Original Research Article

A clinical and biochemical laboratory profile to measure the severity of dengue fever in paediatric population and their outcome

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ABSTRACT

Background: Aim of the study was to assess various clinical manifestations of dengue fever, and complications, to establish the diagnosis of dengue fever based on dengue antigen (NS 1) and antibody (IgM, IgG) and to find the association between the clinical findings with laboratory findings.

Methods: 100 cases of suspected children below 18 years of age with clinical features suggestive of dengue infection and children presenting with fever of acute onset (<2 weeks), pain abdomen, vomiting, rash, flushed appearance and bleeding manifestation were studied. The cases were followed up for the clinical and laboratory parameters and were treated according to WHO guidelines.

Results: Out of total 100 cases studied 36 were classified as classical dengue fever, 33 as DHF, 15 as DSS, 16 as DLI. It was observed that the disease was common in age group of 5-11 year (54%). Most of the patients were male (66%) with an M:F ratio of 1.94:1. The common presenting symptoms were fever (96%), vomiting (49%), abdominal pain (42%), headache (12%), myalgia (7%), arthralgia (4%), retro orbital pain (1%). General physical examination revealed presence of hypotension, tachycardia, rashes, facial puffiness (28%), pedal oedema (21%), and conjunctival congestion (18%). The skin bleeding was the most common manifestation noted in 12 cases (12%) followed by GIT bleeding like hematemesis 4 cases (4%) followed by epistaxis 4 cases (4%), haematuria 2 cases (2%) and gum bleeds 2 cases (2%). In systemic examination patients were found to have hepatomegaly (53%), ascites (13%), splenomegaly (8%), and pleural effusion (27%). 36 (36%) patients in the study had leucopoenia and mean total leukocyte count of 6014.5 cells/cu mm. The highest and lowest TLC was 22000 and 1400 cells/cumm respectively. 85% cases had thrombocytopenia in the present study. The mean platelet in the present study was 41870 cells/cu mm. Elevated liver enzymes and elevated serum creatinine count was found in complicated forms of disease.

Conclusions: The treatment of dengue is mainly supportive, but early institution and meticulous monitoring are the corner stone for positive outcome. Much more awareness, vigilance and research in the diagnostic modalities is further needed to avoid unnecessary panic and platelet transfusions.

Keywords: Dengue fever; Thrombocytopenia; Epistaxis, Liver enzymes, WHO, Haematocrit

INTRODUCTION

Dengue has become hyperendemic in many parts of India. Globally 2.5-3 billon individuals live in approximately 112 countries that experience dengue transmission. The number of cases reported to the national vector borne disease control program (NVBDCP) in 2016, for the first time, more than 100,000 cases were reported (total: 129,166 with 245 deaths).[1]

Dengue is a fast emerging and rapidly spreading systemic viral infection with global estimates of 390 million infections per year, of which 96 million are apparent infections and 3.97 billion people in 128 countries are at risk of dengue infection.[2,3]

Dengue fever (DF) with its severe manifestations such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) has emerged as a major public health problem of international concern.[4] Estimates suggest that annually 100 million cases of dengue fever and half a million cases of dengue hemorrhagic fever (DHF) occur in the world with a case fatality in Asian countries of 0.5-3.5%. 90% of DHF subjects are less than 15 years of age. Early recognition and prompt initiation of treatment are vital if disease related morbidity and mortality are to be controlled.[5]

Dengue fever is caused by an RNA virus of the family *Flaviviridae*; genus *Flavivirus*. It has 4 closely related serotypes DEN 1, DEN 2, DEN 3, DEN 4 which bear partial cross reactivity with each other. The viruses are transmitted to man by the bite of infective mosquitoes, mainly *Aedes aegypti*.

The illness caused by dengue infection manifest either as classical dengue fever or severe dengue (dengue hemorrhagic fever/dengue shock syndrome) which includes severe plasma leakage with severe hemorrhage and organ impairment.

In India the incidence has increased due to deficient water management, unplanned urbanization and migration of population to urban areas.

At present very few studies have been conducted in this part of our country. As also exact clinical and laboratory profile is important for diagnosis and successful management thus crucial for saving life, hence this study was undertaken to analyses varied clinical and laboratory profile of serologically confirmed.

METHODS

Source of data

Suspected cases of dengue fever in outpatients and admitted inpatients department of pediatrics, Narayana medical college, Nellore.

Method of collection of data

100 cases of suspected dengue fever children who fulfilled the inclusion criteria were selected. Pre-test counseling was given to parents/guardian. After taking written informed consent from parents, case was enrolled, data was collected.

Blood samples were collected from children with suspected Dengue infection for complete blood count, hematocrit, liver function tests, prothrombin time, APTT, dengue viral Ag, IgG and IgM investigations.

WHO classification and case definition were used to classify dengue fever, dengue hemorrhagic fever, dengue shock syndrome and dengue like illness.

Study design

Hospital based descriptive design was used for this study.

Duration of study

Duration of study was from May 2018 to March 2020.

Inclusion criteria

All children below 18 years of age with clinical features suggestive of dengue infection admitted as inpatients and outpatients in the department of paediatrics.

Child presenting with fever of acute onset (<2 weeks), pain abdomen, vomiting, rash, flushed appearance and bleeding manifestation.

Exclusion criteria

Febrile illness of >2 weeks duration and patients with any identified specific infection like malaria, typhoid, UTI, etc. were excluded.

Investigations

Complete blood count, blood test (serology) for dengue fever, urine routine, serum electrolytes, random blood sugar, QBC for MP, WIDAL/blood culture, liver enzymes-SGOT, SGPT, serum albumin, chest x-ray, ultrasound abdomen, PT, APTT, blood urea, and serum creatinine.

Statistics

One-way analyses of variance were used to test the difference between groups. When comparing more than two means, an ANOVA F-test was used to measure the significance between the means.

RESULTS

Out of total 100 cases studied, 36 children met WHO specified criteria for DF, 33 children with DHF, 15 children with DSS and 16 children with DLI.

Age and gender

The highest number of cases were found in age group of 5 to 8 years (31%), followed by in age group of 9-12 years (26%) (p=0.198). Out of the 100 children 66 were male and 34 were female. The ratio M:F=1.94:1. 96 (96%) children presented with fever as the predominant complaint.

Temperature

Sixty percent of children in the study group had fever and remaining 40% were non-febrile.

Symptomatology

Ninety-six (96%) children presented with fever as the predominant complaint followed by vomiting 49 (49%), abdominal pain 42 (42%), headache 12 (12%), cough 10 (10%), diarrhoea 7 (7%), myalgia 7 (7%), joint pain 4 (4%), edema 3 (3%), cold 3 (3%), convulsion 2 (2%), retro orbital pain 1 (1%), menorrhagia 1 (1%).

Signs

The most common signs were hepatomegaly (53%),

followed by facial puffiness (28%), pedal edema (21%), conjunctival congestion (18%), ascites (13%), splenomegaly (8%).

The most common sign was hepatomegaly (53%).

Respiratory system

On respiratory system examination, 27% of cases were observed to have decreased air entry.

Relationship between various sites of bleeding

Bleeding was noted in 24% of the total number of cases. The skin bleeds were the most common manifestation noted in 12 cases (12%) followed by GIT bleeding like hematemesis 4 cases (4%) followed by epistaxis 4 cases (4%), haematuria 2 cases (2%) and gum bleeds 2 cases (2%). The bleeding manifestations were more in DHF, DSS group than DF group.

Table 1: Distribution of signs according to clinical spectrum.

Signs	DF (n=36)		DHF (n=33)		DLI (n=16)		DSS (n=15)		Chi square value	P value
	N	%	N	%	N	%	N	%		
Conjunctival congestion	3	8.3	8	24.2	1	6.3	6	40	9.566	0.023
Facial puffiness	2	5.6	14	42.4	1	6.3	11	73.3	31.447	<0.001
Pedal edema	1	2.8	11	33.3	1	6.3	8	53.3	21.782	<0.001
Temp (febrile)	6	16.7	0	0.0	4	25	2	13.3	7.828	0.050
Hepatomegaly	13	36.1	25	75.8	5	31.3	10	66.7	15.147	0.002
Splenomegaly	3	8.3	3	9.1	1	6.3	1	6.7	0.162	0.984
Ascites	1	2.8	7	21.2	1	6.3	4	26.7	8.415	0.038

Table 2: Relationship between various sites of bleeding and dengue fever according to clinical spectrum.

Site of Bleeding	DF(n=36)		DHF (n=33)		DLI (n=16)		DSS (n=15)		Chi square value	P value
	N	%	N	%	N	%	N	%		
Rashes	0	0.0	8	24.2	0	0.0	4	26.7	14.830	0.002
Melaena	0	0.0	0	0.0	0	0.0	0	0.0		
Hematuria	0	0.0	2	6.1	0	0.0	0	0.0	4.143	0.246
Hematemesis	0	0.0	4	12.1	0	0.0	0	0.0	8.460	0.037
Epistaxis	1	2.8	3	9.1	0	0.0	0	0.0	3.659	0.301
Gum bleeds	0	0.0	2	6.1	0	0.0	0	0.0	4.143	0.246

Skin rashes

Most common type of skin rash observed in the present study was flushing 54%, followed by petechiae 33%, macular rash 21% and ecchymosis in 11% of cases.

Dengue serology

Dengue Ag was positive in 43 cases (43%), IgM was positive in 58 cases (58%) and IgG was positive in 22 cases (22%) in this study.

Chest x-ray

Chest x-ray was done in all the 100 cases, in 38 children (38%) there was pleural effusion. In the DHF and DSS group the number of cases were more compare to DF

and DLI group. (Chi square=21.460, p<0.001) It was statistically significant.

Ultrasonography

About 33 patients had gall bladder wall thickening, 37 patients had pleural effusion, 32 patients had ascites, 14 patients had acalculous cholecystitis.

Platelet count

A mean value of platelet count was 41870 cells/cu mm. The WHO criteria of low platelet count of <1,00,000 cells/cu mm was observed in most of the cases (85%). With maximum number of cases having platelet count in the range of <20000 cells/cu mm in DHF and DLI groups.

Hemoglobin levels (Hb g%)

The hemoglobin level ranged from 6.5-18.9 gm%, with a mean level of 12.721 gm%.

Hematocrit (PCV%)

The haematocrit ranged from 18.7-54.2% with a mean value of 37.86%.

Total leucocyte count

Normal: 4000-11000 cells/cu mm. The range of total leukocyte count varied from 1400-22000 cells/cumm with a mean count of 6014.5 cells/cu mm. 36 (36%) patients had leucopenia i.e., <4000 cells/cu mm.

Prothrombin time

PT-normal 10-13 sec. The prothrombin time ranged from 11.6-54 sec with a mean of 18.88 sec.

APTT

APTT-Normal range is 26-36 sec.

The activated partial thromboplastin time ranged from 28.2-69.0 sec with a mean of 43.86 sec.

Blood urea

The range for blood urea was 14-136 mg/dl with a mean of 42.9 mg/dl.

Serum creatinine (mg/dl)

The range for serum creatinine was 0.4-1.8 mg/dl with a mean of 0.735 mg/dl.

Liver function test

SGOT-normal 1-55 IU/lt. The range for SGOT was 10-1072 IU/lt with a mean of 168.58 IU/lt.

SGPT-normal 5-45 IU/lt. The range for SGOT was 6-829 IU/lt with a mean of 98.82 IU/lt.

Serum albumin (g/dl)

Normal 3.4-5.4 gm%. The range for serum albumin was 1.0-4.2 gm% with a mean of 3.066 gm%. Serum albumin of <3.4 gm% was seen in 62% of children, more in DHF and DSS group. It is statistically significant. (Chi square=29.856, $p \leq 0.001$).

Serum electrolytes

The range for serum sodium was 122-148 meq/l with a mean of 134.85 meq/l. The range for serum potassium was 2.8-6.3 meq/l with a mean of 4.35 meq/l. The range for serum chloride was 90-107 meq/l with a mean of 98.55 meq/l.

DISCUSSION

In the present study of 100 cases-36% cases were DF, 33% cases were DHF, 15% cases were DSS group and 16% cases were DLI. The 5-11-year age group dominated the Present study, accounting for 54% of the total. Among the subgroup, there is a tendency for DSS to occur at younger age. However previous studies have not noted any difference in age between dengue with or without shock. The youngest child in the present study was 8 months old.

The incidence of male children that were affected is slightly more in our study, the ratio being 1.94:1. Similar observation made by others also showed increased preponderance among boys as in WHO study in 1999 due to increased outdoor activities of male children.[5-8]

In present study fever (96%) was the predominant symptoms followed by vomiting (49%), abdominal pain (42%), bleeding (24%), rashes (24, retro-orbital pain (28%). Similar observation was made by others.[10-12]

The evaluation of immediate micro and macroenvironments of the patient's habitat revealed following observations. Storage of water in containers was present. The scope for mosquito breeding was present. Those children got infected in the immediate monsoon or post monsoon months, being responsible for the increase in the number of cases in that period. Efforts were made to educate parents about disease from which their children were suffering and the possible modes of spread, the environmental factors that might have been responsible, the ways and means to prevent spread of disease, like keeping the surrounding clean using mosquito curtain etc., as a long-term measure.

Of the 100 children in the study 96% children had fever and no child was in category of hyperpyrexia.

In the present study bleeding manifestations were found in 24% of cases.

Apart from petechiae, which usually associated with bleeding manifestations, hematemesis and epistaxis were the predominant modes of bleeding. Hematemesis was the most common bleeding manifestation reported in other Indian studies.[13,14]

The systemic examination revealed non-specific signs, as like any other viral illness. Hepatomegaly was seen in 53 children (53%) in the present study. Other studies also reported hepatomegaly in significant

percentage.[15-17]

The mean hemoglobin and hematocrit in the present study were 12.721 gm% and 37.86% respectively.

Butt et al, in their series found that, out of 104 patients, 55 (52.8%) had leukopenia. The mean leucocyte count was 5200 cells/cu.mm, which almost correlates with the present study.[18]

Thrombocytopenia and dysfunctional platelets remain a central hallmark of dengue fever, surprisingly little is known about the interaction of dengue virus with platelets.[19]

Platelets counts carry one of the most important keys for diagnosis. On taking the WHO limit of <100000/cmm for low platelet count, 85% had thrombocytopenia in the present study. The mean platelet in the present study was 41870 cells/cmm. The platelet counts at the admission was neither an indicator of prognosis nor of bleeding tendencies or progression of the disease. This suggest that other factors like platelet dysfunction or disseminated intra-vascular coagulation may have role in bleeding in dengue fever cases. However, studies which include only DHF cases shows correlation between low platelet count and bleeding manifestations.[20]

The studies by Gomber and Narayanan et al have documented the same opinion.[21,22]

The present study findings concurred with the previous studies and we found that thrombocytopenia was the most commonly associated finding.[23,24]

Many studies have noted high transaminases levels. Kalayanarooj et al in 1997 in their study at Bangkok reported higher levels of SGPT in patients of DHF than in DF.[25] The present study did not demonstrate a significant difference in the LFT's between the clinical subgroup of dengue. The high incidence of vomiting, hepatomegaly and elevated liver enzymes can score as markers of suspicion of dengue during an epidemic.[6,13,15]

Larreal et al study showed that laboratory test findings showed transaminase values fivefold higher than the normal values (p<0.005) observed in 36.8 and 74.4% of patients with CD and DHF respectively, AST was predominant in both groups as their results suggest liver damage during the course of dengue.[23]

Petdachai in his study found that in children with dengue shock syndrome, AST levels were elevated in all cases and were more than ALT levels. Hepatic dysfunction is common in Dengue infection and aminotransferase levels were useful in predicting the occurrence of hepatic dysfunction.[26]

Plasma leakage, which indicates that dengue causes hypoalbuminemia, is an indicator of severity. In our study, albuminemia lesser than 3.4 g/dL was associated with higher incidence of DHF. Usually, high values of albuminemia may reflect the integrity of the vascular endothelium, whereas albumin levels less than 3.4 g/dL may be an early indicator of vascular permeability alteration. Therefore, this parameter may be an early indicator of plasma leakage and a useful prognostic marker.

The dengue Ag was positive in 43 children, IgM was tested positive in 58 children, IgG was positive in 22 cases in the study

The present study had DF 36 (36%), DHF 33 (33%), DSS 15 (15%) and DLI 16 (16%) cases among total of 100 cases.

According to WHO, pleural effusion is a supporting evidence of plasma leakage, the distinguishing feature of DHF. It also mentions that extent of pleural effusion correlates with the severity of the disease and bilateral pleural effusion is common in shock.

The most striking USG-abdomen finding in our study population was GB wall thickening/edema that was seen in 33% of the patients. Splenomegaly, hepatomegaly and ascites were also seen.[9,27]

CONCLUSION

In our present study classical dengue fever was the most common presentation followed by other complicated forms such as dengue hemorrhagic fever and dengue shock syndrome. On investigation deranged liver function test, renal function test, secondary dengue infection, thickened gall bladder wall, hepatosplenomegaly on ultrasound abdomen, pleural effusion on chest radiogram were associated with DHF and DSS. Much more awareness, vigilance and research in the diagnostic modalities is further needed to avoid unnecessary panic and platelet transfusions.

During epidemic, dengue should be considered as the differential diagnosis of any child presenting with fever.

The treatment of dengue is mainly supportive, but early institution and meticulous monitoring are the corner stones for positive outcome.

REFERENCES

1. The World Health organization, Dengue: guideline for diagnosis, treatment, prevention and control, new edition. 2009;1.
2. Bhatt S, Gething P, Brady WOJ. The global distribution and burden of dengue. Nature. 2013;496:504-7.
3. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG et al. Refining the Global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Negl Trop Dis. 2012;6:e1760.
4. Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakorn S et al. Early clinical and laboratory indicators of acute Dengue illness. J Infect Dis. 1997;176:313-21.
5. Malavige GN, Fernando S, Fernando DJ, Seneviratne SL. Dengue viral infections. Postgrad Med J. 2004;80:588-601.
6. Chandrakanta, Kumar R, Garima, Agarwal J, Jain A, Nagar R et al. Changing clinical manifestations of dengue infection in north India. Dengue Bull. 2008;32:118-25.
7. Cam BV, Fonsmark L, Hue NB, Phoung NT, Poulsen A, Heegaard ED, et al. Prospective case control study of encephalopathy in children with dengue hemorragic fever. Am J Trop Med Hyg. 2001;65:848-51.
8. Panchareon C, Thisyakorn U. Neurological manifestations in dengue patients. Southeast Asian J Trop Med Public Health. 2001;32(2):341-5.
9. Gurdeep SD, Deepak B. Clinical profile and outcome in children of dengue hemorrhagic fever in North India. Iran J pediatr. 2008;18(3):222-8.
10. Sajid A, Ikram A, Ahmed M. Dengue fever outbreak 2011: clinical profile of children presenting at madina teaching hospital faisalabad. JUMDC. 2012;3(1):42-7.
11. Anuradha S, Singh NP, Rizvi SN, Agarwal SK, Gur R, Mathur MD, et al. The 1996 outbreak of dengue hemorrhagic fever in Delhi, India. Southeast Asian J Trop Med Public Health. 1998;29(3):503-6.
12. Misra UK, Kalita J, Syam UK, Dhole TN. Neurological Manifestation of dengue viral infection. J Neurol Sci. 2006;244(1-2):117-22.
13. Kumar ND, Tomar V, Singh B, Kela K. Platelet transfusion practice during Dengue fever epidemic. Indian J Pathol Microbiol. 2000;43:55-60.
14. Rahman M, Rahman K, Siddque AK, Shoma S, Kamal AH, Ali KS et al. First outbreak of Dengue hemorrhagic fever, Bangladesh. Emerg Infect Dis. 2002;8:738-40.
15. Nimmannitya S. Dengue and Dengue Hemorrhagic fever in the South-East Asian Regions. Am J Trop Med Hyg. 1969;18:954-71.
16. Mohan B, Patwari AK, Anand VK. Hepatic dysfunction in childhood Dengue infection. J Trop Pediatr. 2000;46:40-3.
17. Jagadishkumar K, Jain P, Manjunath VG, Umesh L. Hepatic Involvement in Dengue Fever in Children. Iran J Pediatr. 2012;22(2):231-36.
18. Butt N, Abbassi A, Munir SM, Ahmad SM, Sheikh QH. Haematological and Biochemical indicators for early diagnosis of Dengue viral infections. J college physicians Surgeons Pak. 2008;18:282-5.
19. Raghunath D, Durga RC, Basu A. Dengue interaction with platelets; Clinical feature and management; Current status and Research, Tata Mc Graw Hill, New Delhi. 2008;8:147-51.
20. Aggarwal A, Chandra J, Aneja S, Patwari AK, Dutta AK. An epidemic of Dengue hemorrhagic fever and Dengue shock syndrome in children in Delhi. Indian Pediatr. 1998;35:727-32.
21. Narayanan M, Arvind MA, Thilothammal N, Prema R, Sargunam Rex CS et al. Dengue Fever Epidemic in Chennai-A Study of Clinical Profile and Outcome. Indian Pediatr. 2002;39:1027-33.
22. Gomber S, Ramachandran VG, Kumar S, Agarwal, Gupta P, Gupta P et al. Hematological observations as diagnostic markers in dengue hemorrhagic fever – a reappraisal. Indian Pediatr. 2001;38:477-81.
23. Larreal Y, Valero N, Estevez J, Reyes I, Maldonado M, Espina LM et al. Hepatic alterations in patients with Dengue. Invest Clin. 2005;46(2):169-78.
24. Faridi MMA, Agarwal A, Monish K, Abedin S. Clinical and Biochemical profile of Dengue Hemorrhagic fever in children in Delhi. Tropical doctor. 2008;(38):28-30.
25. Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakorn S et al. Early clinical and laboratory indicators of acute Dengue illness. J Infect Dis. 1997;176:313-21.
26. Petdachai W. Hepatic dysfunction in children with Dengue shock syndrome. Dengue bull. 2005;(29):112-8.
27. Venkata Sai PM, Krishnan R. Role of ultrasound in Dengue fever. Bri J Radiol. 2005;78:416-8.