Original Research Article

A study of clinical and laboratory profiles of dengue fever in children

Anand R.[1], Selvakumar L.[2], Sagayaraj B.[3], Sujatha B.[4], Porchelvan[5]

[1]Dr. Anand R, [2]Dr. Selva Kumar L, [3]Dr. Benjamin Sagayaraj, [4]Dr. Balamma Sujatha, all above authors are affiliated with Department of Paediatrics, Saveetha Institute of Medical and Technical Sciences. Chennai, Tamil Nadu, [5]Dr. Porchelvan, Department of Community Medicine, Saveetha Institute of Medical and Technical Sciences. Chennai, Tamil Nadu, India.

Corresponding Author: Dr. Anand R, Department of Paediatrics, Saveetha Institute of Medical and Technical Sciences. Chennai, Tamil Nadu. E-mail: anand160988@gmail.com

Abstract

Background: Early recognition of characteristic clinical and laboratory parameters of is importantto facilitate prompt diagnosis andtreatmentfor a better outcome, particularly in dengue burden countries. **Methods:** Children aged less than 15 years who sought medical care in the pediatric department of Saveetha medical college, diagnosed as Probable Dengue/Dengue fever/ dengue with warning sign/severe dengue according to standard guidelines during the study period (July 2017 – December 2017) comprised the study sample. **Results:** A total of 61 cases were enrolled, of these 36 were boys. The mean age was 6.49 years. Only five patients had severe dengue. Fever (96.7%), loss of appetite (59%), cough and running nose (33%) were common symptoms noted and itching (37.7%) was common during recovery. Only 11.4% of children had bleeding manifestation. Hepatomegaly was noticed in 35 children. Five children went into shock, 2 of whom had hypotension. NS1 was positive in 49%, IgM in 36%, and IgG in 13%. NS1 positivity rate on day 4, day 5 and day 6 of illness were 62.5%, 38.4% and 18.1% respectively. **Conclusion:** Dengue fever is common during monsoon season, and the course and severity are highly variable. Though the manifestations of dengue are similar to other viral infections, morbidity and mortality are more, thus requiring early diagnosis. As observed in our study the presence of prodromal respiratory symptoms does not preclude the diagnosis of dengue. There should be a high index of suspicion of co-infection, notablymalaria and scrub typhus, if there is an unusual persistence of fever.

Keywords: Dengue fever, Severe dengue, Co-infection

Introduction

Day-biting Aedesaegypti and Aedesalbopictus transmitsone of four serotypes of dengue viruses (DEN1-4) of the Flaviviridae family to cause dengue fever. While the primary infection in human has often been in apparent, secondary infection by heterologous types frequently causes severe dengue [1]. Dengue is now endemic in over 100 countries, resulting in 40% of the world's population living mostly in urban and semi-urban settings being at risk for dengue.

Although there is no specific treatment for dengue, careful hemodynamic and hematologic parameters monitoring, volume repletion and close observation for the signs of severe disease can reduce dengue' smorbidity and mortality [2]. Dengue virus transmission is ubiquitous with the highest risk in Asia (70%), Africa (16%) and South American countries (14%) of which over half occurred in Brazil and Mexico [3]. India alone contributes 14% of the global burden which is mainly due to densely populated areas that serve as ideal circumstances for the dengue borne mosquitoes to breed and spread disease [4–6].

Dengue is the leading cause of childhood morbidity and mortality globally than any other vector-borne viral disease [7]. In the last few decades, the number of dengue cases has gradually increased in India. Malaria and dengue were the most common causes of fever among hospitalised patients with acute undifferentiated fever [8].

Various factors like change in temperature and precipitation [4], nutritional status of overweight and undernutrition [9,10], inadequate knowledge and preventive measures among the less privileged population about dengue fever attributes to this scenario [11].

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The lack of effective and safe dengue vaccine is also a major factor for increased morbidity and mortality among high-risk population given the lack of dengue-specific antiviral agents. The recent studies [12,13] show that the overall efficacy of CYD-TDV vaccine is 54% (40-64), while serotype-specific efficacy is 77% (66-85) for DENV4, 75% (65-82) for DENV3, 50% (36-61) for DENV1, and 34% (14-49) for DENV2.15% (174-74) vaccine efficacy for unknown serotype.

Although CYD-TDV vaccine is effective and immunogenic in children, its reduced efficacy against DENV2, which is known for causing severe dengue infection and dengue outbreaks, cause for serious concern. This review aims to address common clinical and laboratory parameters to facilitate early diagnosis of dengue fever, to determine predictors of severe dengue and to initiate appropriate treatment for a better outcome

Material and Methods

Place of study- Department of Pediatric, Saveetha medical college, Chennai

Type of study- Retrospective observational study

Sampling method- Consecutive sampling

Inclusion criteria- All patients aged less than 15 years who sought medical care in the pediatric department of Saveetha medical college, diagnosed as Probable Dengue/Dengue fever/ dengue with warning sign/severe dengue according to standard guidelines [14]

Exclusion criteria- Children with preexisting haematological illnesses

Sample collection- For each patient, basic demographics (name, age, sex, address) was collected. Presenting complaints (duration of fever, myalgia, headache, abdominal pain, vomiting, bleeding manifestations, rash and petechiae) and examination findings (vitals, Hess test, pallor, organomegaly, urine output, signs of fluid retention, circulatory failure)were documented.

Serial laboratory investigations (haemoglobin, total leukocyte count, haematocrit and platelet count) and investigations like Serum glutamic pyruvic transaminase (SGPT), serum glutamic oxalic acid (SGOT) and serum albumin were recorded.

Radiological investigations like ultrasound abdomen and chest X-ray was taken into consideration if available. Details of co-infections/ alternate diagnosis considered at admission/discharge were also recorded.

Statistical method- Statistical analysis was done using SPSS (statistical package for social sciences) software.

Results

A total of 61 cases were enrolled in the months September, October and November, of these 36 were boys and 25 girls. Most of the admissions were in October (61%). There were 14, 37 and 10 admissions in September, October and November respectively. The mean age was **6.49** years; the youngest child isten months old. Of the total cases, the maximum number of admissions was in October (**38**) which constituted to about **61**% of the total patients. Only five patients were diagnosed to have severe dengue.

Table-1: Demographic distribution

Age	Boys	Girls	Total
7-12 months	0	1	1
1-2 years	1	5	6
2-5 years	8	9	17
6-12 years	24	10	34
13-15 years	3	0	3

Fever was the most common symptom seen in 96.7% of children among which 40 (65.6%) had an only mild fever. Only **13**% had temperature>104° F. The next most common symptom was a loss of appetite present in **36 (59%)**. Majority of patients did not have any prodromal symptoms; However, 20 **(33%)** children had cough and runny nose.

A headache was present in **26 (43%)** patients, and 33 **(54%)** had vomiting. During the recovery phase, **23 (37.7%)** children had itching. Loose stools were infrequently present in 7 children **(11.5%).**

Table-2: Clinical features

Clinical Parameters	n (%)
Fever	59 (96.7)
Chills and Rigor	13 (21.3)
Headache	26 (42.6)
Rash	13 (21.3)
Flushed Look	25 (41.0)
Hess Test Positivity	18 (29.5)
Vomiting	33 (54.1)
Loose Stools	7 (11.5)
Arthralgia	26 (42.6)
Myalgia	29 (47.5)
Anorexia	36 (59.0)
Abdominal Pain	28 (45.9)
Cough or Runny nose	20 (32.7)
Itching	23 (37.7)

On clinical assessment, 40**%** of children had rash and flushed skin. Hess test was positive in **29.5%** of the children. Only **11.4%** of children had bleeding manifestation. Hepatomegaly noticed in **35** children and hepato splenomegaly in **2** children. Most children had heart rate within normal limits, and14.7**%** had brady cardia. **Five** children went into shock, **2** of whom had hypotension.

NS 1 was positive in **30** children **(49%)**, IgM in 36**%** and IgG in **13 %**. NS1 positivity rate on day 4, day 5 and day 6 of illness was **62.5%, 38.4% and 18.1%** respectively. SGOT elevation was noticed in **23** children. Most children had mild-moderate thrombocytopenia **(59%)**. Only **26.2 %** had severe thrombocytopenia. The mean day of platelet recovery was between day **7 and 9** of illness. PCV change of > 20% was found in **13 (21.3%)** patients and 35 **(57.4%)** children had < 20% rise in PCV. **24 (39.3%)** of the children had some degree of anaemiaand more than 2/3rd of the patients had leucopenia **(44).**

Table-3: Clinical Signs

Clinical Signs	N (%)
Bleeding Manifestation	7 (11.5)
Oedema	9 (14.8)
Tachycardia	4 (6.6)
Bradycardia	9 (14.8)
Tachypnea	4 (6.6)
Oliguria	4 (6.6)
Compensated Shock	3 (4.9)
Hypotensive Shock	2 (3.3)
Hepatomegaly	35 (57.4)
Hepatosplenomegaly	2 (3.3)

Table-4: Laboratory values

Laboratory Values	n (%)
Anaemia	24 (39.3)
Thrombocytopenia	57 (93.4)
Leucopenia	44 (72.1)
Hyponatremia	5 (8.2)
Hypoalbuminemia	5* (N=49)
Ns1 Antigen Positivity	30 (49.2)
Serology (I) IgM Positive	14 (23)
(Ii) IgG Positive	1 (1.6)
(Iii) Both Positive	8 (13.1)

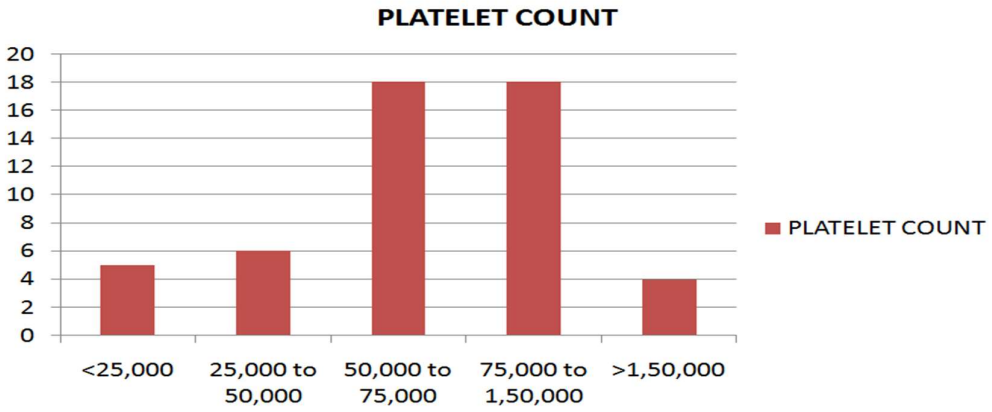

Fig-1: Platelet trend

Table-5: Comparison between severe and non-severe illness (symptoms)

Parameters		Severe illness (n =22)		Non-severe illness n=39	P value (<0.05)
		N (%)		N (%)	
Sex	Boys	18 (81.8)		18(46.2)	0.007*
	Girls	4 (18.2)		21(53.8)	
Duration of stay	≤ 5 days	3 (13.6)		31(79.5)	< 0.001*
	> 5 days	19(86.4)		8(20.5)	< 0.001*
Headache		11(50)		15(38.5)	0.382
Prodromal symptoms		7(31.8)		16(41)	0.881
Fever		21(95.5)		38 (97.4)	0.676
Duration of fever		< 3 days	3 (13.6)	15(38.5)	0.165
		≥ 3 days	19(86.4)	24(61.5)	
Grading of fever	Mild	15(68.2)		25(64.1)	0.436
	Moderate to high*	7(31.8)		14(35.9)	
Chills and rigor		5(22.7)		8(20.5)	0.839
Rashes*		10(45.5)		3(7.7)	0.001*
Flushing		17(77.3)		8(20.5)	<0.001*
Itching		13(59.1)		10(25.6)	0.010*
Vomiting		15(68.2)		18(46.2)	0.097
Loose stool		3(13.6)		4(10.3)	0.691
Arthralgia		11(50)		15(38.5)	0.382
Myalgia		11(50)		18(46.2)	0.773
Anorexia		19(86.4)		17(43.6)	0.001*
Abdominal pain		14(63.6)		14(35.9)	0.037*

Of the total 61 children enrolled in this study, only five children diagnosed with severe dengue, and 17 had dengue with warning signs. These two categories were combined to form a single severe illness group and compared with the remaining who had either dengue fever or probable dengue (non-severe illness group). Among the critical illness groups, 18 were boys. Nineteen children belonging to the severe illness group stayed in the hospital for more than five days. Flushing and the rashes were significantly more common in the severe illness group. Similarly, anorexia, abdominal pain, edema and itching were more frequent in the critical illness group. However, no significant difference was noted between the two groups in the occurrence of other symptoms (chills, vomiting, loose stool, headache, arthralgia and myalgia).

Table-6: Comparison between children having a severe and non-severe illne (signs and laboratory parameters)

Heart rate	**Tachycardia**	4(18.2)	0	0.015*
	Bradycardia	4(18.2)	5(12.8)	
Tachypnea		4(18.2)	0	0.006*
Hypotension		2(9.1)	0	0.056
HESS test positivity		15(68.2)	3(7.7)	<0.001*
Edema		7(31.8)	2(5.1)	0.005*
Oliguria		4(18.2)	0	0.006*
Hepatomegaly		16(72.7)	21(53.8)	0.080
Anemia		5(22.7)	19(48.7)	0.033*
Severe thrombocytopenia		14(63.6)	7(17.9)	<0.001*
Leukopenia		18(81.8)	26(66.7)	0.205
Na < 135 Meq/L		5(22.7)	0	0.002*
SGOT(>120 IU/L)		11(50)	14(35.9)	0.788
Hypoalbuminemia (< 2.5 gm/dl)		5(22.7)	0	0.002*
Hydrops gall bladder		1(4.5)	2(5.1)	0.631

Among the clinical sign tachycardia (disproportionate to the degree of fever), tachypnea and oliguria were seen only in the severe illness group. The occurrence of bradycardia and hepatomegaly were similar in the two groups. Hyponatremia and low albumin noticed in 5 (22.7%) children who had severe illness. Elevated liver enzyme and leucopenia were distributed similarly in the two group.

Discussion

Boys were more commonly affected in this study group and they also had higher tendency to have severe illness. Similar male preponderance was noted in other studies which may be attributed to the presence of more exposed area leading to more significant chance of mosquito-borne diseases [15,16]. Majority of the children belonged to the 6-12 age group which was also reported in other studies [15, 17].

Fever was the most common symptom. Vomiting and anorexia were also commonly seen in our patients. Other widelyrecognisedsymptoms were arthralgia, abdomen pain and headache. This symptom pattern is similar to those reported in several studies [17, 18]. Tourniquet test was positive only in few cases. Similar results observed in other Indian studies, probably due to the darker complexion of the study patients here [19, 20] However, it was more frequently seen in children with severe illness. Similarly, flushing was also seen more commonly in children with severedisease. These features can be used as an early marker to identify such children. More than a third of the children in our study reported itching during the recovery period. Some of them also had an erythematous rash which was different from the rashes noticed during the initial part of the illness. This rash was not blanchable, more confluent with islets of healthy skin which has been describedas “white islands in a sea of red” [21, 22].

One-tenth of the total cases had bleeding manifestations with petechiae being the most common manifestation. A similar result was noticed in the study conducted by Mishraet al [19]. Nearly one-third of children in our study had prodromal symptoms like a cough and runny nose. Other studies did not report these symptoms. The difference could be because this study was conducted during an epidemic of dengue infections, and there was a high index of suspicion among health professionals to screen for dengue. Similar illness presenting with a cough and runny nose during the non-epidemic season would have been regarded as non-specific viral illnesses. More than half of the children [57%] in this study had hepatomegaly similar to previous reviews [23]. However, two children had hepato splenomegaly. Both of them were found to have malariaco-infection.

Thereby suggesting that in our setting whenever there is associated splenomegaly in children with dengue, co-infections with other vector-borne diseases that share similar seasonal trends like malaria and scrub typhus should be considered [24]. Apart from patients with malarial co-infection, two other patient had persistent fever spikes lasting for more than 7 days. These children were found to have gram negative bacterial sepsis complicating their underlying dengue infection, highlighting the need for evaluating children with persistent fever to look for co-infections.

Among the various laboratory parameters, thrombocytopenia was the most frequently noticed abnormality. Majority of them had mild to moderate thrombocytopenia, and a small proportion showed normal platelet counts. Almost three fourth of the children had leucopenia [20, 25]. Isolated elevation of SGOT (>120 IU/L) was present in 40% of the children in our study. A similar pattern of transaminitis was described in previous studies, and they observed a positive correlation between the level of SGOT and the severity of illness [26]. Hyponatremia and low albumin noted in children with severe disease, highlighting the importance of these parameters in assessing the risk of severe disease.

Conclusion

Dengue fever is a common cause of acute febrile illness, especially during monsoon season. Though the manifestations of dengue are similar to other viral infections, the disease severity and mortality is more in dengue, thus requiring early diagnosis. As observed in our study the presence of prodromal respiratory symptoms does not preclude the diagnosis of dengue. The course and severity of the illness are highly variable. Apart from the described warning signs, flushing, positive tourniquet test and laboratory derangements like hyponatremia and hypoalbuminemia can be considered as markers of severe illness. The presence of splenomegaly should raise the suspicion of co-infection if there is an unusual persistence of fever considering their common epidemiological background.

Clinical implications of this study- This study highlights the importance of suspecting and evaluating patients for dengue even if they present with prodromal respiratory symptoms and also highlights the need to screen for co-infections if the disease course is atypical.

Contributions

- Dr. Anand Ramakrishnan and Dr. Selvakumar- Data collection and analysis
- Dr. Benjamin Sagayaraj and Dr. BalammaSujatha- manuscript preparation
- Dr. Porchelvan- Statistical analysis

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