International Journal of Contemporary Pediatrics
Mogra G et al. Int J Contemp Pediatr. 2016 Nov;3(4):1405-1410
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20163687

Original Research Article

Classification and study of the clinico-hematological profile of patients with dengue fever in the pediatric age group

Gaurav Mogra, Radha Gulati Ghildiyal, Smilu Mohanlal*

Department of Pediatrics, T. N. M. C. and BYL Nair Ch. Hospital, Mumbai, Maharashtra, India

Received: 14 August 2016
Accepted: 24 September 2016

***Correspondence:**
Dr. Smilu Mohanlal,
E-mail: drsmilu@gmail.com

ABSTRACT

Background: Dengue fever has become a major public health issue constituting a major burden of monsoon related illnesses. New WHO classification of dengue fever was introduced in 2009. There is a need to study the factors which can predict the severity of dengue fever for timely interventions and management to decrease the mortality and morbidity.
Methods: An observational prospective study was conducted in the pediatric ward and intensive care unit at a tertiary care center in Mumbai to study the correlation between severity and clinical and laboratory parameters, morbidity and mortality in patients with dengue fever. The qualitative data was represented in the form of frequency and percentage tables with the help of SPSS 17.
Results: This study spanning an 18 month period enrolled 100 hospitalized patients.45% of them were classified as probable dengue, 44% as dengue with warning signs and 11% were severe dengue. 64% had a normal nutritional status, 28% moderate malnutrition and 8% severe malnutrition. Most common symptom was fever in 100% children, 57% vomiting, 50% rash, 49% malaise, 44% abdominal pain, 45% headache, 37% petechiae, 26% bleeding manifestation, 3% altered sensorium and 2% convulsion.46% of them had hepatomegaly ,45% with positive tourniquet test, 17 % tachycardia, 10% splenomegaly, 8% signs of circulatory failure and 7% had hypotension. Of the laboratory parameters 72% had abnormal total counts, 58% with thrombocytopenia, 45% deranged liver function tests, 41% had hemoconcentration, 22% deranged renal function test, 13% electrolyte disturbances and 6% metabolic acidosis.48% had pleural effusion and 33% had ascitis. The mortality rate was 2%.
Conclusions: A significant association ($p<0.05$) was found between abdominal pain, petechiae, bleeding manifestation, altered sensorium, convulsion, tachycardia, hypotension, hepatomegaly, splenomegaly, signs of circulatory failure, positive tourniquet test, hemoconcentration, platelet count, electrolyte disturbances, deranged liver and renal function tests, pleural effusion, ascitis and duration of stay with severity of dengue fever.

Keywords: Dengue fever, WHO classification

INTRODUCTION

Dengue Fever is one of the arthropod borne diseases that are on the rise in India.[1] The south-east Asia region shares 52% of global risk for DF/DHF.[2]

Dengue fever is characterized by sudden onset of fever of 3-5 days, intense headache, rash, myalgia, retro-orbital pain, anorexia and gastrointestinal disturbances. Dengue viruses are flavivirus, which include four serotypes 1, 2, 3 and 4. They are responsible for dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The viruses are transmitted to man by the bite of infective mosquitoes, mainly Aedes aegypti.

80% of the people infected with dengue, remain asymptomatic or have only mild symptoms such as uncomplicated fever, 5% have more severe illness and in

a small proportion it is life threatening. The incubation period ranges from 3-14 days, but most often is 4-7 days.[3] Children often experience symptoms similar to those of the common cold and gastroenteritis, but are more susceptible to the severe complications and in contrast to many other infections it is more common in well-nourished children.[4] Females are more at risk than males.

In the initial years dengue was classified as dengue fever, dengue hemorrhagic fever and dengue shock syndrome. According to WHO criteria 2009 the patients are to be classified as dengue fever (either probable or laboratory-confirmed), dengue fever with warning signs, severe dengue (which may have severe plasma leakage, severe hemorrhage, severe organ impairment).[5]

Dengue fever is also diagnosed by microbiological laboratory testing which is done by virus isolation in cell cultures, nucleic acid detection by PCR, viral antigen detection or specific antibodies (serology).[6] Cases detected early by clinical suspicion and corroboratory laboratory evidence can help to limit number of cases that progress to developing complications such as plasma leakage, hemorrhage and organ impairment with timely intervention.

Dengue fever (DF) with its severe manifestations has emerged as a major public health problem. There is an increased potential for breeding of Aedes aegypti which has led to the increase in geographical distribution.

With early recognition and prompt initiation of treatment disease related morbidity and mortality can be limited. With there being an increasing number of cases detected, a study of the basic clinical and hematological aspect of the disease was considered important. Considering the morbidity and mortality associated with dengue fever, classification of the disease is imperative. Thus this study was undertaken to classify and study the clinico-hematological profile of the patients with dengue fever (as per WHO guidelines 2009) at a tertiary care centre attached to one of medical colleges in Mumbai.

METHODS

A prospective observational study was conducted at a tertiary care centre in a metropolitan city after obtaining approval from the institutional ethics committee. Patients in 1-12 year age group during an 18 month period (April 2013 to October 2014) who fulfilled the criteria were included in our study. Patients enrolled were classified according to the WHO 2009 criteria as probable dengue, dengue with warning signs and severe dengue (Table 1).[5] Detailed demographic profiles of patients, IPD no, duration of stay, PICU admission, duration of PICU stay, nutritional status according to WHO classification were noted in the case record form. Symptoms and signs like fever (temp more than 380 C), tachycardia or bradycardia, tachypnea, hypotension, delayed CRT, oliguria, raised JVP as per age norms, pallor, icterus, signs of circulatory failure, significant hepatomegaly that is more than 2 cms, splenomegaly or any other systemic findings like ascites, pleural effusion were also noted. Laboratory investigations like complete hemogram, blood urea nitrogen, serum creatinine, serum electrolytes,blood gases, serum bilirubin and liver enzymes, urine routine microscopy were done.

Anemia was defined as hemoglobin less than specific for that age, leucopenia as total leucocyte counts less than 4000/cubic mm, thrombocytopenia as platelet count less than 1.5 lakh/ cubic mm, raised hematocrit as increase in 20% from baseline.[7-10] Blood urea nitrogen >20 mg/dl, serum creatinine >1 mg/dl were considered as a deranged RFT.[7] Serum sodium (135-145 meq/litre), serum potassium (3-5.5 meq/litre). PH less than 7.35 on ABG or less than 7.31 on VBG or serum bicarbonate less than 21 meq/litre was considered as acidosis. Deranged LFT was considered when serum bilirubin was more than 1 mg/dl, SGOT/SGPT more than 55 U/litre.[7] Presence of more than 5 RBCs/HPF on urine microscopic examination was considered as hematuria.[11] Results of radiological findings such as pleural effusion on chest X-ray or USG thorax; ascites on USG abdomen were noted. Outcome on the basis of mortality and morbidity were noted.

The patients were treated and discharged according to the WHO 2009 guidelines.

SPSS Version 17 was used for analysis. Results were graphically represented wherever deemed necessary.

Inclusion criteria

- Any patient, male or female, between age 1 month to 12 years diagnosed as having dengue fever which was laboratory confirmed on the basis of Presence of antibodies (IgM/IgG) in serum against dengue fever virus or tested positive for dengue NS1 antigen in serum or tested positive for dengue PCR.
- Fulfilling the WHO criteria (2009) for dengue fever.
- Patient whose parents or guardians were willing to give written informed consent fulfilling the above mentioned criteria.

Exclusion criteria

- Patients having other co-infections like malaria, typhoid or infective hepatitis, interfering with interpretation of the laboratory data
- Immunocompromised subjects

Table 1: Who classification of dengue fever.[5]

Dengue fever either Probable dengue or laboratory confirmed	Dengue with warning signs	Severe dengue
Live in or travel to dengue endemic area	Abdominal pain or tenderness Persistent vomiting Clinical fluid accumulation Mucosal bleed Lethargy, restlessness Liver enlargement >2 cm Laboratory: increase in HCT concurrent with rapid decrease in platelet count *(requiring strict observation and medical intervention)	Severe plasma leakage leading to Shock (DSS), Fluid accumulation Withrespiratorydistress,
Fever and 2 of the following criteria Nausea, vomiting Rash Aches and pains Tourniquet test positive Leukopenia Any warning sign		Severe bleeding as evaluated by clinician
Laboratory-confirmed dengue (important when no sign of plasma leakage)		Severe organ involvement Liver: AST or ALT >=1000 CNS: Impaired consciousness Heart and other organs

RESULTS

There were 100 in- patients with dengue who fulfilled our inclusion criteria enrolled in the study. 45 children (45%) were classified as probable dengue, 44 children (44%) as dengue with warning signs, 11 children (11%) as severe dengue. 53% of the children were in the age group of 6 to 12 years, followed by 36% in the > 1-5 year age group and 11% in the age group of < = 1 year. Mean age of presentation was 5.82 years. Out of the total patients 59% were males (59) and 41% were females (41). Male: female ratio being 1.43:1.

Table 2: Association between the symptoms and severity of dengue fever (n = 100).

Factors		Severe dengue	Dengue with warning signs	Probable dengue	Chi-square tests*	P value
Petechiae	Present (37)	10 (27%)	23 (62.2%)	4 (10.8%)	33.373	<0.05
	Absent (63)	1 (1.6%)	21 (33.3%)	41 (65.1%)		
Abdominal pain	Present (44)	9 (20.5%)	35 (79.5%)	0	64.304	<0.05
	Absent (56)	2 (3.6%)	9 (16.1%)	45 (80.4%)		
Altered sensorium	Present (3)	3 (100%)	0	0	25.023 16.529	<0.05
	Absent (97)	8 (8.2%)	44 (45.4%)	45 (46.4%)		
Convulsion	Present (2)	2 (100%)	0	0	16.512 8.538	<0.05
	Absent (98)	9 (9.2%)	44 (44.9%)	45 (45.9%)		

64% of the children (64) had a normal nutritional status followed by 28% of the children (28) having moderate malnutrition and 8% of the children (8) had severe malnutrition. Among the symptoms, most common was fever which was present in 100% of the children followed by 57% who had vomiting, 50% had rash, 49% malaise, 44% abdominal pain, 45% headache, 37% petechiae, 26% bleeding manifestation, 3% altered sensorium and 2% convulsion. Amongst the signs in the study group maximum children i.e., 46% of the children had hepatomegaly followed by 45% having a positive tourniquet test, 17 % tachycardia, 10% splenomegaly, 8% signs of circulatory failure and 7% had hypotension.

Of the laboratory parameters studied 72% of the children had abnormal total counts, followed by 58% having thrombocytopenia, 45% deranged liver function tests, 41% had haemoconcentration, 22% had deranged renal function test (BUN and creatinine), 13% had electrolyte disturbances and 6% had metabolic acidosis. Among the

radiological findings in the study group 48% children had pleural effusion and 33% had ascites. 98% of the children were discharged with a mortality rate of 2%. The mean duration of stay was 9.18, 6 and 3.96 days for severe dengue, dengue with warning signs and probable dengue respectively. A significant association of abdominal pain, bleeding manifestation, altered sensorium, convulsion, tachycardia, hypotension, hepatomegaly, splenomegaly, signs of circulatory failure, positive tourniquet test, haemoconcentration, platelet count, deranged renal function test, electrolyte disturbances, deranged liver function test, metabolic acidosis, pleural effusion, ascites and duration of stay with severity of dengue fever was found (Table 2, 3, 4).

Table 3: Association between the signs and severity of dengue fever (n = 100).

Factors		Severe dengue	Dengue with warning signs	Probable dengue	Chi-square tests*	P value
Tachycardia	Present (17)	6 (35.3%)	10 (58.8%)	1 (5.9%)	18.977	<0.05
	Absent (83)	5 (6.0%)	34 (41.0%)	44 (53.0%)		
Hypotension	Present (7)	7 (100%)	0	0	60.899	<0.05
	Absent (93)	4 (4.3%)	44 (47.3%)	45 (48.4%)	51.516	
Splenomegaly	Present (10)	3 (30%)	6 (60%)	1 (10%)	7.318	<0.05
	Absent (90)	8 (8.9%)	38 (42.2%)	44 (48.9%)	2.224	
Circulatory Failure	Present (8)	8 (100%)	0	0	70.35	<0.05
	Absent (92)	3 (3.3%)	44 (47.8%)	45 (48.9%)	60.821	
Tourniquet test	Positive (45)	8 (17.8%)	26 (57.8%)	11 (24.4%)	14.629	<0.05
	Negative (55)	3 (5.5%)	18 (32.7%)	34 (61.8%)		

Table 4: Association between the laboratory investigations and severity of dengue fever (n = 100).

Factors	Results	Severe dengue	Dengue with warning signs	Probable dengue	Chi-square tests*	P value
Hemoconcentration	Present (41)	11 (26.8%)	29 (70.7%)	1 (2.4%)	55.088	<0.05
	Absent (59)	0	15 (25.4%)	44 (74.6%)		
Thrombocytopenia	Present (58)	11 (19%)	30 (51.7%)	17 (29.3%)	17.392	<0.05
	Absent (42)	0	14 (33.3%)	28 (66.7%)		
Renal function tests	Altered (22)	9 (40.9%)	12 (54.5%)	1 (4.5%)	33.908	<0.05
	Normal (78)	2 (2.6%)	32 (41.0%)	44 (56.4%)		
Liver Function tests	Deranged (45)	11 (24.4%)	20 (44.4%)	14 (31.1%)	16.955	<0.05
	Normal (55)	0	24 (43.6%)	31 (56.4%)		
Metabolic acidosis	Present (6)	6 (100%)	0	0	51.644	<0.05
	Absent (94)	5 (5.3%)	44 (46.8%)	45 (47.9%)	42.426	
Pleural effusion on x ray	Present (48)	9 (18.8%)	24 (50%)	15 (31.3%)	9.674	<0.05
	Absent (52)	2 (3.8%)	20 (38.5%)	30 (57.7%)		
Ascites on USG Abdomen	Present (33)	11 (33.3%)	16 (48.5%)	6 (18.2%)	30.430	<0.05
	Absent (76)	0	28 (41.8%)	39 (58.2%)		

There was no significant association found between severity of dengue fever with age, gender, nutritional status, malaise, vomiting, rash, headache and abnormal total counts.

DISCUSSION

Previously many studies have been conducted regarding the clinico-hematological profile of dengue fever, prognostic factors to predict severity and the outcome of dengue fever. We conducted this study based on the new WHO classification 2009 of dengue fever to know which factors can predict severity so as to facilitate timely intervention. In our study out of 100 patients with dengue fever 45 were classified as probable dengue, 44 as dengue fever with warning signs and all children as severe dengue. However Prasad D et al found 82.1% as severe dengue and Sahana et al found 24.7%.[12,13] This variance in the subject distribution may be attributable to the timing of admission, the awareness in the draining community, timely intervention. The mean age of presentation in our study was 5.82 years with 53% of the children in the 6-12 year age group, a finding similar to that by Gomber S et al and Rasul et al.[14,15] This could be

due to the proneness of this age group to mosquito bites because of their outdoor activities. Though no significant association was found between age and severity of dengue in our study, Shah I et al and Rachel C et al found younger age as one of the predictive markers for Dengue shock syndrome and dengue hemorrhagic fever.[16,17] 1.43:1 was the male: female ratio in our study, similar to study by Rasul et al.[15] Though studies by Anders KL et al and Phuong CX et al found increased risk of shock and death among females, our study did not have a significant association similar to studies by Pongpan S and Ahmed FU et al.[18-21] No significant association was found between the nutritional status of the study subjects and the severity of dengue fever. Pichainarong stated that severe dengue is rarely seen in children with protein energy malnutrition.[22] A robust inflammatory response appears necessary for the severe forms of DHF and DSS, however many studies have been conducted on this with inconclusive results.[23,24]

In various studies thrombocytopenia, bleeding episodes and neurological complications were found to have a significant association with severity of dengue, similar to that of our study.[25,26] Hepatomegaly was found to have a significant association with severity in a study by Sahana et al.[13] Splenomegaly was seen more in non survivors than survivors in a study by Reddy BK et al, we however did not notice such an association in our study.[27] Many studies proposed hemo-concentration as a prognostic factor for the severity of dengue infection.[27,28] Vasculopathy in dengue causes increased vascular permeability, leading to hemo-concentration and shock. A falling trend in platelet count as seen by Jayashree K et al and Mourao et al was associated with poor outcome.[29,30] These findings are similar to that observed in our study. The platelets fall before the patient enters into a state of shock. Low platelets are explained by bone marrow suppression and immune response induced platelet destruction by the liver and spleen.[31] As in our study significant association between the presence of pleural effusion, ascitis and dengue fever was also found by Sahana et al and Dayal A et al.[13] Reported case fatality rate for the world is approximately 1%. Mortality rate in our study was 2% similar to the study by Sahana et al.[13]

Various measures for early diagnosis and prompt intervention with emphasis on the warning signs and good supportive care could help decrease the fatality and morbidity associated with Dengue. Health education would also play a major role.

CONCLUSION

Thus from this study it is possible to conclude that early identification of the significant factors as mentioned above is of paramount importance in early recognition of children likely to developing complications. Various measures for early diagnosis and prompt intervention with emphasis on the warning signs and good supportive care would help decrease the fatality and morbidity associated with Dengue. Health education would also play a major role.

ACKNOWLEDGEMENTS

Authors would like to thank the department, faculty and also the patients who were enrolled in this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Chaturvedi UC, Nagar R. Dengue and dengue hemorrhagic fever: Indian perspective. J Biosci. 2008;33(4):429-41.
2. World Health Organization. Prevention and control of dengue and dengue hemorrhagic fever: comprehensive guidelines. WHO SEARO Regional Publication; 1999:29.
3. Oishi K, Saito M, Mapua CA, Natividad FF. Dengue illness: clinical features and pathogenesis. J Infect Chemother. 2007;13(3):125-33.
4. Ranjit S, Kissoon N. Dengue hemorrhagic fever and shock syndromes. Pediatr Crit Care Med. 2011;12(1):96-100.
5. World Health Organization, Geneva. Dengue: guidelines for diagnosis, treatment, prevention and control. WHO; 2009:1-144.
6. Guzman MG, Halstaed SB, Artsob H ,Buchy P, Farrar J, Gubler DJ, et al. Dengue: a continuing global threat. Nat Rev Microbiol. 2010;8(12):S7-S16.
7. Kliegman RM, Stanton BF, Jenson HB, Behrman RE. Nelson textbook of paediatrics. 18th ed. Philadelphia. Saunders Elsevier; 2007:2944-2949.
8. Kliegman RM, Stanton BF, Schor NF, Behrman RE, Geme JW. Nelson textbook of pediatrics. 19th ed. Philadelphia. Saunders Elsevier. 2011;125:746-52.
9. Kliegman RM, Stanton BF, Schor NF, Behrman RE, Geme JW. Nelson textbook of paediatrics. 19th ed. Philadelphia. Saunders Elsevier. 2011;478:1714-22.
10. Gomber S, Ramachandran VG, Kumar S, Agarwal KN, Gupta P, Dewan DK. Hematological observation as diagnostic marker in dengue hemorrhagic fever - a reappraisal. Indian Pediatr. 2001;38(5):477-81.
11. Kliegman RM, Stanton BF, Schor NF, Behrman RE, Geme JW. Nelsons textbook of paediatrics. 19th ed. Philadelphia. Saun ders Elsevier. 2011;503:1778-1.
12. Prasad D, Kumar C, Jain A, Kumar R. Accuracy and applicability of the revised WHO classification of dengue in children seen at a tertiary healthcare facility in northern India. Infection. 2013;41(4):775-82.
13. Sahana KS, Sujata R. Clinical profile of dengue among children according to revised WHO

classification: Analysis of a 2012 Outbreak from Southern India. Indian J Pediatr. 2015;82:109-13.
14. Gomber S, Ramachandran VG, Kumar S, Agarwal KN, Gupta P, Dewan DK, et al. Hematological observation as diagnostic marker in dengue hemorrhagic fever- a reappraisal. Indian Pediatr. 2001;38(5):477-81.
15. Rasul CH, Ahasan HA, Rasid AK, Khan MR. Epidemiological factors of dengue hemorrhagic fever in Bangladesh. Indian Pediatr. 2002;39(4):369-72.
16. Shah I, Deshpande GC, Tardeja PN. Outbreak of dengue in Mumbai and predictive markers for dengue shock syndrome. J trop pediatr. 2004;50(5):301-5
17. Vicente CR, Lauar JC, Santos BS, Cobe VM, Junior CC. Factors related to severe dengue during an epidemic in Vitória, State of Espírito Santo, Brazil, 2011. Rev Soc Bras Med Trop. 2013;46(5):629-32.
18. Anders KL, Nguyet NM, Chau NV, Hung NT, Thuy TT, Lien le B. Epidemiological factors associated with dengue shock syndrome and mortality in hospitalized dengue patients in Ho Chi Minh City, Vietnam. Am J Trop Med Hyg. 2011;84(1):127-34.
19. Phuong CX, Nhan NT, Kneen R, Thuy PT, van Thien C, Nga NT, et al. Clinical diagnosis and assessment of severity of confirmed dengue infections in Vietnamese children: is the world health organization classification system helpful? Am J Trop Med Hyg. 2004;70(2):172-9.
20. Pongpan S, Wisitwong A, Tawichasri C, Patumanond J. Prognostic Indicators for dengue infection severity. International J Clin Pediatr. 2013;2(1):12-8.
21. Ahmed FU, Mahmood CB, Sharma JD, Hoque SM, Zaman R, Hasan MS. Dengue and dengue haemorrhagic fever in children during the 2000 outbreak in Chittagong, Bangladesh. Dengue Bull. 2001;25:33-9.
22. Pichainarong N, Mongkalangoon N, Kalayanarooj S, Chaveepojnkamjorn W. Relationship between body size and severity of dengue hemorrhagic fever among children aged 0-14 years. Southeast Asian J Trop Med Public Health. 2006;37(2):283-8.
23. Kalayanarooj S, Nimmannitya S. Is dengue severity related to nutritional status? Southeast Asian J Trop Med Public Health. 2005;36(2):378-84.
24. Carlos CC, Oishi K, Cinco MT, Mapua CA, Inoue S, Cruz DJ et al. Comparison of clinical features and hematologic abnormalities between dengue fever and dengue hemorrhagic fever among children in the Philippines. Am J Trop Med Hyg. 2005;73(2):435-40.
25. Gupta V, Yadav TP, Pandey RM, Singh A, Gupta M, Kanaujiya P, et al. Risk factors of dengue shock syndrome in children. J Trop Pediatr. 2011;57(6):451-6.
26. Hendarto SK, Hadinegoro SR. Dengue encephalopathy. Acta Paediatr Jpn. 1992;34(3):350-7.
27. Chacko B, Subramanian G. Clinical, laboratory and radiological parameters in children with dengue fever and predictive factors for dengue shock syndrome. J Trop Pediatr. 2008;54(2):137-40.
28. Shah GS, Islam S, Das BK. Clinical and laboratory profile of dengue infection in children. Kathmandu Univ Med J (KUMJ). 2006;4(1):40-3.
29. Jayashree K, Manasa GC, Pallavi P, Manjunath GV. Evaluation of platelets as predictive parameters in dengue fever. Indian J Hematol Blood Transfus. 2011;27(3):127-30.
30. Mourao MP, Lacerda MV, Macedo VO, Santo JB. Thrombocytopenia in patients with dengue virus infection in Brazilian Amazon. Platelets. 2007;18(8):605-12.
31. Chuansumrit A, Tangnararatchakit K. Pathophysiology and management of dengue hemorrhagic fever. Transfus Altern Transfus Med. 2006;8(1):S3-11.

Cite this article as: Mogra G, Ghildiyal RG, Mohanlal S. Classification and study of the clinico-hematological profile of patients with dengue fever in the pediatric age group. Int J Contemp Pediatr 2016;3:1405-10.