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Spectrum of Liver Dysfunction and the Indicators of Severe Disease in Dengue Patients

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ABSTRACT

Dengue fever the most common arthropod-borne disease, is transmitted by mosquitoes of the Aedes family. Liver damage caused by dengue can range from moderate (high transaminase levels) to severe (hepatocyte destruction). The study's goals were to (1) determine how often hepatic dysfunction occurs in dengue patients and (2) analyze the relationship between hepatic dysfunction severity and illness severity. Methods: One hundred patients with confirmed dengue serology who were admitted to the general medicine department of the Kalinga Institute of Medical Sciences in Bhubaneswar participated in this retrospective cross-sectional observational research. Several laboratory values were obtained in addition to the patient's demographic data. Aspartate aminotransferase (ALP), total and direct bilirubin, serum levels of albumin and globulin, complete blood count, serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT) and clinical symptoms were among the data that were measured. In accordance with the categorization that was established by the World Health Organization in 2009, two distinct groups of patients were identified those who were suffering from severe dengue and those who had dengue with or without warning signals. After doing a One-Way Analysis of Variance (ANOVA) to compare multiple means across illness severity the post-hoc analysis was based on the difference that was found to be the least significant. To find out how transaminases and platelet counts were related, we employed Pearson's correlation coefficient. All of the analyses made use of 95% confidence intervals and $p>0.05$. Elevated SGOT levels were seen in 69% of patients with dengue without warning symptoms, 81% of patients with warning indications and 94% of patients with severe dengue. Serum glutathione concentrations were elevated in 94% of severe dengue patients, 55% of patients with warning indications of the disease and 45% of patients with no symptoms at all. When SGOT and SGPT levels were high, more patients experienced bleeding symptoms. There was a substantial increase ($p<0.0001$) in hypoalbuminemia (53% of cases) and A:G ratio reversal (30%) in cases of severe dengue. A negative correlation ($p<0.0001$) was seen between platelet count and SGOT and SGPT levels. Liver damage was suggested by elevated transaminase levels in 77% of dengue patients. A higher level of SGOT and SGPT indicates a more severe case of dengue. It is common for dengue fever to cause damage to the liver, hence, biochemical markers such transaminitis, hypoalbuminemia and A:G ratio reversal should be applied in order to diagnose and monitor liver dysfunction in dengue patients.

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Key Words

Dengue, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, Alkaline Phosphatase, liver dysfunction

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INTRODUCTION

Aedes mosquitoes are the vectors that are responsible for the transmission of dengue virus (DENV), which is the most serious arthropod-borne sickness that may affect humans[1-4]. It is possible for any of the four serotypes of the dengue virus (DENV-1, DENV-2, DENV-3 or DENV-4) to be the cause of dengue fever (DF), which is a mild sickness that resolves on its own. The two most severe symptoms of the disease, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), are very rare[2-4]. The World Health Organization classified dengue fever into two categories in 2009[1-3] severe dengue and dengue with or without warning signals.

The areas with higher probability of experiencing dengue fever-related public health issues are those that are tropical or subtropical. Dengue fever, which is endemic to almost all of India's states, is the most prevalent reason for hospitalization in the country[5]. In spite of the fact that instances have also been identified in rural and peri-urban settings the illness was originally detected in urban areas a few decades ago[5,6]. The National Vector Borne Disease Control Program received reports of about 1.5 lakh cases of dengue fever in 2019[5-8]. As a result, it's possible that the number of cases of dengue fever recorded in India is exaggerated.

Since 1967, there have been reports of hepatic impairment linked to dengue infection[7]. From relatively minor injuries (a spike in transaminase levels) to complete liver failure, severe injuries can manifest in a variety of ways, including hepatocyte damage and jaundice. Hepatic dysfunction occurs as a consequence of both direct toxicity to the liver and a host immune response that is impaired when the virus is present. A few rare cases of fulminant hepatic failure have been reported, however transaminase abnormalities often resolve on their own and can be used to forecast the severity of the illness[6-9]. We don't know much about the variations in liver involvement among dengue patients because there hasn't been much research in our area. Researching the coastal Indian population allowed us to fill this knowledge gap in the literature. The purpose of this study was to ascertain the frequency with which hepatic dysfunction develops in dengue patients and to investigate whether or not there is a correlation between the severity of the disease and the degree of hepatic dysfunction seen.

MATERIALS AND METHODS

A total of one hundred hospitalized patients at the Kalinga Institute of Medical Sciences who had confirmed dengue serology were included in this retrospective observational cross-sectional investigation. The present study followed all ICH-GCP protocols and has the blessing of the institution's ethical committee. Inclusion criteria for the research were patient's ages and the presence of proven dengue serology (IgM positive by spot). "We excluded from our study patients with a history of non-alcoholic steato-hepatitis or non-alcoholic fatty liver disease, chronic liver disease, a history of long-term use of hepatotoxic drugs, or additional hepatitis-causing infections (malaria, leptospirosis, viral hepatitis, or secondary sepsis)."

In our study, we categorized people as having either severe or moderate dengue, depending on whether or not they exhibited any warning signals[6]. ALP, serum globulin and albumin levels, total and direct bilirubin levels, SGPT and SGOT levels, complete blood count and other laboratory values were recorded together with the patient's demographics, dengue severity, presenting symptoms, and clinical signs. The data was compiled by drawing on the patient's medical history.

Statistical analysis: The statistical program for the social sciences, called SPSS, version 20, was used to manage the data analysis. While percentages and frequencies were used to represent categorical data, averages and standard deviations (SD) were used to explain continuous data. We used the average for continuous data. To compare several means throughout the spectrum of sickness severity, a One-Way Analysis of Variance (ANOVA) and a post-hoc analysis based on the least significant difference were employed. The Pearson's correlation coefficient was employed to determine the type of relationship between transaminase levels and platelet counts. The two-tailed probability value that was deemed statistically significant was less than 0.05 (95% CI).

RESULTS

Forty-five percent of dengue patients without symptoms, 55 percent of cases with symptoms, and 94 percent of cases with severe dengue had elevated SGPT levels. Among patients with severe dengue, 24% had elevated ALP, whereas 13% had no symptoms at all and 61% had warning signals. Patients who had severe dengue, those who had warning indications, and those who did not have any symptoms had the greatest rates of hyperbilirubinemia, which were 28.0%, 17.0-1.8%, respectively. The SGOT/SGPT ratio was also greater than one in ninety percent of dengue patients who did not exhibit any symptoms, in ninety-eight percent of patients who had warning signals and in one hundred percent of patients who had severe dengue. It was shown that hypoalbuminemia was present in 9.4% of cases, 22% of patients with warning signals of dengue and 53% of

cases with severe dengue that were examined. It was noted that the A: G ratio or the A/G ratio <1 had reversed in 1.9% of severe dengue cases, 10% of dengue patients who did not exhibit any warning signs, and 30% of dengue cases that exhibited warning indicators.

Seventy-Eight parent of patients diagnosed with increased liver enzymes had stomach discomfort, ninety percent had continuous vomiting, 94 percent had mucosal bleeding, 100% of them had lethargy or restlessness and 80 percent had hepatomegaly that was >2 centimeters. When compared to patients who were not in shock the average SGOT and SGPT levels were considerably higher in shock patients. The SGOT levels were 1762 (1898.1) IU L^{-1} and the SGPT levels were 528.3 (402.8) IU L^{-1} and 103.2 (182.6) IU L^{-1} respectively. The p-value for each of these values was less than 0.05. In accordance with the findings, those who exhibited elevated levels of liver enzymes exhibited a significantly higher mean hematocrit (45.4% versus 42.1%, p<0.05) in comparison to those who possessed normal levels of that particular enzyme. Platelet count [84894 (61286) vs. 163486 (48942.8) cu.mm, P<0.05] was considerably lower in those with increased liver enzyme levels compared to those with normal values. There was an increased likelihood of bleeding symptoms in a greater number of SGOT (96%) and SGPT (84%). A decrease in platelet count was associated with an increase in dengue severity, as there was a negative correlation (p<0.05) between blood levels of glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase.

DISCUSSIONS

From silent elevations in transaminase levels to catastrophic fulminant hepatic failure, dengue can cause a wide range of liver dysfunctions. A total of 77% of the people who participated in our study had transaminase levels that were too high. Multiple supplementary studies have shown comparable percentages of subjects, with 76% showing increased SGOT and 53% showing increased SGPT[9-11]. By more than 100%, the average SGOT value was higher than the average SGPT value. The high SGPT levels seen in other cases of viral hepatitis stand in sharp contrast to this. One or more of these pathways might be the secretion of SGOT from injured erythrocytes, cardiac muscle, or skeletal muscle. Clinical and laboratory findings that are consistent with acute viral hepatitis, such as a pattern of SGOT/SGPT derangement, thrombocytopenia, and fever that persists after icterus has appeared, may indicate dengue infection[12]. Both an SGOT with a maximum value that was greater than 100 times the normal range and an SGPT with a maximum value that was greater than 30 times the upper limit were included in the sample that we used for our research. Despite the fact that one of these patients passed away as a result of their dengue while they were receiving treatment the other patient achieved a complete recovery. It is important to stress that the first patient did not exhibit any indications of bleeding, and the final diagnosis of death was severe refractory hypotension. This is despite the fact that the patient's course was tumultuous. On the other hand, the second patient, Melena, exhibited serious bleeding symptoms, which lends credibility to the notion that the SGPT is still the gold standard for evaluating liver condition. We discovered that the group with severe dengue had a significantly higher mean alkaline phosphatase level than the other groups, which is in line with the findings of the study that was conducted by[13].

Hypoperfusion, immune-mediated damage, and direct viral cytopathic effects are some of the ways in which dengue can injure the liver. Human postmortem investigations have revealed a variety of changes, including microvesicular steatosis, hepatocellular necrosis, Councilman bodies, inflammatory cell infiltrates and Kupffer cell hyperplasia and death. In addition, research using immunohistochemistry has demonstrated increased production of IFN-γ and the infiltration of CD4+ and CD8+ T cells into the liver acini, indicating the involvement of Th1 cells. Microcirculatory failure and hepatocyte ischemia can occur in the absence of hypotension due to dengue's venular or sinusoidal endothelial damage[14]. Acute or chronic liver failure might aggravate preexisting liver problems in dengue-endemic regions.

Few studies have focused on vhypoalbuminemia as a symptom of dengue hepatic dysfunction. Hypoalbuminemia afflicted 13.9 percent and 16.5 percent of dengue patients, respectively, according to studies[12-16]. In addition, hypoalbuminemia was seen in 17.5% of individuals who sustained dengue. We found that the prevalence of hypoalbuminemia was 36%, which is lower than the prevalence that Itha *et al*.[22] found, which was 76%. It was discovered by us that the average levels of blood albumin in individuals who had severe dengue were much lower than those reported in the general population. The results of a research[14] showed that those who had passed away as a result of dengue had a more robust association with severe dengue than those who had perished from the disease. It is possible for capillary leakage to create hypoalbuminemia even when the patient is in the middle of a severe illness[17]. Because of this, it is plausible to believe that it is correlated with the severity of the condition. Moreover, hypoalbuminemia was shown to be more frequent in individuals who were experiencing shock, as per our findings. When

compared to patients who showed warning indications of dengue (10%) or who showed no warning signals at all (30%), patients who had severe dengue had an A: G ratio that was thirty percent higher. The variations in molecular size that exist between albumin and globulin could supply an explanation for this phenomenon. The ratio of albumin to globulin undergoes a change in the early stages of the illness. This is due to the fact that albumin is a smaller molecule than globulin, which allows it to leak more easily[18].

According to the findings of our study, patients who were in shock had significantly higher mean levels of SGOT, SGPT and ALP than patients who were not in shock. The disruption of microcirculation has been demonstrated to be capable of causing hepatic dysfunction even in the absence of hypotension[19] but shock appears to render the damage even more severe. Significantly greater levels of serum bilirubin, SGOT, SGPT and ALP were also seen in individuals who experienced bleeding symptoms in comparison to participants who did not have any bleeding symptoms. Because those with increased liver enzymes exhibited considerably higher levels of hemoglobin and hematocrit ($p<0.05$ and $p<0.05$, respectively), it may be inferred that hemoconcentration played a significant role in their condition.

CONCLUSION

Elevated transaminase levels, an indicator of liver damage, were observed in 77% of dengue patients. Because of their inverse relationship, SGOT and SGPT blood levels increase as dengue severity increases. The indication of this is a decrease in the platelet count. Dengue patients had reduced SGPT levels compared to SGOT levels. Dengue fever can cause liver damage, which is rather frequent. Reversal of the A:G ratio and hypoalbuminemia are biochemical markers that can be used to detect and track hepatic impairment in dengue patients.

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