Original Article

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Effect of Dengue Fever on Liver Enzymes

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ABSTRACT

Background and Objectives: Dengue fever is a disease that is commonly found in endemic areas and is caused by the dengue virus which is spread by mosquitoes, specifically the Aedes aegypti mosquito. To determine the platelet count in dengue fever patients on the 5th day of diagnosis. To determine the correlation of dengue fever with liver enzyme.

METHODOLOGY: A retrospective study was conducted in the Bahria Hospital in Lahore, Pakistan. The study was conducted during the 3 months from May to July, 2023. The study included a total of 140 individuals with confirmed dengue fever, comprising 58 women and 82 men with ages ranging from 1 to 90. The study was conducted to determine the platelet count on the 5th day of diagnosis and to find out the correlation of dengue fever with liver enzymes. Patients were dived into 3 groups according to the age range 5-30, 31-60, and 61-90 years. Hematology results of these patients indicated low platelet count (<130×109/L). The instrument or machines we used for platelet count and liver enzyme measurement were Cell-DYN Ruby and Alinity ci-series respectively. A self-designed Performa was used to collect the patient data. Data were entered and analyzed by using excel and displayed by using Tables and Bar Charts.

RESULTS: According to the study, adults between the ages of 31 and 60 were most frequently affected by low platelet counts. Aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) levels were also found to be increased in individuals between the ages of 5 and 30 in 26%, 27%, and 8.5% of instances, respectively. The majority of patients with higher AST, ALT, and ALP values were between the ages of 31 and 60, with 53.5%, 52%, and 15.7% of patients displaying increased levels, respectively. In 14%, 14%, and 3.7% of patients between 61 and 90 years old, respectively, increased levels of AST, ALT, and ALP were found.

CONCLUSION: In conclusion, patients between the ages of 31 and 60 were found to have the highest prevalence of increased aminotransferases among all age categories, with AST and ALT levels being twice as high as ALP levels.

KEYWORDS: Aspartate transaminase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP).

INTRODUCTION

Dengue fever is caused by positive single-stranded, mosquito-borne dengue virus. The virus belongs to a family of Flaviviridae having 1 of 4 serotypes (DEN1, DEN2, DEN3, and DEN4)(1). Recently 5th serotype of dengue virus (DEN-5) was identified in Malaysia from the blood of patients. On the basis of viral genome changes all these serotypes has further subtypes or genotypes and are categorized by the number of antigens that the virus have in common(2). Female mosquitoes of the Aedes species, particularly Aedes aegypti and Aedes albopictus, carry the dengue virus, which can cause a variety of illnesses ranging in severity from moderate to severe(3). Dengue virus is spherical shaped RNA enveloped virus with 11000 nucleotides and only 1 reading frame(4). The dengue virus's RNA is replicated by the NS1 protein, which also aids in the virus's defence by preventing complement activation. The wide geographical distribution of Aedes aegypti, a mosquito species, poses a significant threat to approximately 2.5 billion individuals, increasing their vulnerability to dengue infection. Each year, an alarming 50 million cases of dengue are reported, highlighting the severity of the issue. Aedes aegypti serves as the primary carrier for various

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vector-borne diseases, including dengue, zika, and chikungunya. This emphasizes the crucial role of this mosquito species in transmitting these diseases(5).

The clinical manifestation of dengue fever varies from mild (fever, headache) to severe fever, arthralgias, myalgia, cephalea and gastrointestinal disorders. According to signs and symptoms dengue virus is classified into 3 forms dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) (6). The mortality rate of dengue shock syndrome (DSS) is 1-5%(4). Lab diagnosis indicates low level of platelets and white blood cells. Platelets are anucleated, small sized discoid shaped cells that are derived from megakaryocytes. In terms of abundance, platelets rank as the second most numerous type of cellular components found in the circulating blood, typically ranging between 150 and 450 billion per liter(7). Thrombocytopenia or low platelet count is the important factor in dengue infection. Low platelet count is observed in mild dengue fever but it become lowest in case of severe dengue fever. In dengue fever, suppression of bone marrow or consumption of platelets at periphery cause the alternation of platelets number and their functions which leads to thrombocytopenia(8). Dengue virus also damage the liver by direct affecting on hepatocytes that cause hepatocellular injury(9).

The liver, positioned in the right upper abdomen beneath the rib cage, is the second largest organ in the human body. Liver has a wide range of functions like liver helps in supporting metabolism, immunity, and vitamin storage. It also acts as a storehouse of blood and synthesizes 50% of lymph in the body. It also maintains blood sugar level, helps in the production and excretion of bile(10). Liver is considered as a unique organ because of its dual blood supply from the portal vein (75%) and the hepatic artery (25%). About 2% of adult`s body weight is made up of liver(11). Any abnormality that affects or damage the liver is known as liver disorder. Liver function test are performed to indicate if any inflammation or damage in liver cells. Following are the parameters of liver function test (LFTs), alanine transaminase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), aspartate transaminase (AST), bilirubin, total protein, and albumin. In dengue patient the elevation of transaminase varies in different cases. Globally dengue cases have been reached up to 400 million per year. This is because of certain factors like climate changes, globalization, travel, trade, socioeconomics and viral evolution(12). About 100 billion cases are reported out of which 390 million people are infected every year in worldwide. Countries like Pakistan, Bangladesh, India and Sri Lanka are adversely affected by dengue viral infection(13).

Half of worldwide population is at risk due to dengue infection. In Pakistan, dengue cases are increasing due to limited resources and lack of public health awareness which is an alarming situation. The hotspot for many vector-borne diseases (e.g., dengue hemorrhagic fever) is Pakistan. All four serotypes of dengue virus (DENV1-DENV4) are circulating in Pakistan and outbreak occurs mostly during monsoon period(14).

METHODOLOGY

It was a retrospective study. Data was collected from the medical ward of Bahria Hospital Lahore, Punjab. Total 140 samples of dengue patient were collected. The patients who were diagnosed with dengue fever on the 5th day of the onset of disease.

A Performa were used to collect patient data of dengue patients. Aseptic phlebotomy procedures were used to obtain intravenous blood samples from dengue patients. The methods and instruments we used for analysis were; Cell-DYN Ruby and Alinity ci-series.

The cell-DYN is a hematology analyzer used in many laboratories. It works on the principle of electrical impedance (allow the passage of one cell at a time from electrode), flow cytometry (when laser beam hits the moving cells, scattering of light occurs and the detector then detect the number of cells) and absorption spectrophotometry (absorption of light is directly proportion to the concentration of a substance in the sample). The system also utilizes MAPSS (Multi-Angle Polarized Scatter Separation) technology.

The Alinity ci-series is a clinical chemistry analyzer used for diagnostic test in clinical laboratories. It works on the principle of immunoassay like enzyme immunoassay (EIA) and chemiluminescence immunoassay (CLIA) and spectrophotometry (Beer Lambert law). Beer Lambert law stated that the absorption of light is directly proportional to the concentration of substance in sample.

Data were entered and analyzed by using excel for statistical analysis. Tables and Bar charts were used to display the data.

RESULTS

The study was conducted at the medical ward of Bahria Hospital Lahore, Punjab. 140 diagnosed patients of dengue fever were selected during the study. Out of these 140 patients 82(59%) were males and 58 (41%) were females.

Table No.1 Gender Based Distribution of Dengue patients

Male	Female	Total
82 (58.57%)	58 (41.43%)	140

The age range of patients in our study was 5-90 years. Patients were divided into 3 groups according to the age. In 1st group patients belonged to the age range between 5-30 years having 39 (27.85%) patients out of which 21 were males and 18 were females. The 2nd group patients belonged to the age range between 31-60 years having 80 (57.1%) patients out of which 52 were males and 28 were females. The 3rd group patients belonged to the age range between 61-90 years having 21 (15%) patients out of which 10 were males and 11 were females. The maximum number of patients (57.1%) belonged to the age group of 31-60 years.

Table No.2 Age Distribution

Age range	(0-30yrs)	(31-60yrs)	(61--90yrs)
Patients	39 (27.86%)	80 (57.14%)	21 (15%)

The analysis of platelet count in the patients with dengue fever showed the abnormal results in all patients. The patients were divided into 3 groups. Group 1 include patients with age range between 5-30 years, hematology result showed 39 (27.9%) patients had abnormal platelet count (less than 1 lac). Group 2 include patients with age range between 31-60 years, hematology results indicated low platelets count in 80 (57.1%) patients. While group 3 include patients with age group 61-90, low platelet count was observed in 21 (15%) patients. While the results of the study indicated that low platelet count was most common in adults.

Table No.3 Abnormal Platelets Count in patients with dengue fever

	Age group		
No. of Patients	5-30yrs	31-60yrs	61-90yrs
Patients	39(27.86%)	80 (57.14%)	21(15%)

140 patients were examined with liver function test which indicates abnormal level of liver enzymes in most cases. Patients with age group 5-30 years were observed with high level of alanine transaminase (ALT) in 38 (27%) patients, aspartate transaminase (AST) in 37 (26%) patients and alkaline phosphatase (ALP) in 12 (8.5%) patients respectively.

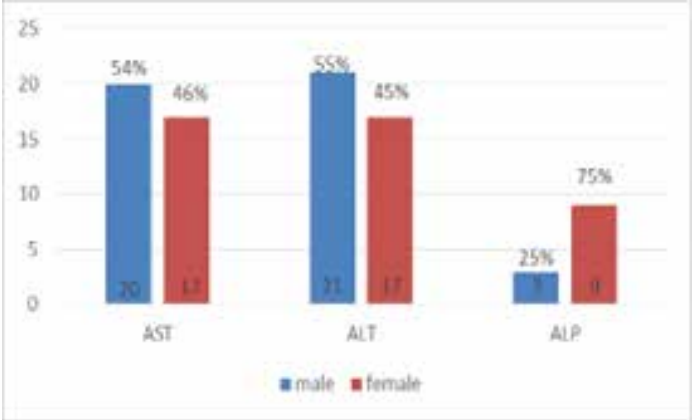

Figure 1 Level of Liver Enzymes between Age Group (5-30yrs)

Patients with age group 31-60 years had high level of alanine transaminase (ALT) in 73 (52%) patients, aspartate transaminase (AST) in 75 (53.5%) patients and alkaline phosphatase (ALP) in 22 (15.7%) patients respectively.

Figure 2 Level of Liver Enzymes between Age Group (31-60yrs)

Patients with age group 61-90 years had high level of alanine transaminase (ALT) in 20 (14%) patients, aspartate transaminase (AST) in 20 (14%) patients and alkaline phosphatase (ALP) in 5 (3.5%) patients respectively.

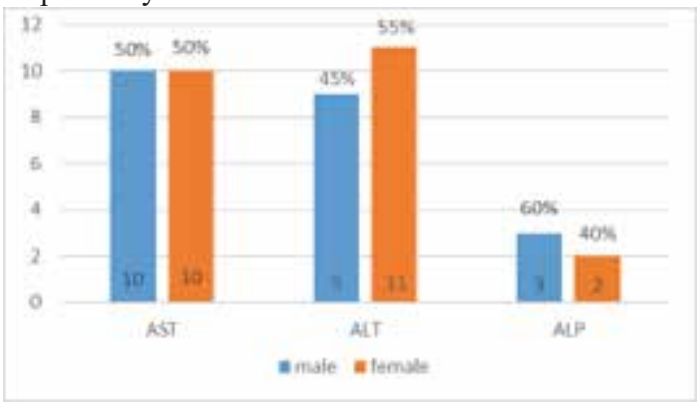

Figure 3 Level of Liver Enzymes between Age Group (61-90yrs)

DISCUSSION

Dengue fever, caused by a mosquito-borne viral infection, is the most notable illness of its kind. This tropical disease impacts a staggering number of individuals worldwide, affecting up to 100 million people. Dengue virus affects the reticuloendothelial system of the host directly that cause dysfunction of liver cells. Liver cells are affected directly by the virus or by dysregulated immune response of the host. Hence, liver function tests play a vital role in diagnosing dengue fever and assessing its severity, as they can indicate an increase in aminotransferase levels.

A study conducted by Kittitrakul and colleagues in Thailand, 127 adult dengue patients are recruited and liver function tests indicated raised level of transaminases in almost all patients at 7th day of infection. The abnormal level of aspartate transaminase (AST) and alanine transaminase (ALT) were found in 88.2% and 69.3% of patients. The ratio of abnormal transaminase (aspartate transaminase and alanine transaminase) was 1:8:1. Abnormal level of aspartate transaminase (AST) was found in febrile stage and it is associated with the bleeding. While abnormal level of alanine transaminase (ALT) is also found in febrile stage but it is associated with shock(15).

Another study conducted by Itha, Srivenu, et al, 45 diagnosed dengue patients were selected out of which 43 (96%) patients had elevated level of aspartate transaminase (AST) and alanine transaminase (ALT) but in severe disease aspartate transaminase (AST) and alanine transaminase (ALT) was increased up to 5-folds. While the raised transaminases were observed in adult patients. It was also observed in the study that 7 patients were died with dengue fever out of which 2 patients were suffered with acute liver failure(16). Similar results were observed in the study undertaken in 2023 at Hayatabad Medical Complex, Peshawar by Nazir Shah and colleagues. Severe increased in the level of alanine transaminase (ALT >300U/L) in dengue fever was associated with prolonged hospital stay and acute liver failure(17).

Saiful Safuan Md Sani, et al., studied the evaluation of creatinine kinase and liver enzymes in identification of severe dengue. The study showed that the data were collected from 365 patients, out of which 22 (6%) patients had severe dengue fever. Liver function tests and creatinine kinase of these patients were performed. The results indicated that the level of liver enzymes were elevated in dengue fever however the level of creatinine kinase did not differ by dengue fever(18).

TL. Nguyen et al., studied the impact of dengue hemorrhagic fever on liver function. The study shows the data were collected from 45 patients with confirmed dengue hemorrhagic fever. The level of serum transaminase was measured in these patients. The results showed abnormal level of aspartate transaminase and alanine transaminase in 97.7% and 37.3% of patients. While the level of aspartate transaminase is 5 times higher than the level of alanine transaminase in mild to moderate cases(19).

In 2018 by Mukker, Payal, and Smitha Kiran, studied 123 dengue cases. The result indicated low level of platelets (thrombocytopenia <1lakh) in 121 patients and more the 1 lakh in 2 patients. While lowest platelet count was observed in patients with low age range(20). Our results are comparable to these studies as it indicates adults between the ages of 31 and 60 were most frequently affected by low platelet counts. Aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) levels were also found to be increased in individuals between the ages of 5 and 30 in 26%, 27%, and 8.5% of instances, respectively. The majority of patients with higher AST, ALT, and ALP values were between the ages of 31 and 60, with 53.5%, 52%, and 15.7% of patients displaying increased levels, respectively. In 14%, 14%, and 3.7% of patients between 61 and 90 years old, respectively, increased levels of AST, ALT, and ALP were found.

CONCLUSION

It is concluded that dengue fever causes low platelet count and elevation in liver enzymes especially in aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP). The elevation of aminotransferases and low platelet count is most common in adults. Dengue virus also affects the hepatic cells and lead to hepatocellular injury that cause elevation of liver enzymes.

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All raw and processed data is available.

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Authors Contributions:

Taha Sahar and Alishba Abid: Substantial contributions to the conception and design of the work.

Rehmat Ullah: Design of the work and the acquisition. Drafting the work.

Alia Bibi: Final approval of the version to be published.

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