International Journal of Medical and Health Research
ISSN: 2454-9142
Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 3; Issue 10; October 2017; Page No. 89-95

Description and classification of severity of Dengue fever using early clinical and laboratory Parameters in paediatric patients

[1]Jai Pratibha Varshney, [2]Neha Sharma, [3]Atul Seth*
[1]Department of Paediatrics, Noble Hospital, Hadapsar, Pune, Maharashtra, India
[2]Department of Paediatrics, Santokba Durlabhji Memorial Hospital, Bhawani Singh Marg, Jaipur, Rajasthan, India
[3]Department of Gynaecology, Armed Forces Medical College, Pune, Maharashtra, India
*Corresponding Author: Atul Seth

Abstract
Objective: Dengue infection, an arthropod – borne viral haemorrhagic fever, continues to be a major challenge to public health. Infection with dengue virus can cause a spectrum of illnesses. Early identification of patients at risk of developing severe dengue is critical to provide timely supportive care, which can reduce the risk of mortality to 1%. Distinguishing dengue from other febrile illnesses early in illness is challenging, since symptoms are non-specific and common to other febrile illnesses. Although the World Health Organization (WHO) has established new clinical guidelines to classify dengue severity, serological, virological, and molecular biological tests are required to definitively diagnose DENV infection. In many endemic countries, laboratory diagnosis of dengue is often problematic. The idea behind this study is to observe the clinical and biochemical characteristics of the patients with Dengue Fever and see if any of these factors are associated with prediction of poor outcome in terms of morbidity.
Methods: This hospital based observational prospective study was conducted in the Paediatric Indoor Unit (Ward and ICU) of a tertiary care hospital over a period of 18 months.378 patients fulfilling the inclusion criteria were included in the study.
Results: While abdominal pain, vomiting, anorexia, respiratory distress, abdominal distention and tachypnoea are early clinical signs of severe dengue. Ascites, pleural effusion and abdominal distension were also important early markers indicating increasing severity of disease. Severity of thrombocytopenia and rise in Serum aminotransferase levels were directly proportional to the severity of the disease. Co-positivity for IgM and IgG antibodies was most common lab parameter in patients with severe dengue infection.
Conclusion: The revised classification of Dengue illness should shift its focus from detecting severity of the disease by hemorrhagic manifestations and circulatory failure to encompassing a more multi-organ evaluation by simple clinical and lab parameters for early intervention resulting in probably lower mortality as compared to the previous years. The acknowledgement of dengue infection presenting differently in pediatric patients as opposed to their adult counterparts and requirement of separate guidelines for this age group has also been recommended.

Keywords: dengue fever, pediatric age group, severity, clinical findings, lab parameters

Introduction

Dengue infection, an arthropod – borne viral haemorrhagic fever, continues to be a major challenge to public health, especially in South-East Asia [1]. It has a wide geographical distribution and can present with a diverse clinical spectrum [2]. It has been estimated that at least 2.5 billion people in tropical and sub-tropical regions worldwide live in areas where there is a significant risk of infection from the dengue virus [3, 4]. Estimates suggest that annually over 50 million cases of dengue infections occur in the world with a case fatality rate of around 2.5%3. An estimated 5, 00,000 people with DHF require hospitalization each year. Of those with DHF, at least 90% are children younger than 5 years old [3].

Infection with dengue virus can cause a spectrum of illnesses including asymptomatic, fever and relatively mild disease, known as classic dengue fever (DF), a more severe form known as DHF earlier, less frequently acute hepatitis with liver failure, disseminated intravascular coagulation, encephalopathy, myocarditis, acute renal failure and haemolytic uremic syndrome [3]. Today, secondary infection by a different dengue serotype is considered the most significant individual risk factor for severe dengue [13, 15]. Some studies have suggested there are differences in the pathophysiology of the different dengue serotypes, but currently no one serotype is considered more dangerous than another [16, 18].

Most cases present as classic dengue fever (DF), a debilitating but self-limited illness that manifests with high fever, retro-orbital pain, severe myalgia/arthralgia, and rash. However, in some cases, mainly children, illness progresses to life-threatening dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS), characterized by vascular leakage leading to hypovolemic shock and a case fatality rate up to 5%. [22, 23]

Early identification of patients at risk of developing severe dengue is critical to provide timely supportive care, which can

reduce the risk of mortality to 1%. [24, 25] However, distinguishing dengue from other febrile illnesses early in illness is challenging, since symptoms are non-specific and common to other febrile illnesses [25, 27]. In addition, many distinguishing clinical features of DHF/DSS generally emerge only after 4–5 days, at defervescence, when the patient is already critically ill. Although the World Health Organization (WHO) has established new clinical guidelines to classify dengue severity, serological, virological, and molecular biological tests are required to definitively diagnose DENV infection. In many endemic countries, laboratory diagnosis of dengue is often problematic [28, 29].

The idea behind this study is to observe the clinical and biochemical characteristics of the patients with DF admitted to a tertiary care hospital and see if any of these factors are associated with prediction of poor outcome in terms of morbidity. The 2009 WHO recommendations for classification of dengue fever was followed during the course of this study [22]. This revised classification is based on severity level. It has a high potential for being of practical use in clinicians' decision in term of where and how intensively the patients should be observed and treated, more consistent reporting in the national and international surveillance system, and as end-point measure in dengue vaccine and drug trials. This model had been suggested by an expert group (Geneva, Switzerland, 2008) and was tested in 18 countries by comparing its performance in practical settings to the WHO 1997 case classification.

Material & Methods

This hospital based observational prospective study was conducted in the Paediatric Indoor Unit (Ward and ICU) of a tertiary care hospital over a period of 18 months. 378 patients fulfilling the inclusion criteria were included in the study.

Inclusion Criteria

1. Serologically confirmed (IgM positive alone or both IgM and IgG) or NS1antigen positive dengue fever patients admitted for at least 4 days.
2. All cases in the paediatric age group (>1 month and <18years) were included irrespective of sex.

Exclusion Criteria

1. Age ≤ 1 month and ≥ 18 years.
2. Serologically negative dengue like illnesses.
3. Cases of enteric fever, scrub typhus, leptospirosis, and malaria by appropriate investigations thrombocytopenia during hospital stay.
4. Patients who were discharged before 4 days of hospital stay.

Sample size and sample technique

The sample size calculation was done with the help of G Power software. Post hoc analysis of the resulting sample size was done to compute the achieved power (1-β) where error probability = 0.05. N = 378, Ng = 3, Nm = 4 gave achieved power of 0.86 where N = Number of cases, Ng = Number of groups and Nm =Number of measurements.

Data collection technique and tools

A detailed history regarding signs and symptoms of patient and a thorough physical examination with preliminary haematological tests and other relevant investigations were conducted at the time of admission and were recorded on a preformed proforma. The children were then divided into non-severe dengue without warning signs, non-severe dengue with warning signs and severe dengue according to their clinical and laboratory presentation.

Data Analysis

The patients' history, clinical presentations, laboratory findings, complications and treatment administered to the children were taken for analysis. Repeated measure ANOVA was used to evaluate the changes in the values of Temperature, Tachypnoea, Tachycardia, Shock, Bleeding score and laboratory investigations at different time intervals (from day 1 to day 4 of admission). All other variables were assessed using one-way ANOVA when difference was to be assessed between the 3 groups: Dengue without warning signs, Dengue with warning signs and severe dengue.

Observations

Table 1: Classification and Distribution of Dengue Cases.

Classification	Dengue without warning signs	Dengue with warning signs	Severe Dengue
Cases (%)	128 (34%)	186 (49%)	64 (17%)

Table 2: Mean age and Standard Deviation of the distributed cases.

Category	Mean and Standard Deviation (years)
Dengue without warning Signs	(128 patients) 10.17 ± 4.73
Dengue with warning signs	(186 patients) 10.83 ± 4.20
Severe Dengue	(64 patients) 9.61 ± 5.11
p value	0.278

Table 3: Age distribution of the cases.

Age (years)	Age (years) Dengue without warning signs Cases (%)	Age (years) Dengue with warning signs Cases (%)	Age (years) Severe Dengue Cases (%)
2 months-5	22 (17.2%)	24 (12.9%)	14 (21.9%)
6-11	49 (38.3%)	62 (33.3%)	24 (37.5%)
12-18	57 (44.5%)	100 (53.2%)	26 (40.6%)
Total	128 (100%)	186 (100%)	64 (100%)

Table 4: Sex distribution.

Sex	Dengue without warning signs Cases (%)	Dengue with warning signs Cases (%)	Severe Dengue Cases (%)
Males	105 (82%)	133 (71.5%)	50 (78.1%)
Females	23 (18%)	53 (28.5%)	14 (21.9%)
Total	128(100%)	186(100%)	64(100%)
p value	0.278		

Table 5: Showing percentage of chief complaints in Cases.

Clinical Manifestations	Dengue Without Warning Signs	Dengue With Warning Signs	Severe Dengue	P Value
Fever	128 (100%)	186 (100%)	64 (100%)	**0.000**
Rash	22 (17.2%)	21 (11.3%)	9 (14.1%)	0.328
Vomiting	Vomiting 71 (55.5%)	135 (72.6%)	42 (65.6%)	**0.007**
Abdominal Pain	2 (1.6%)	129 (69.4%)	45 (70.3%)	**0.000**
Abdominal Distension	0 (0%)	7 (3.8%)	19 (29.7%)	**0.000**
Anorexia	20 (15.6%)	52 (28%)	25 (39.1%)	**0.001**
Bleeding	0 (0%)	19 (10.2%)	16 (25%)	**0.000**
Respiratory Distress	0 (0%)	3 (1.6%)	21 (32.8%)	**0.000**
Reduced Urine Output	3 (2.3%)	7 (3.8%)	14 (21.9%)	**0.000**

Table 6: Showing number and percentage of cases having fever on first 4 days of admission.

	Day	Dengue without warning signs Cases (%)	Dengue with warning signs Cases (%)	Severe Dengue Cases (%)
Temp	Day 1	64 (50%))	73 (39.2%)	27 (42.2%)
	Day 2	60 (46.9%)	68 (36.6%)	25 (39.1%)
	Day 3	37 (28.9%)	43 (23.1%)	25 (39.1%)
	Day 4	21 (16.4%)	28 (15.1%)	23 (35.9%)
	p value	0.000	0.000	0.913

Table 7: Showing number and percentage of cases having tachycardia on first 4 days of admission.

	Day	Dengue without warning signs Cases (%)	Dengue with warning signs Cases (%)	Severe Dengue Cases (%)
Tachycardia	Day 1	43 (33.6%)	53 (28%)	33 (51.6%)
	Day 2	43 (33.6%)	55 (29.6%)	31 (48.4%)
	Day 3	38 (29.7%)	48 (25.8%)	23 (35.9%)
	Day 4	26 (20.3%)	42 (22.6%)	22 (34.4%)
	p value	0.016	0.373	0.151

Table 8: Showing number and percentage of cases having tachypnoea on first 4 days of admission.

	Day	Dengue without warning signs Cases (%)	Dengue with warning signs Cases (%)	Severe Dengue Cases (%)
Tachypnoea	Day 1	28 (21.9%)	30 (16.1%)	27 (42.2%)
	Day 2	30 (23.4%)	30 (16.1%)	29 (45.3%)
	Day 3	29 (22.7%)	23 (12.4%)	23 (35.9%)
	Day 4	25 (19.5%)	22 (11.8%)	13 (20.3%)
	p value	0.382	0.067	**0.003**

Table 9: Showing number and percentage of cases with severe dengue with Shock on the first 4 days of admission.

	Severe Dengue (64 patients)
	Cases (%)
Day 1	14 (21.9%)
Day 2	3 (4.7%)
Day 3	4 (6.3%)
Day 4	3 (4.7%)
p value	0.003

Table 10(a): Showing the bleeding score and its description.

Bleeding score Description	Bleeding score Description
0	No bleeding
1	Petechiae
2	Epistaxis or gingival bleeding, menorrhagia
3	Gastrointestinal bleeding
4	Intracranial bleed, intrapulmonary bleed

Table 10(b): Showing the percentage of cases with bleeding score for 4 days of admission.

		Dengue without warning signs	Dengue with warning signs	Severe Dengue
Day of Admission	Bleeding Score	Cases (%)	Cases (%)	Cases (%)
Day 1	0	00 (0%)	163 (87.6%)	50 (78.1%)
	1	3 (2.3%)	6 (3.2%)	1 (1.6%)
	2	0 (0%)	5 (2.7%)	5 (7.8%)
	3	0 (0%)	12 (6.5%)	8 (12.5%)
Day 2	0	0 (0%)	(90.3%)	43 (67.2%)
	1	2 (1.6%)	3 (1.6%)	4 (6.3%)
	2	0 (0%)	6 (3.2%)	5 (7.8%)
	3	0 (0%)	9 (4.8%)	12 (18.8%)
Day 3	0	0 (0%)	175 (94.1%)	49 (76.6%)
	1	2 (1.6%)	2 (1.1%)	2 (3.1%)
	2	0 (0%)	6 (3.2%)	5 (7.8%)
	3	0 (0%)	3 (1.6%)	8 (12.5%)

Day 4	0	0 (0%)	185 (99.5%)	60 (93.8%)
	1	1 (0.8%)	0 (0%)	1 (1.6%)
	2	0 (0%)	1 (0.5%)	1 (1.6%)
	3	0 (0%)	0 (0%)	2 (3.1%)
p value		0.782	0.098	0. 193

Table 11: Showing number and percentage of cases showing warning signs during the 1st 4 days of admission.

	Dengue with warning signs	Severe Dengue
Clinical findings	Cases (%)	Cases (%)
Pleural effusion	6 (3.2%)	23 (35.9%)
Abdominal distension	6 (3.2%)	22 (34.4%)
Hepatomegaly	29 (15.6%)	36 (56.3%)
Tender abdomen	62 (33.3%)	45 (70.3%)
Ascites	5 (2.7%)	27 (42.2%)
CNS	0 (0.0%)	7 (10.9%)
p value	0.000	0.000

Table 12(a): Showing number and percentage of cases found positive for various serological markers on admission.

Dengue Serology	Dengue without warning signs	Dengue with warning signs	Severe Dengue	p value
	Cases (%)	Cases (%)	Cases (%)	
NS1Ag	93 (72.7%)	128 (68.8%)	43 (67.2%)	0.68
IgM	44 (34.4%)	63 (33.9%)	32 (50%)	0.050
Ig G 39	39 (30.5%)	86 (46.2%)	38 (59.4%)	0.000

Table 12(b): Showing percentage of cases found positive for more than one serological markers on admission.

	NS1Ag+IgM+IgG (%)	IgM+IgG (%)	NS1Ag+IgG (%)	NS1Ag+IgM (%)
Dengue without Warning Signs	11.7%	4.6%	5.4%	10.1%
Dengue with warning signs	9.6%	9.1%	12.3%	10.2%
Severe Dengue	15.6%	18.7%	14%	12.5%

Table 13: Showing mean haemoglobin of patients in all categories admitted for 4 days.

	Dengue without warning signs Mean(SD)	Dengue with warning signs Mean(SD)	Severe Dengue Mean(SD)
Day 1	13.17±1.99	13.43±1.97	13.13±2.91
Day 2	13.26±1.71	13.00±1.66	12.22±2.64
Day 3	13.05±1.60	12.85±1.66	11.35±2.44
Day 4	12.90±1.57	12.76±1.69	11.26±2.05
p value	0.014	0.000	0.000

Table 14: Showing mean haematocrit of patients in all categories admitted for first 4 days of admission.

		Dengue without warning signs Mean (SD)	Dengue with warning signs Mean (SD)	Severe Dengue Mean (SD)
Haematocrit (%)	Day 1	38.8 ± 5.64	39.55±5.06	37.86±8.36
	Day 2	39.62 ± 5.14	38.7±4.88	36.13±7.36
	Day 3	38.17 ± 4.66	38.14±4.86	33.63±6.9
	Day 4	36.81± 4.76	37.23±5.10	33.23±6.14
% fall in haematocrit after treatment		5.4%	5.9%	13.9%
P value		0.000 0.000 0.000	0.000 0.000 0.000	0.000 0.000 0.000

Table 15: Showing mean TLC of patients in all categories admitted for first 4 days of admission.

		Dengue without warning signs Mean(SD)	Dengue with warning signs Mean(SD)	Severe Dengue Mean(SD)
Total leucocyte count (x 103cells/µl)	Day 1	5.52±3.67	6.69±5.37	9.52±5.33
	Day 2	5.55±3.06	6.59±4.81	9.56±5.23
	Day 3	5.86±2.75	6.59±4.63	9.13±4.38
	Day 4	6.16±2.37	6.56±3.85	8.75±3.66
P value		0.058	0.944	0.657

Table 16: Showing mean absolute neutrophil count of patients in all categories admitted for first 4 days of admission.

		Dengue without warning signs Mean(SD)	Dengue with warning signs Mean(SD)	Severe Dengue Mean(SD)
Absolute Neutrophil count (x 103cells/µl)	Day 1	2.48±2.16	16 2.72±2.24	4.38±2.86
	Day 2	2.15±1.84	2.20±1.99	4.14±2.94
	Day 3	1.98±1.21	2.00±1.36	3.89±2.81
	Day 4	2.09±1.00	2.02±1.09	4.09±2.9
P value		0.007	0.000	0.287

Table 17: Showing mean absolute lymphocyte count of patients in all categories admitted for first 4 days of admission.

		Dengue without warning signs Mean(SD)	Dengue with warning signs Mean(SD)	Severe Dengue Mean(SD)
Absolute lymphocyte count (x 103cells/µl)	Day 1	2.45±2.31	2.79±2.39	4.08±3.02
	Day 2	2.62±1.69	3.33±2.43	4.54±3.28
	Day 3	3.11±1.79	3.50±2.47	4.15±2.41
	Day 4	3.33±1.76	3.60±1.98	3.90±1.92
P value		0.000	0.000	0.150

Table 18: Showing mean Absolute monocyte count of patients in all categories admitted for first 4 days of admission.

		Dengue without warning signs Mean(SD)	Dengue with warning signs Mean(SD)	Severe Dengue Mean(SD)
Absolute Monocyte count (x 103cells/µl)	Day 1	0.38±0.34	0.47±0.58	0.61±0.42
	Day 2	0.44±0.31	0.49±0.32	0.69±0.44
	Day 3	0.45±0.26	0.51±0.31	0.76±0.40
	Day 4	0.51±0.28	0.53±0.36	0.77±0.42
P value		0.001	0.355	0.095

Table 19: Showing mean Absolute platelet count of patients in all categories admitted for first 4 days of admission.

		Dengue without warning signs Mean(SD)	Dengue with warning signs Mean(SD)	Severe Dengue Mean(SD)
Absolute platelet count (x 103/µl)	Day 1	116.95±79.03	89.53±76.89	59.41±50.99
	Day 2	104.42±65.61	87.31±59.14	60.55±50.90
	Day 3	119.48±65.26	101.77±60.97	87.47±118.32
	Day 4	159.45±68.55	142.08±69.37	127.14±95.13
P value		0.000	0.000	0.000

Table 20: Showing mean AST of patients in all categories admitted for first 4 days of admission.

		Dengue without warning signs Mean(SD)	Dengue with warning signs Mean(SD)	Severe Dengue Mean(SD)
AST Levels (IU/l)	Day 1	198.10±157.45	264.12±192.98	1541.11±2836.48
	Day 2	157.16±135.62	235.55±181.89	1362.73±2023.47
	Day 3	120.88±113.45	202.15±166.44	1245.41±1245.41
	Day 4	94.66±100.44	172.50±149.97	1006.20±2781.79
P value		**0.000**	**0.000**	0.123

Table 21: Showing mean ALT of patients in all categories admitted for first 4 days of admission.

		Dengue without warning signs Mean(SD)	Dengue with warning signs Mean(SD)	Severe Dengue Mean(SD)
ALT Levels (IU/l)	Day 1	94.52±80.15	115.66±86.05	697.53±1414.75
	Day 2	72.22±70.24	100.51±78.09	651.33±1288.66
	Day 3	53.16±60.77	84.27±72.23	576.84±1323.84
	Day 4	40.60±50.05	70.93±65.30	443.53±951.49
P value		0.000	0.000	0.087

Table 22: Showing number and percentage of patients requiring >105% of maintenance fluid in all categories.

Dengue without warning signs Cases (%)	Dengue with warning signs Cases (%)	Severe Dengue Cases (%)	p value
3 (2.3%)	86 (46.2%)	49 (76.6%)	**0.000**

Table 23: Showing number and percentage of patients requiring colloidal transfusion in all categories.

Dengue with warning signs	Severe Dengue	p value
Cases (%)	Cases (%)	
3 (1.6%)	12 (18.8%)	**0.000**

Table 24: Showing Number and Percentage of Patients Requiring Blood Component Transfusion in All Categories.

Dengue without warning signs Cases (%)	Dengue with warning signs Cases (%)	Severe Dengue Cases (%)	p value
0 (0%)	2 (1.1%)	20 (31.3%)	**0.000**

Table 25: Showing Number and Percentage of Patients Requiring Inotropic support in Severe Dengue.

Severe Dengue (64 patients)		p value
No. of patients	% of patients	
21	32.8%	0.000

Discussion

The present study was carried out with the aim of studying the clinical and laboratory profile of dengue fever in pediatric patients. The study was conducted on 378 serologically confirmed cases of dengue fever. Each case was classified according to the severity of their illness. Data regarding

presenting complaints, thorough clinical examination at presentation and investigations were obtained as they were done.

378 patients of 422 serologically confirmed indoor dengue patients were admitted to our study according to the inclusion criteria. The mortality observed was 1.6% (7 patients).

Out of these, 34% had dengue without warning signs, 49% had dengue with warning signs and 17% had severe dengue. The youngest child admitted to the study was 3 months old.

Among children of 2 months to 5 years, severe dengue (21.8%) was most common while most of the children (53.7%) of preadolescent to adolescent age group (12-18 years) had dengue with warning signs. Young infants and children are thus prone to develop a severe form of the disease. The male to female ratio in the study was approximately 3.2: 1. All patients had fever on admission, vomiting (55.5%), rash (17.2%) and anorexia (15.6%) were the next most common clinical presentations in children who had no warning signs. Vomiting (72.6%), abdominal pain (69.4%), anorexia (28%), rash (11.3%) and bleeding manifestations (10.2%) were the most common presenting complaints in children who had dengue with warning signs. Abdominal pain (70.3%), vomiting (65.6%), anorexia (39.1%), respiratory distress (32.8%) and abdominal distention (29.7%) were the common presenting complaints in children with severe dengue. Among the vital signs, tachypnoea was the earliest sign to decrease, raised temperature and tachycardia persisted in those with severe dengue as compared to those with non-severe dengue. 21.9% of severe dengue patients had shock on presentation. Gastrointestinal bleeding decreased in incidence (6.5% on day 1 and none on day 4 of admission) while mucosal hemorrhage increased in incidence (2.7% on day 1 to 3.2% on day 3) as the days of admission progressed in those with warning signs. Gastrointestinal haemorrhage was more common as the illness progressed (12.5% on day1 to 18.8% on day 3) in those with severe dengue. Tender abdomen and hepatomegaly were the most common warning signs seen in both non-severe and severe dengue. Ascites, pleural effusion and abdominal distension were also important early markers indicating increasing severity of disease.NS1Ag was most commonly positive in all patients and the co-positivity for NS1Ag and IgG antibodies (12.3%) was the most common pattern in those with warning signs while co-positivity for IgM and IgG antibodies (18.7%) was the most common pattern among those with severe dengue. Haemoglobin and hematocrit showed the sharpest fall with intravenous fluid therapy in patients of severe dengue. Total leucocyte counts did not vary much but the absolute monocyte counts showed a persistent rise during the course of the disease. Severity of thrombocytopenia was greater for those with a severe dengue. Serum aminotransferase levels were directly proportional to the severity of the disease. Serum AST levels were a better marker of disease severity and showed a delayed fall in levels as compared to serum ALT levels. The revised classification of Dengue illness has shifted its focus from detecting severity of the disease by hemorrhagic manifestations and circulatory failure to encompassing a more multi-organ evaluation for early intervention resulting in probably lower mortality as compared to the previous years.

Conclusions

This was a prospective hospital based observational study in view of the re-emergence of dengue illness in India. The new classification instead of focusing on the hemorrhagic symptoms takes into account the symptoms due to multiple organ involvement and plasma leakage thus increasing the sensitivity and specificity of the diagnosis. The disease is more severe in infants and hemorrhagic manifestations are more common in young adults. Looking for warning signs of leakage and early institution of fluid therapy on their basis prevents the rise of hematocrit to >20% of baseline levels. Absolute differential leucocyte counts can be further explored for their diagnostic potential. Gastrointestinal bleeding is the most common pattern of hemorrhage. Serum transaminases rise with the severity of the disease. The rise in AST levels is more than the rise in ALT levels and has better correlation with the disease severity. Judicious fluid replacement, under stringent monitoring to prevent its overload, instead of blood component (esp. platelet) transfusions is the mainstay of treatment.

The acknowledgement of dengue infection presenting differently in pediatric patients as opposed to their adult counterparts and separate guidelines, which take cognizance of the distinctive problems faced by this age group, drafted for their management will help clinicians in reducing the morbidity of the disease in them.

The newer case definitions of dengue illness still have a lower degree of acceptance though proven by studies to be more sensitive and specific for the severity of the disease and result in prompt management of cases. We need to adopt these definitions as pertinent in our setup to further reduce the morbidity and economic burden of the disease in our country. Larger case studies are recommended to evaluate the usefulness of absolute neutrophil counts, absolute lymphocytic counts and absolute monocyte counts as early laboratory markers of severity of the disease. The nationwide rise in the incidence of dengue infections in 2012 and 2013 indicate a lack in our vector control strategies as the changing epidemiology of the viruses indicates that there is a rise in the incidence of secondary infections which leaves vector control as the main weapon in our arsenal to combat this problem. Studies indicate that under-reporting of dengue cases is hampering the response of the health sector to the real burden of the disease resulting in ill-preparedness and allowing major outbreaks to happen. The adherence to case definitions based on early clinical signs will result in better management of resources in prevention and control rather than crises management.

References

1. Halstead SB. Dengue. Curr Opin Infect Dis. 2002; 15(5):471-6.
2. Seneviratne SL, Malavige GN, De Silva HJ. Pathogenesis of liver involvement during dengue viral infections. Trans R Soc Trop Med Hyg. 2006; 100(7):608-14.
3. World Health Organisation. Prevention and control of dengue and dengue hemorrhagic fever: comprehensive guidelines. WHO SEARO Regional Publication, 2011; 60.
4. Suaya JA, Shepard DS, Siqueira JB, Martelli CT, Lum

LCS, Tan LH, *et al.* Cost of dengue cases in eight countries in the Americas and Asia: A prospective study. Am J Trop Med Hyg. 2009; 80(5):846-55.
5. Nimmannitya S, Halstead SB, Cohen SN, Margiotta MR. Dengue and chikungunya virus infection in man in Thailand, 1962-1964. I. Observations on hospitalized patients with hemorrhagic fever. Am J Trop Med Hyg. 1969; 18(6):954-71.
6. Bravo JR, Guzmán MG, Kouri GP. Why dengue haemorrhagic fever in Cuba? Individual risk factors for dengue haemorrhagic fever/dengue shock syndrome DHF/DSS. Trans R Soc Trop Med Hyg. 1987; 81(5):816-20.
7. Halstead SB. Dengue: The Syndromic Basis to Pathogenesis Research. Inutility of the 2009 WHO case definition. Am J Trop Med Hyg. 2013; 88(2):212-5.
8. Thomas L, Verlaeten O, Cabié A, Kaidomar S, Moravie V, Martial J *et al.* Influence of the dengue serotype, previous dengue infection, and plasma viral load on clinical presentation and outcome during a dengue-2 and dengue-4 co-epidemic. Am J Trop Med Hyg. 2008; 78(6):990–8.
9. Nisalak A, Endy TP, Nimmannitya S, Kalayanarooj S, Thisayakorn U, Scott RM *et al.* Serotype-specific dengue virus circulation and dengue disease in Bangkok, Thailand from 1973 to 1999. Am J Trop Med Hyg. 2003; 68(2):191-202.
10. Vaughn DW, Green S, Kalayanarooj S, Innis BL, Nimmannitya S, Suntayakorn S *et al.* Dengue viremia titer, antibody response pattern, and virus serotype correlate with disease severity. J Infect Dis. 2000; 181(1):2-9.
11. World Health Organization. Dengue: Guidelines for diagnosis, treatment, prevention and control. Geneva: WHO Press cited 2014 Jun 17, 2009.
12. Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ *et al.* Dengue: a continuing global threat. Nat Rev Microbiol. 2010; 8(12Suppl):S7-16.
13. Chokephaibulkit K, Perng GC. Challenges for the formulation of a universal vaccine against dengue. Exp Biol Med Maywood NJ. 2013; 238(5):566-78.
14. Zavala-Velazquez JE, Yu XJ, Walker DH. Unrecognized spotted fever group rickettsiosis masquerading as dengue fever in Mexico. Am J Trop Med Hyg. 1996; 55(2):157-9.
15. Watt G, Jongsakul K, Chouriyagune C, Paris R. Differentiating dengue virus infection from scrub typhus in Thai adults with fever. Am J Trop Med Hyg. 2003; 68(5):536-8.
16. Ellis RD, Fukuda MM, McDaniel P, Welch K, Nisalak A, Murray CK *et al.* Causes of fever in adults on the Thai-Myanmar border. Am J Trop Med Hyg. 2006; 74(1):108-13.
17. Guzmán MG, Kourí G. Dengue diagnosis, advances and challenges. Int J Infect Dis IJID off Publ Int Soc Infect Dis. 2004 Mar; 8(2):69–80.
18. Cherian T, Ponnuraj E, Kuruvilla T, Kirubakaran C, John TJ, Raghupathy P. An epidemic of dengue haemorrhagic fever & dengue shock syndrome in & around Vellore. Indian J Med Res. 1994; 100:51-6.