Original Article

Spectrum of Hepatic Involvement in Children with Dengue Infection

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Abstract

Background: Nowadays, dengue infection, a viral disease spread by arthropods is the most prevalent and significant for humans. Though not hepatotropic, the dengue virus often causes liver damage. Liver dysfunction in dengue cases may result from direct viral impact on liver cells or uncontrolled immune response by the host.

Objective: To estimate the range of hepatic involvement in dengue infection in children.

Methods: This prospective observational study was conducted at the Paediatric Indoor Department of Combined Military Hospital, Dhaka, Bangladesh from April 2023 to July 2024. A total of 70 dengue NS1 or dengue antibody IgM-positive children aged 2-12 years were enrolled as the study subjects using a purposive sampling technique. For data analysis, SPSS v26 was applied.

Results: Among the participants while analyzing the hepatic involvement it was observed that 56% had hepatomegaly, 49% had ascites and 26% had serum bilirubin levels above 1 mg/dl. Elevated aspartate aminotransferase (AST) levels were found in 91%, elevated alanine aminotransferase (ALT) levels in 81%, elevated alkaline phosphatase (ALP) levels in 70% and 36% had a prolonged international normalized ratio (INR) greater than 1.5.

Conclusion: In children with dengue infection, the most common hepatic involvements are elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT) alkaline phosphatase (ALP) levels and hepatomegaly. Additionally, ascites, hyperbilirubinemia and prolonged INR may also be observed.

Keywords: Dengue fever, Hepatic involvement, Children, NS1, IgM-positive, Hepatomegaly, INR.

Introduction

In Southeast Asia, dengue infection, a mosquito-borne viral hemorrhagic fever, continues to pose a significant public health challenge.[1] Despite not being hepatotropic, dengue frequently presents with hepatomegaly and elevated serum aminotransferase levels.[1] According to the 2009 revised criteria by the World Health Organization (WHO), dengue infections are classified into three categories: severe dengue, dengue fever (DF) with warning signs and DF without warning signs.[2] Hepatic dysfunction in dengue cases arises either from direct viral effects on hepatocytes or from an excessively vigorous immune response by the host.[3] Hepatic dysfunction is a recognized feature of dengue infection, even though the liver is not a primary target organ.[4] Liver involvement may manifest as acute hepatitis, right hypochondriac pain, hepatomegaly, jaundice and elevated aminotransferase levels.[5,6] Hepatic involvement in dengue is marked by hepatomegaly, which is the most prevalent feature among children, with occurrence rates spanning 12% to 80%.[7] Clinical jaundice has been reported in 0.95% to 60% of pediatric cases in various studies.[8] Hyperbilirubinemia has also been observed, though more frequently in adult populations.[9,10] Elevated liver transaminase levels are commonly noted during dengue infections in children. Transaminase levels generally rise during the first week of infection but tend to return to normal within three weeks.[11] In various studies, the average AST levels in children ranged from 78 U/L[11] to 415 U/L[12] while the average ALT levels varied from 52 U/L11 to 253 U/L.[12] Transaminase levels are more than ten times higher in severe dengue cases compared to those with dengue fever (DF) with or without warning signs.[12] Studies consistently show that the risk of liver injury increases with the severity of DF.[11,12] A large pediatric study of 372 children reported that 38.7% had liver injuries; however, only 4.8% had ALT/AST levels exceeding 1000 IU/L, as defined by WHO guidelines for severe dengue.[12] Incidence rates of pediatric dengue-associated acute liver failure (ALF) were recorded at 18.5% and 34.3% in some Asian studies.[13,14]

Materials and Methods

This was a prospective observational study that was conducted in the Department of Combined Military Hospital, Dhaka, Bangladesh from April 2023 to July 2024. A total of 70 children who tested positive for dengue NS1 or dengue antibody IgM were enrolled in the study using a purposive sampling technique. The study received approval from the hospital's ethical committee. Written consent was obtained from all participants before data collection. The inclusion criteria involved all suspected dengue infections as per the

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revised WHO guidelines of 2009, children aged between 2 to 12 years and those who were NS1 positive or serologically confirmed (immunoglobulin M [IgM] positive) by dengue IgM capture enzyme-linked immunosorbent assay (ELISA). The exclusion criteria included children with IgM-negative dengue-like illness, NS1 negative and those aged less than 2 years and more than 12 years, children with pre-existing liver diseases, other concomitant infections affecting the liver such as malaria, typhoid, hepatitis A and B, and patients who refused to be included in the study. All cases were subjected to the following investigations: Dengue NS1(if reported within 72 hours of onset of symptoms), Dengue IgM capture ELISA (if reported after 72 hours of onset of symptoms), hemoglobin (Hb), total count, differential leukocyte count, platelet count (PLC), hematocrit (HCT), peripheral blood smear, serum bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), serum albumin, serum globulin, total proteins, prothrombin time (PT), Activated partial thromboplastin time (APTT), ultrasound abdomen and thorax. The necessary demographic and clinical information of the participants was recorded. Data were analyzed using SPSS v26.

Results

The demographic data of this study indicated that 54% of the participants were male, while 46% were female. The mean age was 7.17 years with a standard deviation of ±0.62 years. As the symptom, fever was found in all the participants. Besides, in more than one-fourth of the participants, body aches (68%), petechial spots (36%), maculopapular rashes (31%) and mucosal bleeds (27%) were observed. Among this study population 37% were diagnosed with dengue fever, 50% with dengue hemorrhagic fever and 13% with dengue shock syndrome. Among the 70 participants, hepatic involvement manifested in various forms. Hepatomegaly was observed in 56% of the cases while ascites occurred in 49%. Serum bilirubin levels exceeded 1 mg/dl in 26% of the participants. Elevated levels of aspartate aminotransferase (AST) were found in 91% of the individuals and 81% showed elevated alanine amino- transferase (ALT) levels. Additionally, 70% had elevated alkaline phosphatase (ALP) levels and 36% exhibited a prolonged international normalized ratio (INR) greater than 1.5.

Table-I: Demographic data of the patients

Characteristics	n	%
Male	38	54%
Female	32	46%
Mean age (years)	7.17±0.62	

Table-II: Status of dengue infections

Status	n	%
Dengue fever (DF)	26	37%
Dengue hemorrhagic fever (DHF)	35	50%
Dengue shock syndrome (DSS)	9	13%
Total	70	100%

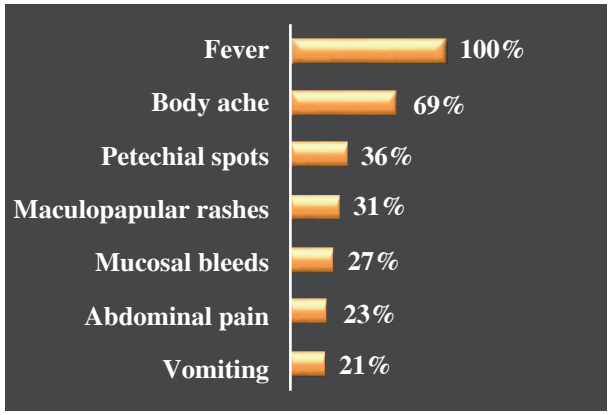

Figure-1: Symptom distribution

Table-III: Hepatic involvement

Involvement	Groups							
	DF (n=26)		DHF (n=35)		DSS (n=9)		Total (n=70)	
Hepatomegaly	2	8%	29	83%	8	89%	39	56%
Ascites	1	4%	24	69%	9	100%	34	49%
S. bilirubin >1mg/dl	1	4%	9	26%	8	89%	18	26%
Elevated AST	22	85%	33	94%	9	100%	64	91%
Elevated ALT	17	65%	31	89%	9	100%	57	81%
Elevated ALP	12	46%	29	83%	8	89%	49	70%
Prolonged INR >1.5	1	4%	16	46%	8	89%	25	36%

AST: Aspartate aminotransferase, ALT: alanine aminotransferase, ALP: Alkaline phosphatase, INR: International normalized ratio

Discussion

Dengue virus infection remains a significant health problem in many parts of the world, with the greatest burden borne by countries in the Asia-Pacific region.[15] Liver involvement in dengue infection is a recognized characteristic, with effects that can range from mild to moderate increases in serum transaminases to severe fulminant liver failure.[16] The main objective of this current study was to estimate the range of hepatic involvement in dengue infection in children. The demographic information from this study showed that 54% of the participants were male and 46% were female. The average age was 7.17 years, with a standard deviation of ±0.62 years. Roy et al[13] also took children of similar demographic status. In this study, fever was observed in all participants. Additionally, over one-fourth of the participants exhibited symptoms such as body aches, petechial spots, maculopapular rashes and mucosal bleeds. Nearly similar findings were observed in a recent study.[17] Within this study population, 37% were diagnosed with dengue fever, 50% with dengue hemorrhagic fever and 13% with dengue shock syndrome. In a recent Bangladeshi study[18] nearly similar results were found. In this study, hepatic involvement among participants manifested in various forms: 56% had hepatomegaly, 49% had ascites and 26% had serum bilirubin levels above 1 mg/dl. Elevated aspartate aminotransferase (AST) levels were observed in 91% of participants, elevated alanine aminotransferase (ALT) levels in 81%, elevated alkaline phosphatase (ALP) levels in 70% and 36% had a prolonged international normalized ratio (INR) greater than 1.5. Importantly, those with more severe forms of dengue, such as Dengue Hemorrhagic Fever (DHF) and Dengue Shock

Syndrome (DSS), exhibited a higher severity of hepatic involvement. Comparable findings were observed in many previous studies.[1,17,18] The findings of this current study may prove valuable for future research in similar areas.

Limitation of the study: This was a single-centered study with a small sample size and conducted over a short period. Therefore, the findings may not accurately reflect the overall situation of the entire country.

Conclusion

In children with dengue infection, the most common hepatic involvements are elevated levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP), along with hepatomegaly. Additionally, ascites, hyperbilirubinemia and prolonged INR may also be observed, indicating significant liver involvement. These findings highlight the importance of careful monitoring and timely intervention to manage hepatic complications in pediatric dengue patients. Understanding these hepatic manifestations can aid healthcare providers in early detection and effective treatment, ultimately improving patient outcomes and reducing the risk of severe complications associated with dengue infection in children.

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