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Original Research Article

Changing trends in clinicopathological parameters in dengue with evaluation of predictors of poor outcome in children

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ABSTRACT

Background: A study was planned to evaluate the changing trends in dengue according to the revised WHO guidelines in children and at identifying and evaluating the association between clinical features the child and the outcome.
Methods: This was a retrospective observational study conducted in Safdarjung Hospital. Children with signs and symptoms of dengue fever along with serological or antigen NS1 positivity were included. Continuous variables were analysed using percentage, mean, standard deviation. Categorical variables were analysed using chi-square test. P value < 0.05 was considered significant.
Results: A total number of 69 patients of dengue were included. The mean age of presentation was 7.1±3 years. All patients with mucosal bleeds had thrombocytopenia which was statistically significant (p<0.002). There was a significant correlation (p < 0.000) between presence of more than three warning signs and prolonged hospital stay (>5 days) (p < 0.000) and progression to shock.
Conclusions: Lethargy, presence of more than 3 warning signs at the time of presentation can be used as predictors of severe dengue.

Keywords: Changing trends dengue, Clinicopathological parameters, Pediatrics, Prognostic factors, Poor outcomes

INTRODUCTION

Dengue is a mosquito borne arboviral disease endemic to the tropical and subtropical regions causing significant morbidity and moratlity and poses as a major public health concern. WHO estimates the incidence to approximately 50-100 million new dengue infections per year out of which 20,000 die annually and identified it as one of the 17 neglected tropical diseases in the year 2010.[1-4]

This increasing incidence of the disease has been attributed to improper water storage, rampant unplanned urbanisation, overcrowding, inadequate sanitation and sewer system leading to proliferation of vector breeding sites in urban, semi-urban and rural areas.

Dengue infection occurs in all age groups including vertical transmission from pregnant women to their foetus (1.6-64%).[5] Infection with dengue is considered a high risk for both morbidity and mortality in children under 15 years.

The clinical manifestations of dengue varies from mild fever to severe haemorrhage, shock and death. WHO IN 2009 reclassified dengue according to levels of severity as: dengue without warning signs, dengue with warning signs (abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver

enlargement, increasing hematocrit with decreasing platelets), and severe dengue (dengue with severe plasma leakage, severe bleeding, or organ failure).[6]

Most of the previous pediatric studies have tried to establish a co-relation between biochemical parameters and outcome. In this study we intend to evaluate and analyse the association between clinical parameters at presentation and the prognosis.

METHODS

This was a retrospective observational study conducted in the pediatric ward of Safdarjung Hospital, a tertiary care hospital of north India during the period of August 2014 to October 2014. Children in the age group between 1-12 years who presented with signs and symptoms of dengue fever along with serological (IgM elisa positive) or non-structural protein antigen NS1 positivity were included for the retrospective analysis in the study.

The children were classified according to the WHO revised guidelines and treated accordingly. All signs, symptoms and biochemical parameters according to the WHO classification were recorded and statistically analysed. Fluid accumulation in body cavities were assessed by sonogram of abdomen (ascitis) and chest x-ray (pleural effusion). Hematological parameters including haemoglobin, platelet count, total leucocyte count and hematocrit were also assessed. Continuous variables were analysed using percentage, mean, standard deviation. Categorical variables were analysed using chi-square test. P value < 0.05 was considered significant. For summarizing clinical features, children were divided into two groups, with cut off at 5 years of age. Warning sings viz. abdominal pain, hepatomegaly, thrombocytopenia, mucosal bleed, fluid accumulation, persistent vomiting, lethargy and shock were considered separately. Outcome of the child was co-related with warning signs, stay in hospital and requirement of fluid or blood.

Clinical features and laboratory parameters were analyzed for frequencies and their predictability to identify severe forms of dengue as per the new WHO criteria.

RESULTS

A total number of 69 patients of dengue, serologically (Ig M Elisa) or antigen (NS1+ve) proven were admitted in pediatric ward of the hospital. The mean age of presentation was 7.1±3 years.

A total number of 43 males (62.3%) and 23 (37.7%) females were admitted. 30 (81.2%) patients of dengue were diagnosed by IgM elisa and the rest 13 (18.8%) by NS1 antigen. All the children had high grade fever with mean duration of fever at presentation of 6±2.9 days. 94.2% children were successfully discharged after a mean duration of stay of 4.5±2 days while 4 (5.8%) children expired.

Table 1: Age-wise distribution of clinical feature (n = 69).

	Age <5 years (21)	Age >5 years (48)	Chi-square (df)	P value
Stay >5 days	4	15	1.09 (1)	0.29
Warning signs>3*	5	6	-	0.29
Abdominal pain	8	12	1.217 (1)	0.27
Fluid accumulation*	5	7	-	0.49
Persistent vomiting	14	30	0.11 (1)	0.74
Mucosal bleed	10	17	0.913 (1)	0.34
Lethargy	18	32	2.656 (1)	0.10
Hepatomegaly	9	26	0.748 (1)	0.39

*Fisher's test

The most common presenting complaints were lethargy (72.5%), abdominal pain (71%), persistent vomiting (63.8%), mucosal bleed (39.1%) mostly as gum bleed and epistaxis. On examination 50.7% of them had hepatomegaly. Third space fluid accumulation was seen in 17% of the children manifesting as ascitis (6 children), pleural effusion (3 children) or both (3 children). Haematological investigations showed the mean haemoglobin 10±2.1g/dl , mean hematocrit value of 32.6±9 ,mean TLC of 7783±4188 /cu mm and the mean platelet count to be 64,130±52,580 /cu mm. Thrombocytopenia (platelet count of <1,00,000/cu mm) was present in 82.6%. All patients with mucosal bleeds had thrombocyopenia which was statistically significant (p<0.002) (Table 2). A hematocrit >20 at admission was found in 94.2% patients. Urea and creatinine were raised in 39.1%, dyselectrolytemia in the form of hyper/hypo natremia or kalemia was found in 65.2% (45/69). All the admitted children were started IV fluids with the mean duration of IV fluid administration 2.9±1.7 days and shock was treated with fluids. 55.07% of the patients required blood transfusion in the form of whole blood (6 children) and platelet rich plasma (32 children). The mean duration of admission was 4.5±2 days.

Table 2: Difference among dengue patients based on presence of thrombocytopenia (n = 69).

	Present (57)	Absent (12)	Chi-square	P value
Stay >5 days*	18	1	-	0.157
>2 blood units given*	10	0	-	0.191
Abdominal pain*	41	8	-	0.734
Fluid accumulation*	10	2	-	1
Persistent vomiting*	39	5	-	0.104
Mucosal bleed*	27	0	-	0.002
Lethargy*	45	5	-	0.014
Shock*	15	1	-	0.270
Hepatomegaly	29	6	0.003	0.956
Fever >7 days*	14	0	-	0.107

*Fisher's test

Table 3: Presence of shock and other clinical features (n = 69).

	Shock absent (53)	Shock present (16)	Chi-square	P value
Hepatomegaly	22	13	7.765 (1)	0.005
Lethargy	34	16	7.915 (1)	0.005
Abdominal pain	35	14	2.75	0.097
Persistent vomiting	31	13	2.76	0.097
Mucosal bleed	18	9	2.56	0.109
Fluid accumulation*	2	10	-	0.000
Stay >5 days*	9	10	-	0.001
Warning signs>3	12	16	30.501 (1)	0.000

*Fisher's test

Table 4: Stay at hospital and clinical feature (n = 69).

	Stay < 5 days	Stay > 5 days	Chi-square	P- value
Warning signs>3	13	6	16.007 (1)	0.000
>2 blood units given*	3	7	-	0.003
Shock*	6	10	-	0.001

Table 5: Clinical features and outcome (n = 59).

	Discharge (55)	Death (4)	Chi-square (df)	P value
Stay >5 days*	19	0	-	0.29
Warning signs>3*	23	4	-	0.04
Abdominal pain*	40	3	-	1
Fluid accumulation*	9	1	-	0.59
Persistent vomiting*	38	3	-	1
Mucosal bleed*	21	4	-	0.03
Lethargy*	42	4	-	0.57
Hepatomegaly	27	2	-	1
IVF duration >5 days*	6	0	-	1

*Fisher's test

Table 6: Course in hospital based on presence of warning signs.

	Warning signs <4	Warning signs >4	Chi-square (df)	P value
Stay >5 days*	13	6	4.78	0.03
Blood units >2*	7	3	-	0.19
IVF duration >5 days*	6	0	-	0.581

*Fisher's test

DISCUSSION

This retrospective study evaluated 69 children with dengue confirmed by by IgM elisa or NS1 positivity, however 72% were IgM positive against only 18% NS1 positive which reflects a higher detection rate by IgM Elisa in comparison to other Indian studies from 2010 and 2012 in which IgM detected only between 20-60% of the cases, IgM is an early marker and hence should be instituted for early detection of dengue. This study also had a male preponderence of 62% and mean age was 8 years which is similar to the other Indian studies.[7,8]

The most common presenting symptom was lethargy, abdominal pain and mucosal bleeds, fever was present universally in all patients. Only one prior study reported abdominal pain as common presenting complaint, thus there should be a high index of suspicion in children presenting with fever and abdominal pain especially during the outbreak of dengue.[7] Lethargy was present in 72% of children and was the only single parameter associated with poor outcome ($p < 0.005$).

There was a significant correlation ($p < 0.000$) between presence of more than three warning signs and prolonged hospital stay (>5 days) ($p < 0.000$) and progression to shock. This finding can hence be used as a predictor of poor outcome and prolonged hospital stay and also to closely monitor and aggressively manage children presenting with them (Table 3).

The most common bleeding manifestation reported in children in various studies over the years have been hematemesis, malena, epistaxis, petechiae and hematuria however in our study we would like to report an unprecedented increase in gum bleed as the most common mucosal bleed at presentation, which has never been reported so commonly before.[7-10] All patients with mucosal bleed had thrombocytopenia and it was statistically significant, however previous pediatric studies have denied any association between bleeding and thrombocytopenia in dengue (Table 4).[7,11]

On examinaton 50% children had hepatomegaly and 17% had third space fluid accumulation, both of these factors independently had significant correlation with shock ($p < 0.005$ and 0.000 respectively) (Table 5).

Acute liver failure has been reported to poor prognostic factor in dengue in several studies.[12-14] However hepatomegaly with liver failure in dengue have been reported only in adult population, some pediatric studies have reported hepatomegaly in dengue but did not have predictive value.[7,15-17]

Most of the pediatric studies of dengue have relied upon biochemical parameters like elevated liver enzymes, hyperglycemia, hypoglycemia, deranged PTT for predicting poor outcome in children, but the disadvantage being the time lapse between obtaining these results and assesing the severity of the disease.[7,18] In this study we have evaluated and analysed clinical features associated with shock and prolonged hospital stay, which can be assesed at the time of admission thereby limiting the delay in predicting severity of the disease which may not be apparent at the onset.

The mean duration of hospital stay was 4.2 days, children having more than 4 warning signs and who received more than 2 units whole blood had hospital stay longer than 5 days ($p < 0.003$) (Table 6).

Four children died, three were aged between 3-5 years and had refractory shock.

WHO revised criteria was used to classify and treat children and so far only three sudies from India have used this new classification in their studies.[7,19,20] The new classification helps differentiate between severe and non-severe dengue and also lays out the protocols for the management of the same, eliminating the occurrence of overlap in diagnosis.

Limitations of the study was the small numbers evaluated which were mostly children with dengue with warning signs (this hospital being a tertiary care centre all children requiring admission and monitoring were referred and admitted) and and unavailabilty of the dengue serotypes.

CONCLUSION

Children between 1-12 years were affected by dengue. Lethargy, abdominal pain and mucosal bleed were the commonest presenting complaints for sick children. Gum bleed was the most common presentation of mucosal bleed with a positive association with thrombocytopenia, this has not been prior reported to the best of our knowledge.

Fever was found in all the patients. Lethargy, presence of more than 3 warning signs at the time of presentation can be used as predictors of severe dengue.

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