International Journal of Contemporary Pediatrics
Kumawat M et al. Int J Contemp Pediatr. 2022 Aug;9(8):719-724
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20221853

Original Research Article

Clinical and laboratory profile in children with dengue viral infection

Mahesh Kumawat, Divya Dave*

Department of Pediatrics, G. M. E. R. S. Medical College and General Hospital, Vadodara, Gujarat, India

Received: 21 April 2022
Revised: 23 June 2022
Accepted: 26 June 2022

***Correspondence:**
Dr. Divya Dave,
E-mail: drdivya99@yahoo.com

ABSTRACT

Background: Dengue infection is the most prevalent arthropod borne viral illness in children associated with liver involvement. In recent studies from India and Thailand, dengue infection was the most important cause of acute hepatic failure in children contributing to 18.5% and 34.3% of the cases respectively.
Methods: Hospital based, prospective, observational study in which 120 dengue patients were included in the study. A detailed history and clinical features were recorded on pre-designed proforma. Investigations for dengue and liver function profile were done as per the standard diagnostic work up followed in our hospital.
Results: The result of study shows that out of 120 children, 73 (60.8%) have dengue with warning sign, 46 (38.3%) have dengue fever and 1 (0.8%) have severe dengue. Abdominal pain was most commonly seen in the age group of 8-12 year. 20 (16.7%) cases had hepatomegaly and 27% patients had icterus, 83.3% had thrombocytopenia. In our study liver enzyme and severity of dengue fever were significantly associated, although there was no significant association between age group and liver enzyme. The 17.5% cases of dengue viral infection had elevated prothrombin time, and 19.2% had hypo-proteinemia. There was no significant difference between male and female liver profile. Younger age group and complicated dengue viral infection had more abnormal liver profile.
Conclusions: Hepatic involvement is more common in severe dengue associated with significant rise of liver enzymes. Hepatomegaly is the most important clinical sign but alteration of liver profile can occur with or without hepatomegaly.

Keyword: Dengue, Liver profile, Hepatomegaly

INTRODUCTION

From 1973 to 1982 liver involvement in dengue infection was mild and manifest by raised liver enzymes. Since 1986 there have been cases of fulminant hepatitis with high mortality reported in pediatric cases in Malaysia and Thailand.[2] The 1996 epidemic in India was mainly due to dengue type 2 virus while the 2003 epidemic appears to be mainly due to dengue type 3 virus.[3] India is one of the seven identified countries in the South-East Asia region regularly reporting incidence of dengue fever/dengue hemorrhagic fever (DF/DHF) outbreaks and may soon transform into a major niche for dengue infection in the near future.[4] Involvement of younger age group and increase in the frequency of epidemics are indicators of higher incidence of infection. If untreated, mortality from complications of DF is as high as 20%, whereas if recognized early and managed properly, mortality is less than 1%.[5] According to world health organization (WHO) approximately 50-100 million infections take place yearly and mostly among children.[6] Dengue infection displays greater variance in its occurrences with high epidemic and non-epidemic variability. It can manifest as vast epidemics of disease along with seasonal variation. Dengue virus has multiple serotypes which are prevalent in India. Multiple epidemics of dengue had happened in India. Reports have come from all geographical regions of the country.[7] This study was undertaken to observe the clinical and laboratory profile of liver involvement in children with dengue viral infection.

METHODS

A hospital based observational study was conducted at department of pediatrics of GMERS medical college and government hospital, Vadodara, from March 2018 to December 2019. Approval of institutional ethical committee was taken before commencement of the study.

The study included children up to 18 years of age presenting with IgM positive and/or IgG positive and/or dengue NS1 antigen positive dengue fever. Informed consent from all the parents of the patients was taken before undergoing the study.

Patients with dengue like illness who did not have supporting lab evidence, children with pre-existing liver diseases, and parents' refusal for participation were excluded from the study.

A detailed history of clinical features including the symptoms of dengue fever was recorded on pre-designed performa.

Investigations like CBC, dengue NS1 antigen, dengue IgM and dengue IgG and serum bilirubin, SGPT, SGOT, ALP, prothrombin time, serum protein, serum albumin, USG abdomen were done as per the standard diagnostic work up followed in our hospital. The normal values were considered as below: haematocrit 36-40%, serum bilirubin 0.3-1 mg/dl, SGOT<35 U/l, SGPT<35 U/l, ALP 100-320 U/l, prothrombin time <14 seconds, serum total protein 6-8 g/dl, serum albumin 3.6-5.2 g/dl. Statistical analysis was done using SPSS-24 software.

Sample size

$n=\frac{4\times p\times q}{L^2}$,

where,

n=required sample size,

p=proportion or prevalence of interest,

q=100-p,

L=allowable error.

An anticipated p value was taken as 50%, as per WHO practical manual on sample size determination in health studies by Lwanga and Lemeshow. Absolute allowable error of 10 percent was taken.

Then, sample size would be,

$N=\frac{4\times 50\times 50}{100}=100.$

Considering non-response rate of 20 % of sample size, total sample size comes out to be 120 for the study.

RESULTS

Total 120 children were enrolled in the study. There was a slight male predominance where male constituted 65 (54.2%) of the study group, while female was 55 (45.8%). That gave a male to female ratio of 1.18:1. The most common age group of presentation of dengue infection in children was 8-12 years. Mean age of children affected with dengue viral infection was 8.5 years and the gender distribution was not statistically significant.

Table 1: Correlation between age and type of dengue.

Age group (years)	Dengue type			Total
	Dengue fever	Dengue fever with warning	Severe dengue	
	N (%)	N (%)	N (%)	
0-4	8 (17.4)	14 (19.2)	0 (0)	22
4-8	14 (30.4)	20 (27.4)	1 (100)	35
8-12	12 (26.1)	30 (41.1)	0 (0)	42
12-16	12 (26.1)	9 (12.3)	0 (0)	21
Total	46 (100)	73 (100)	1 (100)	120

Clinically, 46 (38.3%) patients had dengue fever 73 (60.8%) had dengue with warning sign, and only1 (0.8%) had severe dengue. Dengue fever was the commonest presentation in 4-8 years group (14 patient-30.4%) while dengue with warning signs was the commonest presentation in 8-12-year-old (30 patients-41.1%). Less cases of severe dengue are probably because of public awareness (Table 1).

Table 2: Clinical features of patients with dengue.

Clinical features	No. of cases (n=120)
	N (%)
Fever	120 (100)
Vomiting	120 (100)
Abdominal pain	87 (72.5).
Jaundice	27 (22.5)
Pallor	23 (19.2)
Hepatomegaly	20 (16.7)
Thrombocytopenia	100 (83)
Hyperbilirubinemia	52 (43)
Elevated SGPT	57 (47.5)
Raised prothrombin time	21 (17.5)
Hypoprotenemia	23 (19.2)
Hypoalbumenemia	42 (35)

All the children in the study group presented with vomiting (100%) and fever (100%) and abdominal pain was presented in 87 (72.5%). None of the children presented with retro orbital pain (Table 2).

In our study, out of 120 patients, 27 (22.5%) cases had icterus. The most commonly affected age group is 8-12 years (33.3%). In our study 1 patient of severe dengue,

had jaundice and out of 73 cases of dengue with warning signs, 15 patients (20.5%) had jaundice and 46 cases of dengue fever 11 patients (23.9%) had jaundice which is statistically insignificant (p=0.16) (Table 3).

Table 3: Correlation between type of dengue and icterus.

Icterus	Dengue fever	Dengue fever with warning	Severe dengue	Total
	N (%)	N (%)	N (%)	
No	35 (76.1)	58 (79.5)	0 (0)	93
Yes	11 (23.9)	15 (20.5)	1 (100)	27
Total	46 (100)	73 (100)	1 (100)	120

Table 4: Correlation between type of dengue and hepatomegaly.

Hepato-megaly	Dengue fever	Dengue fever with warning	Severe dengue	Total
	N (%)	N (%)	N (%)	
Present	0 (0.0)	20 (27.4)	0 (0.0)	20
Absent	46 (100)	53(72.6)	1 (100)	100
Total	46 (100)	73 (100)	1 (100)	120

In our study, out of 120 patients 20 (16.7%) cases had hepatomegaly. Out of 20 patients with hepatomegaly, the most commonly affected age group was 8-12 years, 11 (26.2%) cases.

Table 5: Correlation between type of dengue and platelet count.

Dengue type	Normal (%)	Thrombo cytopenia (%)	Total
	N (%)	N (%)	
Dengue fever	15 (33)	31 (67)	46
Dengue fever with warning	5 (7)	68 (93)	73
Severe	0 (0)	1 (100)	1
Total	20 (17)	100 (83)	120

In our study out of 120 cases 100 (83.3%) had thrombo-cytopenia. Out of 100 patients with thrombocytopenia, in 42 cases there was borderline thrombocytopenia and 54 had moderate thrombocytopenia and 4 patients had severe thrombocytopenia (<25000). Out of 100 patients with thrombocytopenia, most patients were seen in 8-12 years age group, 35 (35%) (Table 5).

The 52 (43%) cases had hyperbilirubinemia, (Table 6) the most common age group affected is 8-12 years i.e., 22 (42.3%). However, this was less than clinical jaundice. Also, it did not statistically correlate with the occurrence of complications.

Table 6: Correlation between complications and S. bilirubin levels.

S. bilirubin	Complication		Total
	No	Yes	
	N (%)	N (%)	N (%)
Hyper bilirubinemia	18 (34.7)	34 (65.3)	52 (100)
Normal bilirubin	8 (11.7)	60 (88.3)	68 (100)
Total	26	94	120

Table 7: Correlation between liver enzyme and dengue serology.

Liver enzyme	Dengue NS1 antigen +ve	IGM +ve	IGG +ve	Total
	N (%)	N (%)	N (%)	
Elevated SGOT	80 (73.3)	28 (25.6)	1 (0.9)	109
Elevated SGPT	42 (73.6)	14 (24.6)	1 (1.7)	57
Elevated ALP	1 (50)	1 (50)	0	2
Total	123	43	2	168

In our study 91 **(**81.67%) cases had dengue NS1 antigen positive. The 85.7% of cases with NS1 antigen positive fall within 12-16 age group. This suggests that most patients presented in the first week of illness. In our study, out of 120, 30(25%) cases were IgM positive. The 12 (34.3%) cases with IgM positive fall within 4-8 age group. There was 1 patient with IgG positive. 10 patients had both NS1 antigen and IgM positive. These were the patients who presented on 7th or 8th day of the illness (Table 7). Out of 109 cases with raised SGOT, 80 (73.3%) cases had dengue NS 1 antigen positive, 28 (25.6 %) cases had dengue IgM positive and 1(0.9%) IgG positive. Out of 57 cases with raised SGPT, 42 (73.6%) cases had dengue NS 1 antigen positive, 14 (24.6%) cases had dengue IgM positive and 1(1.7%) IgG positive. There was overlap of patients who had both SGOT and SGPT elevated. Out of 2 cases with raised ALP 1 (50%) was NS1 antigen positive and 1 (50%) was IgM positive. This is suggestive that serologically confirmed with NS1 antigen positive cases have more abnormal liver profile.

In our study 21 (17.5%) cases of dengue viral infection had elevated prothrombin time. The raised prothrombin time was most commonly seen in age group 4-8 years (Table 8). Out of 21 cases of raised prothrombin time dengue fever consists of 6 (28.6%), 14 (66.7%) cases of dengue Fever with warning and 1 (4.8%) of severe dengue.

In our study 26 (21.7%) cases had complication that was more common in age group of less than of 4 years (31.8%). In our study, complication of dengue was more

common in dengue with warning sign (35.6%) (Table 9). In our study 26 (21.7%) cases have complication that is more common in age group of less than of 4 years (31.8%).

Table 8: Correlation between dengue type and prothrombin time.

Dengue type	Raised prothrombin time	Normal prothrombin time	Total
	N (%)	N (%)	
Dengue fever	6 (28.6)	40 (40.4)	46
Dengue fever with warning	14 (66.7)	59 (59.6)	73
Severe dengue	1 (4.8)	0 (0)	1
Total	21 (100)	99 (100)	120

Table 9: Correlation between age and complications of dengue.

Age group (years)	Complication, n (%)		Total
	No	Yes	
	N (%)	N (%)	
0-4	15 (16.0)	7 (26.9)	22
4-8	32 (34)	3 (11.5)	35
8-12	31 (33)	11 (42.3)	42
12-16	16 (17)	5 (19.2)	21
Total	94 (100)	26 (100)	120

DISCUSSION

Abdominal pain was most commonly seen in the age group of 8-12 years. In a study done in Andhra Pradesh, conducted on 100 children of dengue viral infection, abdominal pain was seen in 50% of cases.[8] In a study by WHO in Delhi, abdominal pain was seen in 40-50% of cases.[9] In our study 23 (19.2%) cases have pallor. The most commonly affected age group is less than 4 years (39.1%). Severe dengue is most commonly seen in children less than 4 years, which may cause internal bleeding, therefore there is an increased incidence of pallor in these patients (Table 2).

Patients with jaundice have poor prognosis and are at a greater risk of developing severe dengue. In other studies, number of cases of severe dengue were high, because of less public awareness and delayed intervention. In a study conducted at Nagpur out of 50 cases of severe dengue, 24% had jaundice (Table 3).[10]

In a study done at Indonesia hepatomegaly was seen in 47.2% of cases.[11] In our study out of 20 cases of hepatomegaly, all 20 patients had dengue with warning signs which is statistically significant (p=0.01) (Table 4). Patients presenting with hepatomegaly indicate increased severity of dengue viral infection.

Out of 46 cases of dengue fever, 31 (67%) had thrombocytopenia, and amongst case with dengue with warning signs, 68 (93%) had thrombocytopenia (Table 3). There was only one case with severe dengue and had thrombocytopenia. Therefore, decreased platelet count predicts the severity of dengue viral infection. In the cell count analysis majority of cases associated with leucopoenia which is most common in age group of 8-12 years. In a study at New Delhi, leucopoenia was seen in5.8% of cases and leucocytosis was seen in 26.5% of cases (Table 5).[12]

In a study by Itha et al hyperbilirubinemia was seen in 30% of the cases.[13] In another study hyperbilirubinemia was seen in 13.4% of cases.[14] Out of 52 cases of hyperbilirubinemia 34 (65.3%) had complication and 18 (34.7%) no complication. this is suggesting that hyperbilirubinemia predicts the severity of dengue viral infection. Out of 52 cases of hyperbilirubinemia, dengue fever consists of 3 (5.8%), 48 (92.3%) of dengue with warning sign and 1 (1.9%) of severe dengue. This also suggests that hyperbilirubinemia predicts the severity of dengue viral infection. In a study done at Assam 1 out of 3 patients of severe dengue 33.3% had hyperbilirubinemia.[1] In a study Nagpur out of 50 cases of severe dengue, 24% had hyperbilirubinemia (Table 6).[10]

In a study at Karnataka, India 80.7% of cases had dengue NS1 antigen positive, 26.3% of cases had dengue IgM positive (Table 7).[4]

In a study conducted at Bangalore, Karnataka, India 34% of patients had raised SGPT levels, 36% had raised SGOT and 42% had raised ALP.[15] In a similar study which included 110 children aged between 2 months to 14 years it was observed that 69.4% of the patients had raised SGPT levels, 88% had raised SGOT levels.[13,16] In our study out of 120 children 102(85%) had raised SGOT levels, and 2 patients (1.7%) had elevated ALP levels. The elevated level of SGOT most commonly found in age group of 8-12 years. Previous study shows that most affected age group was 1-6 years.[15]

In a study done at Nagpur suggests that amongst patients with elevated prothrombin time, dengue fever consists of (1.6%), (29.92%) cases of dengue fever with warning and (46%) of severe dengue (Table 8).[4]

Another study done at Chennai, shows that children less than 5 years were most commonly affected by severe dengue (70%) with infant forming the largest group (Table 9).[18]

In our study hypo-proteinemia was seen in 19.2% of 120 patients. The most common age group affected is 0-4 years (27.3%). In our study hypo-proteinemia in severe dengue is 100%, dengue with warning signs is 26% and

dengue fever is 6.5% which is suggestive that liver function is more abnormal in severe dengue. In our study 35% of the patients had hypoalbuminemia. The most commonly affected age group is 12-16 years. In our study hypoalbuminemia in severe dengue is 100%, and is 39.7% in dengue with warning signs and 26.1% in patients with dengue fever which is suggestive that liver function is more abnormal in severe dengue. Average hospital stay was 4.8 days (Maximum 11 days). Patients with dengue fever with warning signs and severe dengue required a longer hospital stay.

Out of 52 cases of hyper-bilirubinemia, dengue fever consists of 3 (5.8%), 48 (92.3%) of dengue with warning sign and 1 (1.9%) of severe dengue. This also suggests that hyper billirubinemia predicts the severity of dengue viral infection. In our study 91 (81.67%) cases had dengue NS1 antigen positive. The 85.7% of cases with NS1 antigen positive fall within 12-16 age group. This suggests that most patients presented in the first week of illness.

In our study out of 102 cases of elevated SGOT, 38 (37.2%) have dengue fever, 63 (61.7%) cases had dengue with warning sign and one (0.9%) have severe dengue. In our study out of 53 cases of elevated SGPT, 10 (18.9%) have dengue fever, 42 (79.2%) cases had dengue with warning sign and one has (1.9%) severe dengue. In our study out of 2 cases of elevated ALP, 1 (50%) has dengue fever, 1 (50%) case had dengue with warning sign and none have severe dengue.

Limitations

Small sample size was the limitation of this study. Repetition of liver function tests was not done, there was no follow up of cases included in the study.

CONCLUSION

Hepatic involvement is more common in severe dengue. Significant rise of liver enzymes helps in recognition of severe form of dengue infection. Hepatomegaly is the most important clinical sign but alteration of liver profile can occur with or without hepatomegaly. High suspicion of dengue should be borne in patients presenting with thrombocytopenia, lymphocytosis and haemoconcentration. The most sensitive indicator being PCV which helps in monitoring the progression of disease from dengue with warning signs to severe dengue. SGOT was elevated more than SGPT and ALP.

Recommendations

Dengue fever should be recognized and managed appropriately to avoid unnecessary complication and mortality**.** Awareness of the doctor should be raised about the clinical presentation, careful examination. Vitals should be monitored in all children of dengue viral infection to prevent complication and mortality. Public awareness should be raised about prevention and control of vector.

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

REFERENCES

1. Das M. Liver Profile in Children with Dengue Viral Infection. J Dental Med Sci. 2018;17(8):47-9.
2. Lum LC, Lam SK, George R, Devi S. Fulminant hepatitis in dengue infection. Southeast Asian J Trop Med Public Health. 1993;24(3):467-71.
3. Chaturvedi UC, Shrivastava R. Dengue Hemorrhagic Fever: A Global Challenge. Indian J Med Microbial. 2004;22:5-6.
4. Tejaswi CN, Patil SS, Shekharappa KR. Study of clinical manifestations of dengue cases in a tertiary care hospital, Bangalore, Karnataka. Int J Med Sci Public Health. 2016;5:2503-7.
5. Narayanan M, Aravind MA, Thilothammal N. Dengue fever epidemic in Chennai--a study of clinical profile and outcome. Indian Pediatr. 2002;39(11):1027-33.
6. Ayesha F, Zahra F, Samina F. Dengue Fever: Hepatic Involvement in Children Up To 12 Years Of Age Professional Med J. 2017;24(11):1605-9.
7. Goyal V, Ahmed A. Spectrum of hepatic involvement in patients with dengue infection. Int J Med Sci Educ. 2018;5(1):2-6.
8. Manohar B, Madhavi N. Clinical Profile and Liver Function in Dengue. new Indian J Pediatr. 2015;4(1);15-21.
9. Halstead SB. Pathophysiology and pathogenesis of dengue hemorrhagic fever. in. thongchareon p, ed monograph on dengue/dengue hemorrhagic fever. New Delhi, World Health Organization, Regional Office for South- East Asia. 1993;80-103.
10. Bokade CM, Chauhan U, Kamat P. Study of Hepatic Dysfunction in Dengue Fever And It's Predictor of Outcome. Int J Recent Sci Res. 2016;7(9):13360-63.
11. Setyoboedi B, Angelika D, Zuraida E, Darmowandowo W, Arief S, Setiono PB. Liver Involvement In Children With Dengue Infection. Folia Medica Indonesiana. 2011;47(4):215-8.
12. Faridi MM, Aggarwal A, Kumar M, Sarafrazul A. Clinical and biochemical profile of dengue haemorrhagic fever in children in Delhi. Trop Doct. 2008;38(1):28-30.
13. Itha S, Kashyap R, Krishnani N, Saraswat VA, Choudhuri G, Aggarwal R. Profile of liver involvement in dengue virus infection. Natl Med J India. 2005;18(3):127-30.
14. Wong M, Shen E. The Utility of liver function tests in Dengue. Ann Acad Med. 2008;37(1):82-3.
15. Khandelwal R, Khandelwal LM, Susheela C. Effect of dengue fever on serum aminotransferases in children. Int J Contemp Pediatr. 2016;3:324-7.

16. Jagadishkumar K, Jain P, Manjunath VG, Umesh L. Hepatic involvement in dengue Fever in children. Iranian J pediatr. 2012;22(2):231-6.
17. Tirumani HB, Bejugam VK, Naseem A, Hussain A, Nizarlalani. Study of hepatic involvement in children with dengue infection. Int J Contemp Pediatr. 2017;4:2012-4.
18. Kamath SR, Ranjit S. Clinical features, complications and atypical manifestations of children with severe forms of dengue hemorrhagic fever in South India. Indian J Pediatr. 2006;73(10):889-95.
19. WHO. Fact sheet: Sample size determination in health studies: A practical manual, 1991. Available at: https://apps.who.int/iris/handle/10665/40062. Accessed on 1 April 2022.

Cite this article as: Kumawat M, Dave D. Clinical and laboratory profile in children with dengue viral infection. Int J Contemp Pediatr 2022;9:719-24.