediatric Age Group at a Tertiary Care Hospital of West Bengal - A Comparison of Two Subsequent Years

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ABSTRACT

BACKGROUND

Dengue is a major public health concern in tropical Asian countries and a most rapidly spreading mosquito borne viral disease with a 30 fold increase in global incidence over the last five decades. Dengue is among the ten leading causes of death in children ranging from 1 to 15 years of age in tropical Asian countries. Complications of dengue fever are common in children. But very limited studies are available on paediatric populations. The virus or non-structural protein (NS1) interacts with platelets and coagulation factors. A combined effect of mild disseminated intravascular coagulation, liver damage and platelet dysfunction results in bleeding in dengue fever. With this scientific knowledge background, the present study was undertaken to identify and document the changing pattern of dengue infection in paediatric age group with a special emphasis on laboratory findings of dengue cases in paediatric age group.

METHODS

The present descriptive study was conducted for two years in a state run paediatric referral hospital. The sample was purposive by design and consisted of patients who have been diagnosed as having dengue fever with warning signs and admitted.

RESULTS

Fever was typically high grade (> 103 F) and most patients presented with warning signs within 5 days of illness (64.2 % in year 2016 and 76.6 % in year 2017). Persistent vomiting and abdominal pain were the most common warning signs in both the years. Thrombocytopenia was the commonest laboratory finding. Bleeding in study subjects lead to < 50000 / cu mm platelet count. Most common bleeding was gastrointestinal bleeding (39.2 % of study subjects with platelet count < 50000 / cu mm presented with G. I bleeding).

CONCLUSIONS

Dengue illness comes with varied presentation. Atypical presentations can delay the diagnosis. Early recognition of warning signs keeping the atypical presentation in mind is important.

KEYWORDS

Dengue Fever, Paediatric Age Group, Non-Structural Protein (NS1), Thrombocytopenia

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DOI: 10.18410/jebmh/2021/405

How to Cite This Article:
Sikdar S, Bandyopadhyay U, Das S, et al. Clinical and laboratory profile of dengue fever in the paediatric age group at a tertiary care hospital of West Bengal - a comparison of two subsequent years. J Evid Based Med Healthc 2021;8(25):2162-2167. DOI: 10.18410/jebmh/2021/405

Submission 30-12-2020,
Peer Review 10-01-2021,
Acceptance 05-05-2021,
Published 21-06-2021.

BACKGROUND

Dengue is an acute febrile illness caused by mosquito borne viruses of genus flavivirus.[1,2] It is characterized by biphasic fever, rash, myalgia or arthralgia, thrombocytopenia, capillary leakage, coagulopathy and shock in severe cases.[2] Dengue subgroup is composed of four antigenically distinct members.[1,2,3,4,5] These four are closely related antigenically but do not provide complete cross protection from infection by any of them.[6,7] Dengue is a major public concern in tropical Asian countries and a most rapidly spreading mosquito borne viral disease with a 30 fold increase in global incidence over the last five decades.[3,8] Dengue is among the 10 leading causes of death in children ranging from 1 to 15 years of age in tropical Asian countries.[3] Every year, severe dengue cases take thousands of lives.[8] The loss to the economy is 264 disability - adjusted life years (DALYS) per million per year.[8] Average case fatality rate (CFR) is estimated to be less than 1 %.[9] Although in some tropical countries case fatality rate is as high as 5 %.[3,9] Both severe forms of dengue namely dengue shock syndrome (DSS) and dengue haemorrhagic fever (DHF) are frequently reported in India.[10] The mosquito, *Aedes aegypti* flourishes in urban environments, breeding in stagnant water.[11] Rapid urbanization explains the increasing rates of Dengue infections.[11] Complications of dengue fever are common in children. But very limited studies are available on paediatric populations.

The virus or non - structural protein (NS1) interacts with platelets and coagulation factors.[2] Platelet dysfunction is both qualitative and quantitative.[6] A combined effect of mild disseminated intravascular coagulation, liver damage and platelet dysfunction results in bleeding in dengue fever.[3,6]

Objectives

- To describe the clinical profile of dengue fever in paediatric age group.
- To compare the changing patterns of dengue fever between subsequent two years of the paediatric age group.

METHODS

The present descriptive study was conducted for two years from January, 2016 to December, 2017) in a state run paediatric referral hospital. The sample was purposive by design and consisted of patients who were diagnosed with dengue fever along with warning signs and admitted.

Inclusion Criteria

- Patients who have been diagnosed by IgM antibody test or both NS1Ag and IgM reactivity.
- Patients who have been diagnosed as "Dengue with Warning signs" or developed symptoms after admission: Following are the warning signs - abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy, restlessness, liver enlargement > 2 cm, increase in haematocrit concurrent with rapid decrease in platelet count.

Exclusion Criteria

- Dengue like illness confirmed by negative result on IgM antibody test.
- Patients not giving consent.

Laboratory Investigations

- Complete blood count, ESR, Malaria parasite.
- Liver Function Tests: Serum Albumin, Alanine aminotransferase, Bilirubin.
- Urea, creatinine.
- Dengue serology: NS1 antigen assay, IgM antibody detection.
- Cerebrospinal fluid study if indicated.
- Echocardiography if indicated.
- Radiological studies e.g. X-Ray, USG, CT scan, MRI scan if indicated.

The study began after receiving approval from the Institutional Ethics Committee. Patients were selected as given in the inclusion criteria and recruited in the study after getting an informed consent in writing. Clinicoepidemiological and laboratory data were collected from dengue patient with warning signs[2] for the year 2017. This data was compared with the data collected retrospectively from patients admitted in the institute in the year 2016. Detailed clinical history, physical examination and laboratory investigations of all patients were done. A pre- designed semi structured proforma was used. The data collected and entered in the Microsoft excel and analysed. Fever grades were defined as High (39.4 - 40.5 ° C, measured in axillary region.), moderate (37.8 - < 39.4 ° C) and low grade (37.2 - < 37.8 ° C).

Any signs of fluid accumulation oedema - ascites, pleural effusion, facial puffiness were grouped as signs of plasma leakage. Decreased urine output (< 0.5 ml / kg / hr.) for less than 7 hours was taken as oliguria. Acute kidney injury was defined from - risk, injury, failure, loss of kidney function, end stage kidney (RIFLE) criteria.[2] More than 3 episodes of vomiting in 12 h, preventing adequate oral hydration was taken as persistent vomiting. Haematocrit value at admission was compared with the normal range of value for age.[6] Leucocyte counts were grouped by Pittsburgh Guidelines.[2]

Data Analysis

All recorded data were analysed using standard statistical methods (SPSS software) including standard diagrams and graphs and the findings were discussed in details to draw appropriate conclusion. chi square test and fisher's exact test were used as test of significance.

RESULTS

In this study total admissions of dengue with warning sign cases were 157 and 171 for the year 2016 and 2017 respectively. Percentages of infant admissions were 5.7 % more in year 2017 than 2016. The difference was significant (P < 0.05, chi square test). Admissions were 4.9 % and 0.7 % less in year 2017 than 2016 for age group 1 - 5 yrs. and > 5 - 12 yrs. respectively.

Infants		Count	3	13
		% within year of admission	1.9 %	7.6 %
Age group	Age 1 - 5 yrs.	Count	50	46
		% within year of admission	31.8 %	26.9 %
	Age 5 -12 yrs.	Count	104	112
		% within year of admission	66.2 %	65.5 %
	Total	**Count**	**157**	**171**
		% within year of admission	**100.0 %**	**100.0 %**
Gender	Male	Count	76	93
		% within year of admission	48.4 %	54.4 %
	Female	Count	81	78
		% within year of admission	51.6 %	45.6 %
	Total	**Count**	**157**	**171**
		% within year of admission	**100.0 %**	**100.0 %**

Table 1. Distribution of Cases According to Age and Gender

Grade of Fever	Moderate Grade	Count	7	6	P Value
		% within year of admission	4.5 %	3.5 %	P value 0.66
	High grade	Count	150	165	
		% within year of admission	95.5 %	96.5 %	
Total		**Count**	**157**	**171**	
		% within year of admission	100.0 %	100.0 %	
Duration of fever		≤ 5 days	98 (62.4 %)	131 (76.6 %)	P value : 0.005
		> 5 days	59 (37.6 %)	40 (23.4 %)	
Rash	Not present	Count	79	53	
		% within year of admission	50.3 %	31.0 %	
	Present and non - itchy	Count	31	66	
		% within year of admission	19.7 %	38.6 %	
	Present and itchy	Count	47	52	
		% within year of admission	29.9 %	30.4 %	
Total		**Count**	**157**	**171**	**P Value < 0.001**
		% within year of admission	100.0 %	100.0 %	
Arthralgia, Body ache.	Absent	Count	128	88	
		% within year of admission	81.5 %	51.5 %	
	Present	Count	29	83	
		% within year of admission	18.5 %	48.5 %	
Total		**Count**	**157**	**171**	**P Value < 0.001**
		% within year of admission	**100.0 %**	**100.0 %**	

Table 2. Distribution of Cases According to Grade of Fever, Duration of Fever, Year of Admission, Rash, Arthralgia, and Body Ache (Chi Square Test)

Most patients presented with high grade fever (103 - degree F) in both years. P - value was 0.66. There was no significant difference between 2016 and 2017. In this study, in the year 2017 most cases (76.6 %) presented warning signs with less than 5 days' fever than 2016 (62.5 %) and this difference was significant. In this study, rash was 19.3 % more in the year 2017 than 2016 and this difference was significant. Rash was found to be itchy in approximately 30 % cases. In this study, Arthralgia & Body ache were 30 % more in the year 2017 than 2016 and this difference is significant.

Platelets			2016	2017	
	> 150000 / mm^3		31 (19.7 %)	44 (25.7 %)	
	> 100000 – ≤ 150000 / mm^3		33 (21.0 %)	30 (17.5 %)	
	> 50000 – ≤ 100000 / mm^3		50 (31.8 %)	62 (36.3 %)	
	> 10000 – ≤ 50000 / mm^3		42 (26.8 %)	33 (19.3 %)	
	≤ 10000 / mm^3		1 (0.6 %)	2 (1.2 %)	**chi sq test**
Total			**100 %**	**100 %**	**P value 0.34**
GI Bleeding			**Absent**	**Present**	
Platelets	> 150000 / mm^3	Count	75	0	
		% within platelets	100.0 %	0.0 %	
	> 100000 – ≤ 150000 / mm^3	Counts	63	0	
		% within platelets	100.0 %	0.0 %	
	> 50000 – ≤ 100000 / mm^3	Count	107	5	
		% within platelets	95.5 %	4.5 %	
	> 10000 – ≤ 50000 / mm^3	Count	56	19	
		% within platelets	74.7 %	25.3 %	
	≤ 10000 / mm^3	Count	0	3	
		% within platelets	0.0 %	100.0 %	**Fisher's exact test**
Total		**Count**	**301**	**27**	**P value < 0.001**
		% within platelets	91.8 %	8.2 %	
Petechiae & Purpura			**Absent**	**Present**	
Platelets	> 150000 / mm^3		75 (100.0 %)	0	
	> 100000 – ≤ 150000 / mm^3		61 (96.8 %)	2 (3.2 %)	
	> 50000 – ≤ 100000 / mm^3		95 (84.8 %)	17 (15.2 %)	
	> 10000 – ≤ 50000 / mm^3		14 (18.7 %)	61 (81.3 %)	
	≤ 10000 / mm^3		0	3 (100.0 %)	**Fisher's exact test**
Total			**74.7 %**	**25.3 %**	**P value < 0.001**

Table 3. Distribution of Cases According to Platelet Count

Platelets * Year of admission Cross tabulation, Platelets * G.I. Bleeding Cross tabulation , Platelets * Petechiae / Purpura Cross tabulation

Thrombocytopenia was 4.6 % less in the year 2017 but there was no significant difference. Only 0.6 % (year 2016) and 1.2 % (year 2017) presented with platelets ≤ 10000 / cu mm. 26.8 % (in 2016) and 19.3 % (in 2017) had platelet count > 10000 ≤ 50000. There was a significant difference in platelet count between GI Bleeding present (M = 35740.74, SD = 17439.11) and absent groups (M = 120694.02, SD = 99634.48); [t (230.15) = 12.77, P = .000].

	N	Minimum	Maximum	Mean	S.D.
Haematocrit 2017	171	13.0	58.2	37.419	7.5326
Haematocrit 2016	157	14.0	56.1	37.438	6.8142

Table 4. Haematocrit on Admission

Haematocrit	28 - 40	Count	96	99	
		% within year of admission	61.1 %	57.9 %	
	< 28	Count	14	14	
		% within year of admission	8.9 %	8.2 %	
	> 40	Count	47	58	
		% within year of admission	29.9 %	33.9 %	chi sq test
Total		**Count**	**157**	**171**	**P value 0.74**
		% within year of admission	100.0 %	100.0 %	
ALT		< 45 U / L	50 (31.8 %)	53 (31.0 %)	
		≥ 45 < 90 U / L	54 (34.4 %)	78 (45.6 %)	
		≥ 90 U / L	53 (33.8 %)	40 (23.4 %)	chi sq test
Total			**100 %**	**100 %**	**P value 0.058**
Leucocytes		Leukopenia (< 5000)	68 (43.4 %)	47 (27.5 %)	
		Normal	85 (54.1 %)	114 (66.7 %)	
		Leucocytosis (> 15000)	4 (2.5 %)	10 (5.8 %)	chi sq test
Total			**100.0 %**	**100.0 %**	**P value 0.07**
Albumin		Albumin ≥ 3.5 gm / dl	128 (81.5 %)	129 (75.4 %)	
		≥ 2.5 - < 3.5 gm / dl	29 (18.5 %)	35 (20.5 %)	
		< 2.5 gm / dl		7 (4.1 %)	fisher's exact test
Total			**100 %**	**100 %**	**P value 0.026**

Table 5. Distribution of Cases According to Haematocrit on Admission, Fisher's Exact Test

HCT * Year of admission Cross tabulation, ALT * Year of admission Cross tabulation, Leucocytes * Year of admission Cross tabulation, Albumin * Year of admission Cross tabulation

Gastrointestinal bleeding was present in 25.3 % of the patients with platelet count > 10000 ≤ 50000 / cubic mm and in all the cases with platelet count less than 10000 / cu mm. A significant difference was also found in platelet count between petechiae / purpura present (M = 42542.17, SD = 20093.86) and absent groups (M = 137807.76, SD = 102610.84); [t (291.26) = 13.77, P = .000]. 81.3 % of cases presented with petechiae and purpura among cases with thrombocytopenia < 50000 / cubic mm. Only 15.2 % with platelet counts above 50000 / cu mm presented with petechiae. Mean haematocrit was 37.419 with standard deviation of 7.531 in the year 2017 and 37.438 with standard deviation of 6.814 in the year 2016.

In this study, more than half of the children presented with normal haematocrit (61.1 % in 2016 and 57.95 % in 2017) on admission. In 33.9 % of the cases haematocrit was > 40 % in the year 2017 and 29.9 % in year 2016). Haematocrit < 28 % was found in approximately 8 % of the cases in both the years. There was no significant difference between 2016 and 2017. In this study patients with leucopenia were 15.6 % lesser and patients with Leucocytosis were 3.3 % higher in the year 2017 than 2016. The difference was significant. Most of the cases had normal leucocyte count (54.1 % in 2016 and 66.7 % in 2017). Hypoalbuminemia was 6.1 % more in the year 2017 and the difference was significant. In the year 2017, 4.1 % cases presented with ≤ 2.5 gm / dl albumin level.

DISCUSSION

Dengue is an important arboviral infection in India. Incidence of Dengue is rising steadily in recent years and case fatality has increased as well. Few studies are based on WHO 2009 classification of dengue fever. This study is based on the new revised classification and compares clinico- epidemiological data of 2016 and 2017 of patients admitted in the institute. All the cases included in this study had presented with warning signs at admission or developed the warning signs after admission. Total number of analysed cases with warning signs were 157 and 171 for the year 2016 and 2017 respectively. The cases were classified as dengue with warning signs and severe dengue. Percentages of infant admissions were 5.7 % more in the year 2017 than 2016. The difference was significant. Admissions were 4.9 % and 0.7 % less in year 2017 than 2016 for age group 1 - 5 yrs. and > 5 - 12 yrs. respectively. (Table 1)

Similar findings were reported by Mishra et al.[12] They observed that 61.8 % of the cases were in the age group of more than 8 years [8 - 11 yrs. (27.8 % cases) and > 11 years (34 % cases)] Banerjee et al.[13] also reported that school age children (> 6 years) were most vulnerable to dengue infection. It may be due to the fact that dengue transmission is facilitated by crowded places like school. The school premises and buildings are also potential breeding grounds. Outdoor activities also increase in school age children and thereby makes them vulnerable to dengue infection. In this study (Table 1) males (48.4 %) were less affected than females (51.6 %) in the year 2016. But in 2017 males (54.4) were more affected than females (45.6 %). There was no significant difference. Murugananthan et al.[14] reported 50.7 % females and 49.4 % males in their study. Banerjee et al.[13] reported 58 % males and 42 % females.

Fever is the most common symptom affecting 100 % of the cases. The grade of the fever was typically high grade > 39.4° C [95.5 % in 2016 and 96.5 % in 2017]. Few cases presented with moderate grade fever (37.8 - 39.4 °C). (Table 2) According to Nelson textbook of paediatrics[2] majority of infected older children experienced sudden onset of fever (grade 103 - 106° F or 39.4 - 41.1° C). Most of the cases were admitted with fever of < = 5 days' duration [62.4 % in 2016, 76.6 % in 2017]. According to WHO[15] critical phase of dengue fever occurs usually on days 3 - 7 of illness. Most of the cases in this study were presented within 5 days of fever with warning signs. In 2017 admission within 5 days of illness were 14.2 % more than 2016 and the difference was significant. (Table 2) The difference may be due to increased awareness of warning signs or the increased severity of dengue illness. More than half of the patients presented with rash [49.7 % in 2016 and 69 % in 2017]. The difference was significant. In approximately 30 % of cases rash was itchy [29.9 % in 2016 and 30.4 % in 2017]. (Table 2)

Banerjee et al.[13] reported skin rash in 25.5 % of cases of all dengue fever. Upadhyay et al.[16] reported high incidence of rash in case of dengue haemorrhagic fever (84 %). The study selected only cases with warning signs which may progress to severe dengue. This explains high incidence of rash in this study. Rash was 19.3 % more in the year 2017 which indicated increased severity of illness in the year 2017 than 2016. In this study arthralgia and body ache were present in 18.5 % and 48.5 % of the cases in the year 2016 and 2017 respectively. Arthralgia and body ache were significantly more in the year 2017 than 2016 (Table 2). Banerjee et al.[13] reported Myalgia / Arthralgia in 63 % of cases. Thrombocytopenia (Platelet count < 150000 / cu mm) was the most common laboratory finding [80.3 % cases in 2016 and 74.3 % in 2017] in dengue fever with warning signs. Petechiae / Purpura was present in 81.3 % and 15.2 % of patients with platelet count > 10000 < = 50000 and > 50000 - < = 100000 / cu mm platelet count respectively. All cases (100 %) with < 10000 / cu mm platelet counts presented with bleeding. 31.3 % of cases with platelet count less than 50000 / cu mm presented with gastrointestinal bleeding. (Table 3)

Pothapregada et al.[17] observed 80.3 % thrombocytopenia and severe thrombocytopenia in 16.9 % of cases. Mallhi et al.[18] reported thrombocytopenia in 59.2 % of cases. Ramachandran et al.[19] reported thrombocytopenia (platelet count of < 1,00,000 / cu mm) in 82.6 % of the cases. In this study, mean haematocrit was 37.419 with standard deviation of 7.531 in the year 2017 and 37.438 with standard deviation 6.814 in the year 2016. (Table 3, 4). Rapid increase in haematocrit (HCT) is one of the WHO criteria of warning signs. But it was difficult to diagnose haemoconcentration as no previous haematocrit (base line) data was available in most cases. Most of the cases in this study were referred cases. Most of the cases were already treated in other hospitals with fluid therapy or had taken oral rehydration solution at home. Various studies (38 – 41) documented haematocrit values taking different range of cut off. In this study haematocrit above 40 % was found in 29.9 % (year 2016) and 33.9 % of the cases (year 2017). Haematocrit < 28 % was found in 8.9 % (year 2016) and 8.2 % (year 2017) of cases (Table 5). Taking reference range from Nelson Textbook of paediatrics (2), 19.1 % (2016) and 24.6 % (in 2017) of cases were found to be above reference range.

In this study 68.2 % and 69 % of cases presented with deranged Alanine amino transferase level (> 45 U / L) in the year 2016 and 2017. Value more than twice of normal (> 90 U / L) was found in 33.8 % (year 2016) and 23.4 % (year 2017) of cases. (Table 5). Fernando et al.[20] observed ALT > 40 – 160 IU / L in 69.6 % (of total non-severe) and 50 % (severe dengue); > 160 IU / L in 9.09 % (of total non-severe) and 72.2 % of cases (of total severe dengue). However, Mishra et al.[12] found elevated ALT (> 50 IU / L) only in 30.92 % of cases. Leucopenia (< 5000) was found in 43.3 % (year 2016) and 27.4 % (year 2017) of dengue patients with warning signs. Leukocytosis was found in 2.5 % (2016) and 5.8 % (2017) of study subjects. (Table 5) However Mishra et al.[12] found Leukopenia (< 4000 cells / cu mm) in 25.77 % of cases and leukocytosis in (> 11000 cells / cu mm) 15.46 % of cases. Pothapregada et al.[17] found Leukopenia (< 4000 / cu mm) in 19.7 % of cases. Significant difference in leucocyte count between two years is present in our study (Table 5). In present study, 18.5 % (year 2016) and 24.6 % (year 2017) presented with Hypoalbuminemia (< 3.5 gm / dl) and the difference between two years was significant. In the year 2017, 4.1 % of cases presented with < 2.5 gm / dl albumin. (Table 5) Increased incidence of hypoalbuminemia may be due to increased severity of illness in year 2017. Pothapregada et al. [17] observed hypoalbuminemia (< 3 gm / dl) in 7.55 % of cases. However, Fernando et al[20] reported low albumin (< 3.5 gm / dl) in 72 % of cases.

CONCLUSIONS

Dengue is a common disease in the tropical countries. It is one of the most important febrile illnesses during the monsoon and post monsoon season. It can affect any age group. But children of 5 - 12 years' age group are commonly affected. Both sexes are equally affected in dengue. This study shows that dengue can present with typical symptoms along with other atypical manifestations. Fever was typically high grade (> 103 F) and most patients presented with warning signs within 5 days of illness (64.2 % in year 2016 and 76.6 % in year 2017). Persistent vomiting and abdominal pain were the most common warning signs in both the years. Thrombocytopenia was the commonest laboratory finding. Bleeding in study subjects increased with < 50000 / cu mm platelet count. Most common bleeding was gastrointestinal bleeding (39.2 % of study subjects with platelet count < 50000 / cu mm presented with G.I. bleeding). Dengue illness comes with varied presentation. Atypical presentations can delay the diagnosis. Complications can be severe. Early recognition of warning signs keeping the atypical presentation in mind is important.

Limitations

- It is a hospital based single centre study. Study population may not be representative of the general population. Larger population - based study is required.
- Sample size was limited.
- Costs and feasibility were a limiting factor.
- Measurement of the dengue viral serotype could not be done in our setting.
- Primary and secondary dengue infection could not be differentiated.
- This study was compared with other studies. But other studies have their own representative population.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

Authors acknowledge immense support of the patients and their parents who participated in the study. Authors also acknowledge immense help of the scholars and authors whose articles are cited and included in reference of the manuscript. The authors are also grateful to authors, editors and publishers of all those articles, journals and books from where the literature of this article has been reviewed.

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