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PREVALANCE OF ACUTE HEPATITIS IN DENGUE FEVER

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Abstract

Background: *Dengue fever, a mosquito-borne viral illness, has emerged as a major public health concern in tropical and subtropical regions. Among its various systemic complications, hepatic involvement is frequently observed, ranging from mild transaminase elevation to acute hepatitis. This study aims to determine the prevalence of acute hepatitis among patients diagnosed with dengue fever.*

Methods: *A cross-sectional observational study was conducted on 150 patients admitted with confirmed dengue fever over a 6-month period at a tertiary care hospital. Dengue infection was diagnosed via NS1 antigen and/or IgM antibody testing. Acute hepatitis was defined as serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels elevated to more than 10 times the upper limit of normal. Liver function tests were performed on all patients upon admission and monitored throughout hospitalization.*

Results: *Out of 150 dengue patients, elevated liver enzymes were found in 91 (60.7%) patients, and they were further divided into mild, moderate and severe derangement. Abdominal ultrasound showed increased hepatic echotexture in 26.6% and periportal fibrosis in 24.6% Based on biochemical parameters i.e. raised liver enzymes, acute hepatitis was found in 91 (60.7%) patients, and according to radiological studies, acute hepatitis was present in 106 (70.6%) patients.*

Conclusion: *The study highlights that acute hepatitis is a common complication in dengue fever, Routine liver function monitoring in dengue cases is crucial for early identification and management of hepatic involvement, which may contribute to improved clinical outcomes.*

INTRODUCTION

Dengue fever, a viral infection transmitted by the Dengue virus (DENV), is a mosquito-borne disease that has four serotypes (DENV-1 to DENV-4). It is vector-transmitted mainly by the Aedes aegypti mosquito that thrives in urban settings and bites during the day. Dengue fever is quickly becoming a

worldwide health issue with a particular burden in tropical and subtropical regions [1].

The symptoms of dengue typically occur 4–10 days after a person is bitten by an infected mosquito. Symptoms of dengue fever include: acute fever, severe headaches, pain behind the eyes (retro-orbital pain), severe muscle and joint pains (hence "breakbone fever"), nausea, vomiting, rashes, and mild bleeding patterns (e.g. nose bleeds, bleeding from the gums). Dengue fever can precipitate severe dengue, also called Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS). Severe symptoms can include plasma leakage, accumulation of fluid (fluid in lungs), respiratory distress, and death.[2]

The earliest recorded outbreaks of a dengue-like illness occurred in the 18th century. The virus was not genetically characterized and confirmed to be a dengue virus until the 1940s, when it was isolated during World War II (Gubler, 1998). Since then, the process of globalization, urbanization, and climate change have fostered the spread of dengue worldwide, primarily in heavily populated urban areas.[3]

Ever since dengue fever has spread around the globe and is now endemic in over 100 countries. The World Health Organization estimates the number of dengue infections a year at 390 million, with 96 million of those having clinical symptoms (WHO, 2024). Although no effective antiviral agents for treatment exist, dengue prevention primarily relies on vector control and personal protective measures. [4]

Hepatitis is an inflammatory condition of the liver most frequently caused by viral infections, although toxins, alcohol use, autoimmune diseases, or medications may also cause it. Hepatitis A, B, C, D, and E represent the five main types of viral hepatitis; hepatitis B and C contribute the most human health burden every year around the world. The signs and symptoms of hepatitis are highly dependent on the etiology and stage of the disease. Acute hepatitis may present with fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, pale stool, and jaundice (yellowish discoloration of the skin and eyes). With chronic hepatitis (in particular hepatitis B and C), there might not be any symptoms for years, until serious liver damage has occurred.[5,6]

Currently, there are over 354 million people living with chronic hepatitis B or C worldwide. Hepatitis B has the highest prevalence in sub-Saharan Africa and East Asia while hepatitis C occurs in large numbers in central and eastern Asia, north Africa, and the Middle East. Vaccination of susceptible individuals has greatly impacted reducing hepatitis B prevalence in many areas but unfortunately, no vaccine exists for hepatitis C.[7]

Untreated chronic hepatitis can result in significant health consequences, such as liver cirrhosis, liver failure, and hepatocellular carcinoma which regards hepatitis C as the chief cause of liver transplantation in the world.[8]

Liver injury is a recognized complication of dengue disease, especially in patients with severe forms of the illness. The pathogenesis is thought to be due to both the direct cytopathic effects of the virus on the liver hepatocytes as well as immune-mediated injury. The end result is elevation in liver enzymes, hepatomegaly, and even acute liver failure in rare cases. Dengue virus-associated hepatitis can have serious clinical symptoms, including jaundice, right upper quadrant pain, and coagulopathy—all features commonly associated with viral hepatitides. Although various studies have demonstrated that hepatic impairment is common with dengue, unlike with truly viral hepatitis, it is surprising that levels of aspartate aminotransferase (AST) are usually 3 to 4 times higher than levels of alanine aminotransferase (ALT). Furthermore, unlike traditional acute viral hepatitis, severe forms of liver involvement appear to be more common in dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), possibly suggesting the severity of the underlying infection parallels levels of liver injury. Moreover, patient co-infection with other hepatotropic viruses, or underlying liver disease, may serve to enhance liver injury.[9,10]

The purpose of our study is to observe relationship between the prevalence of acute hepatitis in dengue fever.

Methodology:

This cross-sectional observational study was done in CMH Lahore from ____ to ____ after taking informed consent from institutional review board. The aim of the study was to assess the prevalence of acute hepatitis in patients with dengue fever. The study was carried out over a period of six months. The confidentiality of patients was preserved throughout the period of the study.

1. Study Population:
Patients of both sexes, age 18 years and above, were included in the study if they were admitted with confirmed dengue fever – diagnosed by positive NS1 antigen and IgM. The exclusion criteria were patients with chronic liver (hepatitis B, hepatitis C, alcoholic liver disease) or other viral or drug-induced liver injuries.

2. Sample Size and Sampling Technique:
A consecutive sampling instrument was adopted; a total of 150 patients were included into the study. All patients who met the inclusion criteria and were admitted during the study period were included until the sample size was met. A WHO Sample Size calculator was used to calculate the sample size with a confidence interval of 95% and a margin of error of 5%.

3. Data Collection:
Demographic information (age, sex), clinical features (duration of fever, symptoms), and laboratory results were documented using a structured proforma. On admission, liver function tests (serum alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin, alkaline phosophatase) were performed. Acute hepatitis was defined as ALT serum levels that were more than three times the upper limit of normal.

4. Statistical Analysis:
Data were entered and analysed using SPSS version 22. Descriptive statistics with frequencies and percentages for categorical variables and means ± standard deviation for continuous variables. The prevalence of acute hepatitis was determined as the proportion of patients with dengue with elevated ALT, AST, raised bilirubin levels and alkaline phosphatase levels. Chi-square or t-tests were used to explore associations between clinical variables and acute hepatitis, with a significance level of p-value < 0.05.

Results:
One hundred and fifty patients diagnosed with dengue fever completed the study. Of these, 88 (58.7%) patients were males and 62 (41.3%) were females. The mean age of patients was 32.6 ± 5 years. The most common presentations included fever (94%), headache (76%), myalgia (69%), nausea/vomiting (52%), and abdominal pain (38%).
Elevated liver enzymes were noted in 91 (60.7%) patients with categorization into mild, moderate and severe elevations. Mild elevation (AST/ALT up to 2× ULN) was noted in (25.3%) patients, moderate (2–5× ULN) was found in 36 patients (24%), and 17 (11.3%) patients had severe elevation of liver enzymes.
Ultrasound of the abdomen was also performed in order to establish that acute hepatitis included hepatomegaly, increased hepatic echogenicity and peri-portal echoes. Hepatomegaly was noted in 29 (19.3%) patients, evidence of peri-portal echoes was present in 37 (24.6%) and increased echogenicity of the liver was noted in 40 (26.6%) patients.
Acute hepatitis either by biochemical parameters i.e. liver enzymes would be considered raised in 91 patients (60.7%) and radiological studies, acute hepatitis would be considered raised liver enzymes in 106 (70.6%) patients.
Furthermore in our study, we also found evidence of thrombocytopenia relating to acute hepatitis and it was found in 94 (62.6%) patients. The average hospital stay of our patients in our study was 6 ± 2 days.

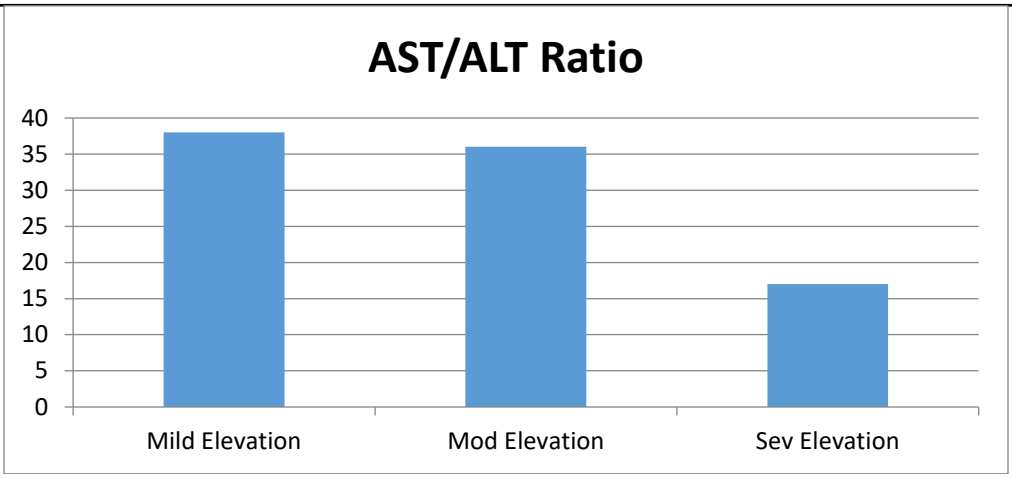


Chart 1.1 (Trends of AST/ALT ratio)

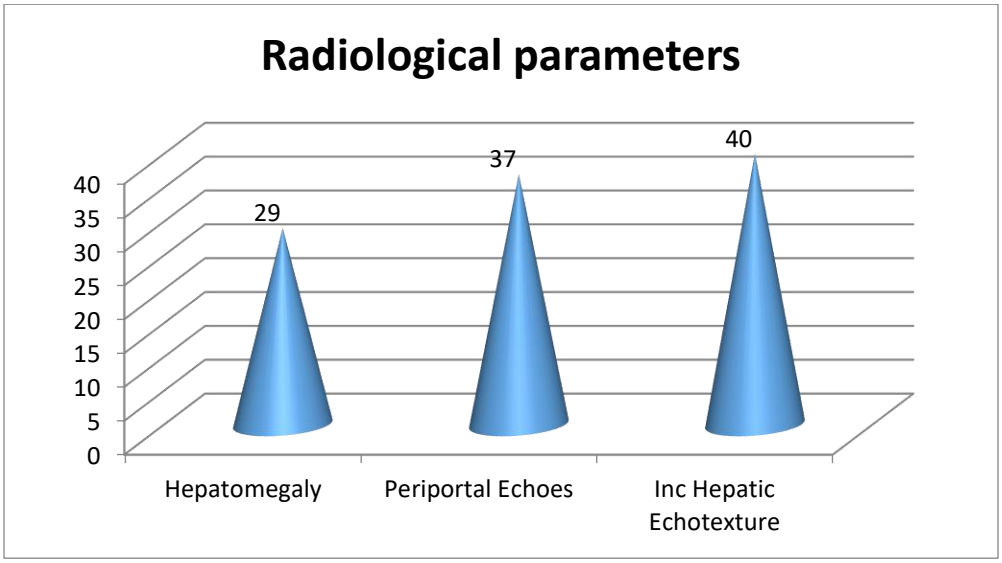
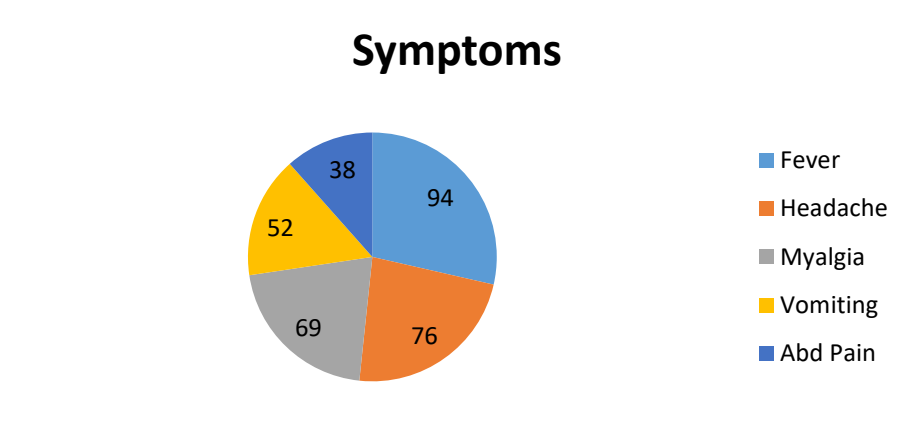
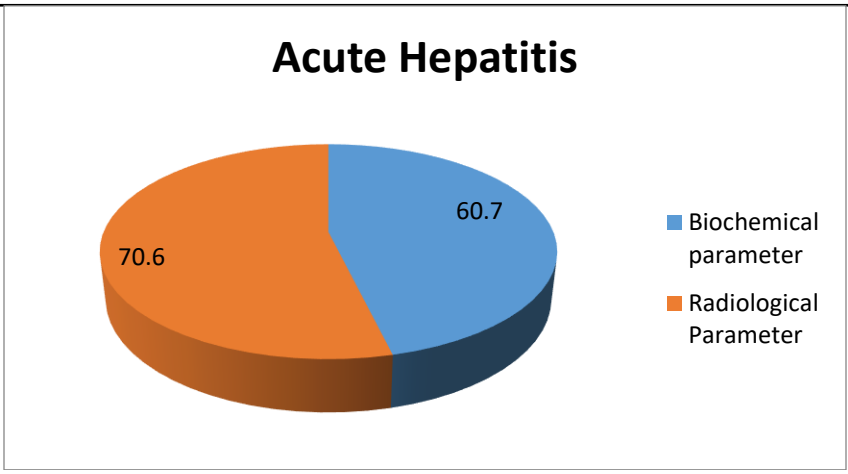


Figure 1.2 (Radiological Parameters of acute hepatitis)



Pie chart 1.3 (symptoms of Dengue Fever)



Pie-chart 1.4 (Acute Hepatitis prevalence)

Discussion:

Dengue fever, a mosquito-borne viral infection caused by the dengue virus (DENV), has emerged as a relevant global public health challenge, particularly in tropical and subtropical countries. One of the significant extra-hematological complications that are increasingly being recognized in dengue patients is hepatic involvement, which can vary from asymptomatic elevations of liver enzymes to overwhelming hepatitis. Hepatic dysfunction is common in dengue fever and can be due to a combination of direct cytopathic effects of the virus, immune-mediated liver injury, and hypoxic injury from hemodynamic instability in severe dengue. Hepatitis in dengue is typically characterized by elevated aminotransferases, hepatomegaly, jaundice, and occasionally hepatic failure. The World Health Organization (WHO) has deemed liver involvement as an important organ involvement in severe dengue.[11]

In a prospective cohort in Brazil by Souza et el. 70% of patients had mild to moderate elevations in alanine aminotransferase (ALT) while 15% had transaminases higher than ten times the upper limit of normal (ULN) compatible with acute hepatitis. Trung et al. similarly recorded a prevalence of 45% in their dengue cohort. A retrospective study in Taiwan by Kuo et el. defined acute hepatitis associated with dengue fever as ALT >100 IU/L; of the 81 patients, they found a 37% prevalence of acute hepatitis. This finding was corroborated in a study by Mohan et al. in India.[12,13]

In contrast, other studies have reported lower prevalence. For example, Parkash et al. (2010) in Pakistan documented transaminase elevation in 63% of dengue patients, but only 12% met the criteria for acute hepatitis.[14]

While these studies consistently demonstrate that liver involvement is common in dengue fever, the reporting of acute hepatitis shows significant variation. One complicating factor is the lack of consensus guidelines for determining "acute hepatitis" in patients infected with dengue. Some studies use ALT/AST levels to define a cutoff for acute hepatitis (e.g., >100 IU/L or >10x ULN) while other studies use clinical findings like jaundice and hepatomegaly. For example, Fernandez and Vazquez performed a systematic review of 23 studies and found that acute hepatitis (defined as ALT >200 IU/L) was about 30% in dengue afflicted patients across Asia. While most studies reported acute hepatitis, it did have an increased prevalence in cases of severe dengue, with some studies reporting up to 55% in severe cases.[15]

The prevalence of liver involvement may also vary geographically depending on the viral serotype. DENV-2 and DENV-3 are more often associated with severe liver injury than DENV-1 and DENV-4. In endemic areas, where reinfections and co-infections are commonplace, the risk of severe hepatic impairment may be compounded by antibody-dependent enhancement and escalation of immune responses.[16]

In a study conducted in coastal India by Nayak et al., liver involvement, primarily raised transaminases, was present in 74.2% of dengue patients. The severity of

dengue was directly related to higher SGOT and SGPT levels, with hypoalbuminemia significantly related to severe dengue. In another study by Kamboj et al., hepatic dysfunction was also found in 67.3% of paediatric dengue patients, again suggesting age-independent vulnerability, however, there was no acute liver failure.[17,18]

In a study in Pakistan, Aslam et al, reported that 15% of dengue patients had severe hepatitis (ALT >300 IU/L), the study showed that acute hepatitis was associated with bleeding complications, renal failure, and increased mortality. Ahmed et al. (2019) further stated that acute hepatitis was very common in adult male dengue patients, and that AST was elevated more than ALT and it could reflect muscle damage.[19]

Limitation of study:

The study was conducted in limited number of patients, with limited sample size and single center, hence results cannot be generalized.

Funding: Nil

Conclusion:

Acute hepatitis is a common but variably reported complication of dengue fever. Liver involvement should be actively monitored, given its prognostic value and potential for contributing to severe outcomes. Hepatic dysfunction may predict severe disease and complicate fluid management due to hypoalbuminemia and coagulopathy. Additionally, dengue-associated hepatitis must be distinguished from other causes of viral hepatitis.

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