ORIGINAL ARTICLE

Spectrum of hepatic dysfunction in dengue epidemic in Rawalpindi Pakistan in 2023

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ABSTRACT

Background: To study the relationship of spectrum of hepatitis dysfunction with other clinical features in Dengue fever. This research article aims to unravel the intricate spectrum of hepatic involvement in individuals afflicted by dengue fever during Dengue epidemic in year 2023.

Material and Methods: This cross-sectional study was done on adult patients with dengue fever confirmed by NS-1 antigenemia. We recorded clinical features and classified patients into different groups of severity as defined by WHO guidelines. Liver function tests were also done in all cases. Different clinical features were compared amongst patients with mild to moderate and severe hepatitis.

Results: There were 235 patients, including 184 (78%) males and 51 (22%) females, out of which 191 (81%) of patients had fever, Rigors and chills 182 (77 %), Vomiting in 115 (49%). Patients with dengue hemorrhagic fever 83 (35%), while dengue shock syndrome was present in 8 (3.40%) of patients. Our study showed statistically significance in terms of hepatic involvement based on its dysfunction and bleeding tendencies with mild / moderate hepatitis (median = 112.15) and severe hepatitis (median = 57.64), p = 0.0001, r= 0.184.

Conclusion: This study showed dengue fever has adverse impact on liver parenchyma and hepatic function resulting in a higher level of transaminases. Early intervention and supportive treatment will result in a better outcome.

Keywords: Dengue, Hepatitis, Hospital stay

BACKGROUND

The year 2023 marked a pivotal moment in the epidemiological landscape of Rawalpindi, Punjab, as the region grappled with a severe dengue epidemic. Dengue, a mosquito-borne viral infection caused by the *flavivirus*, has been a persistent public health challenge in tropical and subtropical regions, including Pakistan. While the clinical manifestations of dengue are well-documented, the focus on hepatic dysfunction during the 2023 epidemic in Rawalpindi warrants comprehensive exploration. This research article aims to unravel the intricate spectrum of hepatic involvement in individuals afflicted by dengue fever during this critical period.[1]

Dengue fever is known for its diverse clinical manifestations, ranging from mild flu-like symptoms to severe manifestations such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[2] Among the multiple organ systems affected, the liver plays a crucial role in dengue pathogenesis. Hepatic involvement in dengue fever has been observed in various forms, including hepatomegaly, elevated liver enzymes, and, in severe cases, hepatic failure.[3] The 2023 epidemic in Rawalpindi presented an opportunity to delve deeper into the nuances of hepatic dysfunction in the context of dengue, with a focus on understanding the variations in clinical presentation, severity, and outcomes.

This research is crucial for several reasons. Firstly, the severity of hepatic involvement in dengue can significantly impact patient management and outcomes. Timely recognition and appropriate intervention for hepatic dysfunction can be life-saving, especially in regions where resources may be limited. Secondly, the specific strains of dengue virus prevalent during the

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2023 epidemic may have exhibited unique interactions with the hepatic system, necessitating a focused study on this aspect.

Furthermore, the socio-demographic profile of the affected population, environmental factors, and existing healthcare infrastructure all contribute to the complex interplay influencing the spectrum of hepatic dysfunction in dengue cases. By investigating these multifactorial dimensions, our research seeks to provide a comprehensive understanding of the hepatic manifestations of dengue.

In this article, we will present a detailed analysis of the clinical, laboratory, and radiological features of hepatic dysfunction in dengue patients. Additionally, we aim to explore the correlation between hepatic involvement and disease severity, emphasizing the importance of early detection and management strategies. Our findings aspire to contribute valuable insights to the existing body of knowledge on dengue, potentially informing future public health interventions and clinical guidelines tailored to the unique dynamics observed during the 2023 epidemic in Rawalpindi, Punjab.

MATERIAL AND METHODS

This descriptive cross-sectional study was carried out at Pak Emirates military hospital from March 2023 to October 2023. The study was conducted after due approval of ethical review committee letter no. A/28/EC/566/2023. All patients, aged greater than 12 years with history of acute fever and confirmed Dengue Non-structural protein 1 antigen positive test were included in the study. Known patient of malignancy, patients receiving chemotherapeutic agents, anti-tuberculosis treatment, massive ascites/ pleural effusion and preexisting congenital platelet or coagulation disorders were excluded from study.

The sampling technique employed was non probability consecutive sampling. Sample size was calculated using WHO sample size calculator assuming 35%, prevalence of liver dysfunction in dengue patients (4) with 95% confidence interval and p-value of less than 0.05 was considered to be clinically significant. A total of 670 suspected dengue patients were evaluated in Emergency and outdoor patient department, out of which 235 confirmed cases of Dengue infection, admitted in Dengue ward were included in the study. Data was collected by conducting one on one interviews with the participants in accordance with a structured questionnaire. The participants were counselled in detail and their verbal consent was sought. A detailed medical history and clinical examination were carried out for all enrolled subjects. A 5ml venous blood was drawn from ante cubital vein and sent for baseline investigations (CBC, Liver function tests, coagulation profile) and ultrasound abdomen and chest X-ray was carried out to confirm organomegaly, cardiomegaly and evidence of serositis. The subjects were followed up and managed indoor till discharge from hospital data was recorded.

Data included demographic details (age, gender, co-morbidities), day of Illness, clinical findings, laboratory parameters and duration of hospital stay. Mortality at 30^{th} day was also recorded. Patients developing dengue complications like bleeding and shock were monitored. Laboratory parameters recorded were serum ALT, serum creatinine. We divided patients into two groups based on ALT levels, mild to moderate hepatitis with ALT levels up till 299 IU/ L and severe acute hepatitis with ALT levels greater than 300 IU/L.[4] Patients were also classified into groups of dengue fever, dengue hemorrhagic fever and dengue shock syndrome. Statistical analysis was done using Statistical package for social sciences (SPSS) version 23.0. Descriptive statistics were used to analyze categorical variables while continuous variables were computed as mean, standard deviation and interquartile range. Categorical variables were represented as frequency and percentages. Normality of data was checked through Komogorov-Smirnov test. Variables including age, hospital stay, transaminases and bleeding disorders were found to be non-normally distributed. Mann-Whitney U test was applied to compare bleeding tendencies and transaminases derangements. Chi square test was applied to determine statistical significance among two variables and p value of <0.05 was considered statistically significant.

RESULTS

A total of 235 patients with dengue fever were enrolled in this study out of which 184 (78 %) were male and 51 (22 %) were females. Median age of sample size was 39 years (interquartile range 95 - 13 years) with 75% of the sample size less than 50 years of age. Median duration of illness while reporting at the hospital was 6 days (interquartile range 16-3 days). The clinical

manifestations in our study showed 191 (81%) of patients had fever, Rigors and chills 182 (77 %), Vomiting in 115 (49%). Patients with dengue hemorrhagic fever 83 (35%), while dengue shock syndrome was present in 8 (3.40%) of patients. Table-I shows distribution of clinical manifestations of dengue fever in sample size.

Patients below 299 IU/ L had limited disease course while above 300 IU/ L had prolonged illness and had more complications. Major Bleeding and Dengue shock was seen in 6 (100%) of the patients having ALT more than 300 IU/L. On the other hand, patients with ALT less than 299 IU/L (mild to moderate disease) had major bleeding disorder and shock in 2 (0.87%). In the group with mild/moderate hepatitis, mean hospital stay was 5 days, (IQR: 11-2 days) whereas the mean hospital stay in group with severe hepatitis was 9 days (IQR: 16-5 days). The duration of hospital stay among group with mild/moderate hepatitis and group with severe hepatitis was found statistically significant (p<0.001). Dengue shock syndrome was more prevalent in severe hepatitis group 6(100%).

Table-I: Distribution of clinical manifestations of dengue fever (n=235)

Clinical Presentation	Cases n (%)
Fever	191 (81)
Myalgias	187 (79)
Rigors & Chills	182 (77)
Headache	180 (76)
Vomiting	115 (49)
Bleeding/Epistaxis	83 (35)
Abdominal Pain	53 (22)
Hepatomegaly	52 (22)
Pleural Effusion	20 (9)
Ascites	18 (7)
Serositis	10 (4)
Sepsis/DSS	8 (3)

Table-II: Statistical analysis of various variables between patients with mild-moderate and severe hepatitis (n=235).

Variables	Hepatitis severity		p-value
	Mild to moderate (gum bleeding, mild epistasis) (ALT<299U/l) n=229	Severe (requiring transfusion) (ALT>300U/l) n=6	
Patients with minor bleed	77 (33%)	6 (100%)	0.003
Patients with major bleed	2 (0.87%)	6 (100%)	<0.001
Patients with no bleed	150 (65%)	0 (0 %)	0.64
Dengue shock syndrome	2 (0.87%)	6 (100%)	<0.001
Mean hospital stay(days)	5 (11 – 2)	9 (16 – 5)	<0.001

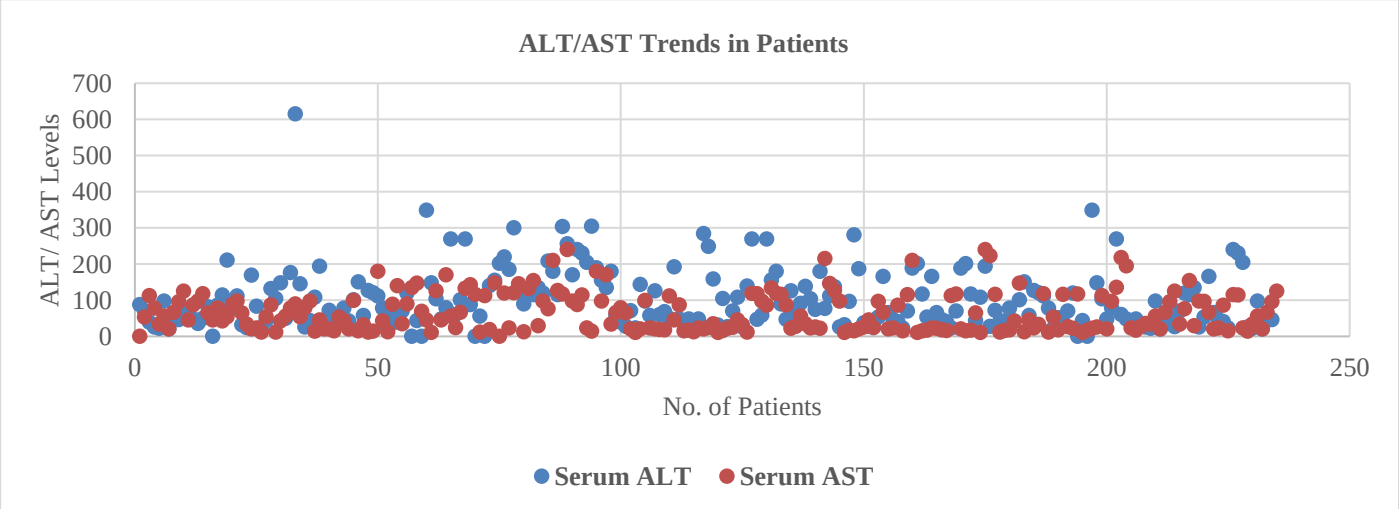

Figure-I: ALT/ AST levels in dengue patients. (n = 235)

DISCUSSION

Dengue fever illness has now been mostly reported in form of epidemics especially in South-east Asian countries.[5] First case of dengue fever was reported in Pakistan in 1994,[6] since then there have been many epidemics reported. Peak season of dengue fever in Pakistan is from July to September.[7] This study revealed males were more affected with dengue fever illness reason being clothing and other outdoor physical activities.[8]

Fever was reported as main symptom in dengue fever illness as illustrated by Khan *et al*.[9] Our study showed that 81% patients having dengue infection presented with fever associated with rigors and chills. Myalgia and arthralgia were found in 79 % of our patients which is quite comparable to study conducted by Khosavanna *et al*, where it was reported in 70% of the patients.[10] In our study, 23% patient had abdominal pain whereas Vanamali *et al* reported abdominal pain in 45% of his patients.[11] Headache was reported in 76 % of the patients in our study which is higher to study done by Fujimoto *et al* whereas it was found in 58%.[12] Vomiting occurred in 53% of our patients which is slightly higher in comparison to study done by Ren *et al* where it was reported in 46.8%.[13]

Hepatomegaly was seen in 21 % of our patients, similar trends were reported by Ahmed.[14] Our study showed 9% dengue patients had pleural effusion whereas other studies showed that 31% of dengue patients had pleural effusion.[15] Daniel *et al* reported ascites in 12% of cases while our study showed ascites in 9 % of the patients.[16] In our study DSS was reported in 3.4 % of all the dengue patients. However, Wasay *et al* reported a lower incidence of DSS (2.9%) in severe dengue fever patients in comparison to our study.[17] Mortality reported in literature ranges from 0.15 % to 7 % .[17] Mortality at 30th day in our study was none whereas in literature it has been reported 0.15 % to 7 %.[18] The likely reason of low mortality in our patients is owing to early detection with more specialist care or may be our patients are infected with different strain of dengue virus in comparison to studies conducted in patients with high mortality.

The emphasis of our study relies on hepatic involvement in dengue patients and its correlation with complicated dengue fever illness. Nearly all patients in our study had raised levels of transaminases. The liver injury caused by dengue virus is multifactorial. The leading mechanisms include cytopathic effects of virus, hepatic injury due to immune mediated mechanism and lastly liver hypoperfusion. A variety of histopathological findings are reported following postmortem of patients died of dengue. Among frequently found pattern are; hepatic micro-steatosis, necrosis, councilman bodies and hyperplasia of Kupffer cells. The hepatic hypoperfusion injury is due to microcirculatory dysfunction that leads to hepatic ischemia irrespective of patient hemodynamic status.

Innate immunity and cytokines released by dengue virus resulted in liver parenchymal injury as this was reiterated in another study done by Chaturvedi *et al* that B-Cells, monocytes and T-Lymphocytes release cytokines which in turn cause hepatocellular damage.[19] Host response plays major role in hepatic parenchymal injuries as reported by postmortem studies done on patients who died of dengue fever illness.[20]

CONCLUSION

This study showed that dengue fever has adverse impact on liver parenchyma and hepatic dysfunction resulting in higher level of transaminases. Liver involvement in dengue fever patient resulted in higher risks of complications along with longer hospital stays. Early intervention and supportive treatment results in better outcome.

LIMITATION

Study was conducted in a single tertiary care setup where patients were entitled to treatment, this study does not represent the population of a specific region.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Usama Zahid: Conceptualization, writing, methodology, data analysis

Shazia Nisar: Conceptualization, writing, revisions overall supervision

Salman Saleem: Conceptualization, overall supervision

Muhammad Arif Sadiq: Writing, methodology, data analysis

Abdul Rehman Azeem: Writing, methodology, data analysis

Ahreema Siddiqui: Data collection

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