e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(2); 1719-1722

Original Research Article

A Prospective Observational Study on Liver Dysfunction in Pediatric Dengue Infection

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Received: 25-12-2023 / Revised: 23-01-2024 / Accepted: 22-02-2024
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Conflict of interest: Nil

Abstract:
Liver involvement is quite common in dengue fever and can lead to fatal complication like acute liver failure (ALF). No single method can accurately identify patients at risk for disease progression and poor outcome. We aimed to determine the relationship between liver function tests (LFTs) and outcome in paediatric dengue infection.

Methods: We conducted a prospective observational study of hospitalized children (1–12 years) with dengue infection (June 2020–Dec 2021). Serial monitoring of LFTs was done in confirmed dengue cases. Patients were classified into non-severe (NSD) and severe dengue (SD).

Results: 90 children (55 boys) with mean age of 7.21 ± 3.74 years, were analysed (NSD, n = 59(65.6%) SD, n = 31(34.4%)). Deranged LFTs were seen in all study population which were more in severe disease group (>1000). Aminotransferase levels were more deranged than bilirubin level. AST level were more deranged than ALT levels and in 1st week of illness. Serum bilirubin was raised in 7(7.8%) of study population. All patients were in severe disease group which were 7(22.6%) population of severe disease group which was statistically significant ($p<0.001$). Hypoalbuminemia and hypoproteinemia were more in severe disease group. Total 54(60%) cases had low albumin level in which 23(74.2%) were in severe disease group and 31(52.5%) cases were in nonsevere disease group which was not statistically significant ($p>0.005$). Death occurs in 8 (25.8%) cases which all were belongs to severe disease group.

Conclusions: Liver involvement was seen in all cases of dengue fever. Severe hepatitis in dengue is associated with poor outcome.

Keywords: Children, Dengue, Hepatitis, Liver Function Tests.

Introduction

Dengue is one of most rapidly emerging infection of tropical and subtropical regions affecting rural area more than urban area. India contributed to 34% of global dengue infection [1]. Disease symptoms range from those of a mild febrile illness to a countless of symptoms, including frank dengue fever, dengue hemorrhagic fever and dengue shock syndrome [2]. Any organ system can be involved but liver involvement is well recognized as a common complication [3].

The Liver injury can range from mild asymptomatic transaminase elevation to fatal acute liver failure which is more common in children, females and certain ethnic groups. Liver involvement tends to be more severe in children with previous dengue infection [3]. The frequency of hepatic dysfunction is more in dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF). Aminotransferase levels are useful in predicting the occurrence of hepatic dysfunction and spontaneous bleeding, hence early recognition and prompt initiation of appropriate supportive treatment can decrease the morbidity and mortality [4].

There is ample literature on liver involvement in dengue illness in adults however the pattern of liver dysfunction and changes in LFT in children with dengue has not been extensively studied.

Methods

This was a prospective observational study conducted on 90 confirmed dengue patients aged between 1 to 12 years admitted in Pediatric Medicine Department of SMS Medical College and Hospital during June 2020–Dec 2021. The present study was conducted after obtaining approval from the institutional ethics committee and in accordance with ICH-GCP guidelines. Patients below 1 year and more than 12 years, diagnosed with fever from other causes, given NSAIDs for the treatment of dengue prior to an admission, those with pre-

existing liver disease and in which a written consent was not obtained were excluded.

The patients were categorized based on the modified WHO classification of 2009 into dengue with or without the warning signs and severe dengue. The patients enrolled underwent a complete medical workup at presentation that incorporated a detailed history and examination including a general and systemic examination. In emergency room, resident doctors were instructed to obtain blood samples (routine and LFTs), chest radiograph and ultrasonography at admission.

Confirmation of dengue will be done by detection of IgM antibodies specific to dengue (anti-DEN IgM capture enzyme-linked immunosorbent assay, ELISA using CDK KIT), demonstration of protein of dengue (dengue NS1) and detection of dengue genomic sequences by polymerase chain reaction in the plasma obtained at the time of admission. A repeat dengue IgM test was performed after 1 week if the initial test was negative. Dengue confirmed case will be defined by the presence of positive DENV IgM or Dengue NS1or detection of DENV RNA by polymerase chain reaction in plasma, provided that the clinical picture was consistent with dengue, and no alternative diagnosis was established.

Estimated minimal sample size required for this study was 100 cases of Dengue infection. Statistical methods were carried out through the SPSS for Windows (version 16.0). Statistical methods employed for data analysis are Descriptive statistics, Cross tabs, Chi-Square test for categorical outcomes and t-test for comparison of means. Comparison of multiple means/non parametric data was done using One Way-ANOVA.

Results

There were total 90 study subjects, 55(61.1%) and 35(38.9%) were males and females respectively. Out of which 24(26.7%) cases were below 5 year of age, in which 17 were from nonsevere dengue and 7 were from severe dengue. 36(40%) patients were in the age between 5-10 year in which 23 were from nonsevere dengue and 13 were from severe dengue. 30 (33.3%) cases were above age 10 year in which 19 were from nonsevere disease and 11 were from severe disease. Mean age group of the study subject was 7.21 ± 3.74years so it was seen that majority of patients were in the age group 5 to 10 years. Majority of cases were non-severe 59(65.6%).

Derangement of LFTs was seen in both severe and non-severe disease group which was more in severe disease group. Hypoalbuminemia and hypoproteinemia were more in severe disease group. Total 54(60%) cases had low albumin level in which 23(74.2%) were in severe disease group and 31(52.5%) cases were in nonsevere disease group. Raised bilirubin level was found in 7 cases, all cases were in severe disease group. SGOT level increase in all dengue cases in which maximum increase was found on day 2 of observation which was mostly day 6th or7th of disease severity. SGPT increases in both severe and nonsevere disease, more increase was present in severe disease group, more increase in day 2 of observation. GGT deranged both in severe and non-severe disease but more in severe disease group.Serum bilirubin, PT/INR comparisons were more increased in severe group.

Table 1: Abnormal liver function test in relation to disease severity among study subjects

Abnormal liver function test	Non severe disease (N=59)		Severe disease (N=31)		Total (N=90)		p value
	N	%	N	%	N	%	
Raised SGOT	59	100	31	100	90	100	1.000
Raised SGPT	59	100	31	100	90	100	1.000
Raised ALP	5	8.5	8	25.8	13	14.4	0.054
Raised GGT	59	100	31	100	90	100	1.000
Low albumin	31	52.5	23	74.2	54	60	0.077
Low total protein	46	78	29	93.5	75	83.3	0.112
Raised bilirubin	0	0	7	22.6	7	7.8	<0.001(S)

Table 2: Time trend of SGOT (U/L) in relation to disease severity

Time	Non severe disease(N=59)	Severe disease(N=31)	p value
Day 1	125.31 ± 104.46	600.63 ± 885.99	<0.001 (S)
Day 2	138.92 ± 123.14	1693.78 ± 3463.94	0.001(S)
Day 3	142.51 ± 126.94	1025.35 ± 1748.19	<0.001 (S)
Day 4	137.42 ± 127.55	893.55 ± 1348.7	<0.001 (S)

Table 3: Time trend of SGPT (U/L) in relation to disease severity

Time	Non severe disease(N=59)	Severe disease(N=31)	p value
Day 1	112.66 ± 128.12	418.74 ± 545.97	<0.001 (S)
Day 2	109.17 ± 100.06	846.42 ± 1379.25	<0.001 (S)
Day 3	144.17 ± 147.71	622 ± 805.16	<0.001 (S)
Day 4	124.69 ± 106.33	665.06 ± 1149.03	0.001(S)

Table4 : Comparison of INR value in relation to disease severity

	Non severe disease(N=59)	Severe disease(N=31)	p value
INR	1.19 ± 0.16	1.39 ± 0.31	<0.001 (S)

Table 5: Outcome of Dengue disease

Outcome	Non severe disease		Severe disease		Total	
	N	%	N	%	N	%
Discharged	59	100	23	74.2	82	91.1
Death	0	0	8	25.8	8	8.9
Total	59	100	31	100	90	100
Fisher Exact Test - p<0.001 (S)						

Discussion

Dengue is an arboviral infection transmitted by the bite of an insect vector, the Aedes mosquito. Any organ system can be involved; liver involvement is well recognized as a common complication. There are a series of hematologic and biochemical changes which occur during the course of the illness. Recently, most reports have demonstrated elevated hepatic transaminases or aminotransferases [aspartate transaminase (AST), alanine transaminase (ALT)] levels in dengue infection, suggesting that the liver is one of the main targets for the dengue virus. In our study, deranged LFTs were seen in all study population. Aminotransferase levels were more deranged than bilirubin level. AST level were more deranged than ALT levels and in 1st week of illness. Serum bilirubin was raised in 7(7.8%) patients of study population. All were in severe disease group. Jayanta Samanta et al[5] conducted a similar study .Clinical jaundice was detected in 1.7%-17% in various series and hyperbilirubinemia had been found to be as high as 48%. Similar study conducted by Samitha Fernando et al [6)] shows that aspartate transaminase (AST), alanine transaminase (ALT) and gamma glutamyl transferase (GGT) levels were elevated in patients with dengue infection throughout the illness. The highest AST levels were seen on day 6 of illness and both AST and GGT levels were significantly higher in patients with severe dengue (SD), when compared to those with non-severe dengue (NSD) on day 5 and 6 of illness. Three patients with SD had AST and ALT values of >1000/IU in the absence of any fluid leakage or a rise in the haematocrit (≥20 %). The peak of the AST levels and the lowest serum albumin levels were seen 24 h before the maximum fluid leakage and 24 h after the peak in viraemia.

In a large study from Brazil, out of 1585 dengue cases, elevation in AST and ALT were seen in 63.4% and 45% of patients respectively, with 3.8% of cases having 10 fold increase in transaminase levels[1]. Similar increase of more than 10 fold rise in the liver enzymes was recorded by other authors also in adults and it varies between 1.8%-11.2%.[7,8,1]

In our study, out of 90 cases 82(91.1%) were discharged successfully in which 59(100%) were belongs to non-severe disease group and 23(74.2%) cases belongs to severe disease group. Death occurs in 8 (25.8%) cases which all were belongs to severe disease group. Anil Sachdev [9] et al conduct a study during the study period of 42 months, 172 patients with dengue fever were admitted to PICU. A total of 78 (45.3%) patients with severe dengue fever were included and analysed. There were 20 (25.6%) deaths.

Limitations of the study: 1) the study sample is small, may be statistically less accurate compared to studies with a larger population 2) The patients were selected from a tertiary care centre which usually tends to see a clustering of more severe cases as the less severe ones may be treated on out-patient basis. Hence the results of the study may not be an accurate representation of the entire population.

Conclusion

It was observed that LFTs monitoring done during acute illness was a predictor of mortality in children with Dengue illness. Higher level of derangement in LFTs like bilirubin PT/INR in children with dengue illness associate with higher rate of mortality. The application of LFT monitoring is quite simple because it utilizes laboratory parameters which are routinely used in clinical practice and available at all levels of patient

care Centre and therefore can be used by clinicians to identify which patients are at high risk for developing severe disease and thus can be used in prognostication.

Competing interests: The authors declare no competing interests.

Authors' contributions: All the authors have read and agreed to the final manuscript.

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