



## FREQUENCY AND SEVERITY OF LIVER INVOLVEMENT IN DENGUE VIRUS INFECTION.

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**ABSTRACT...** To determine the frequency & severity of liver involvement in dengue infection among adults at tertiary care hospital. **Study Design:** Cross-sectional study. **Setting:** Department of Gastroenterology and Department of Medicine Liaquat National Hospital, Karachi. **Period:** Six months (9th May 2016 to 9th Nov 2016). **Materials and Methods:** A total of 343 patients with Dengue fever were selected to conduct this study with mean age of  $34.67 \pm 9.09$  years. **Results:** Mean duration of the fever was  $7.31 \pm 1.62$  days. Mean duration of hospital stay of the patients came out to be  $3.50 \pm 0.82$  days. Severity of liver enzymes derangement was mild in 80 patients (23%), moderate in 246 (72%) & severe in 17(5%). Mortality was seen in 14% (47 patients) & 100% mortality was seen in dengue fever patients with severely deranged Liver enzymes. **Conclusion:** Dengue fever patients with deranged liver enzymes had statistically worse outcome thus can lead to early recognition of high risk cases.

**Key words:** Bleeding Diathesis, Dengue Virus, Hepatitis, Liver.

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### INTRODUCTION

Dengue virus infection (DI) is an important health problem in many southeast Asian Countries.<sup>1-2</sup> In recent years, several epidemics of DI have been reported from India.<sup>3-4</sup> Liver involvement is known to occur in children with DI;<sup>4-7</sup> a few patients have presented with clinical illness resembling liver failure.<sup>6,7</sup> The severity of liver dysfunction varies according to the type of clinical presentation of DI, being more common in patients with complicated dengue.<sup>8-10</sup> A study reports that severe hepatitis was present in 15% and mild to moderate hepatitis in 71%.<sup>11</sup> Literature further shows that dengue fever has also been associated with acute liver failure.<sup>12,13</sup> It has also been reported that high bilirubin level may act as a bad prognostic marker in patients with dengue infection.<sup>14</sup> Another study shows that higher AST and ALT have association with worse outcome thus can lead to early recognition of high risk cases.<sup>15</sup> Severe disease leads to two issues i.e. abnormal endothelial function & blood clotting system.<sup>16</sup> Endothelial malfunction causes leakage of fluid from blood vasculature in the abdominal and chest cavities while coagulation malfunction

responsible for bleeding diathesis. Multiplication of viral load in serum and involvement of organs (liver) associated with severe disease and spread of infection.<sup>17</sup> The rationale of this study was to assess the frequency of deranged liver function tests with severity of dengue fever. As this study was conducted in a well-known tertiary care hospital where people come from every nook and corner so on that basis we were able to pick the severity earlier and manage accordingly and save lives.

### PATIENTS AND METHODS

This cross-sectional study (9th May 2016 to 9th Nov 2016) was conducted in department of Gastroenterology and department of Medicine Liaquat National Hospital, Karachi for the evaluation of frequency of severity of liver involvement in dengue fever patients in a tertiary care hospital. The inclusion criteria were;

1. Either gender
2. Age 20-60
3. Ability and willingness to sign informed consent
4. Available for the study period

- Dengue diagnosed pt as per operational definition

While the exclusion criteria were;

- History of auto-immune disease
- Pt having MP/ICT test +ve
- Patient with ITP, Liver Disease [i.e. HBV, HCV]
- Currently taking anti-coagulant medication, aspirin or non-steroidal anti-inflammatory drugs (NSAIDs), Hakeem medication
- Hepatotoxic drug for the last 6 months
- Pregnant patients
- Age < 20 and > 60 years

### Liver Involvement

Liver involvement was assessed in terms of mild, moderate and severe and assessed on SGPT level. The range for ALT was taken 7 - 32 IU/L: normal 33 - 66 IU/L (SGPT more than normal but less than 3 times): mild disease, 67 - 319 IU/L (SGPT more than 3 times but less than 10 times): moderate disease 320 IU/L and above: (SGPT more than 10 times of normal) severe disease.

For AST, the grouping was 5 - 40 IU/L: normal 41 - 80 IU/L: mild disease, 81 - 250 IU/L: moderate disease 251 IU/L and above: severe disease.

### Dengue Fever

The diagnosis was made on the basis of Positive serology & Immunoenzymatic assay presence of any one or both were labeled as dengue patient; Platelet count  $\leq 100,000/\text{mm}^3$ , any spontaneous hemorrhagic manifestation, evidence of plasma leakage (i.e., pleural effusion, hypoalbuminemia, ascites, or a variation in hematocrit > 10%).

All patients attended inpatient department of General Medicine & gastroenterology in Liaquat National Hospital, Karachi, who fulfill the inclusion criteria were included in the study. Positive serology & Immunoenzymatic assay was used to Diagnose Dengue fever. Outcome variables according to liver involvement were defined as mild, moderate & severe while the exclusion criteria were followed strictly to avoid confounding variables. SPSS version 17 was used for data analysis. Frequencies and percentages and mean

$\pm$  SD were computed. The post stratification chi-square test was used and the  $p \leq 0.05$  was considered level of significance.

### RESULTS

A total of 343 patients with dengue fever were selected to conduct this study. The mean age  $\pm$  SD was  $34.67 \pm 9.09$  years. The distribution of age and gender is presented in Figure-1 and 2. The descriptive statistics of age is presented in Table-I. The age was stratified in two groups, 223 patients (65%) were males & 120 patients 35% were females. Mean duration of the fever was  $7.31 \pm 1.62$  days. The frequency and percentages are presented in Table-I to III.

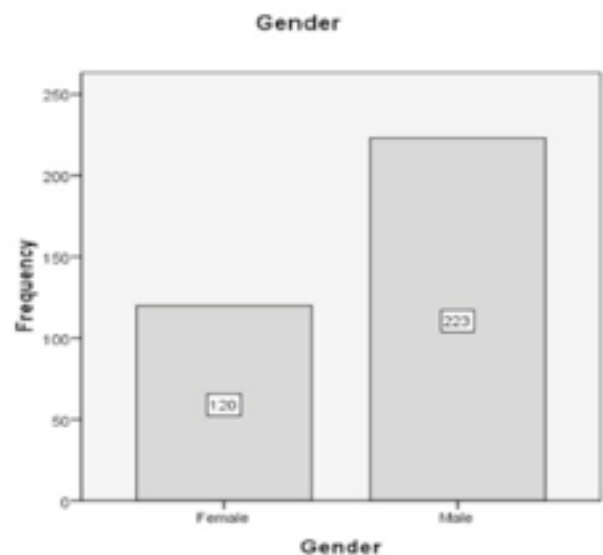


Figure-1. Frequency distribution of gender

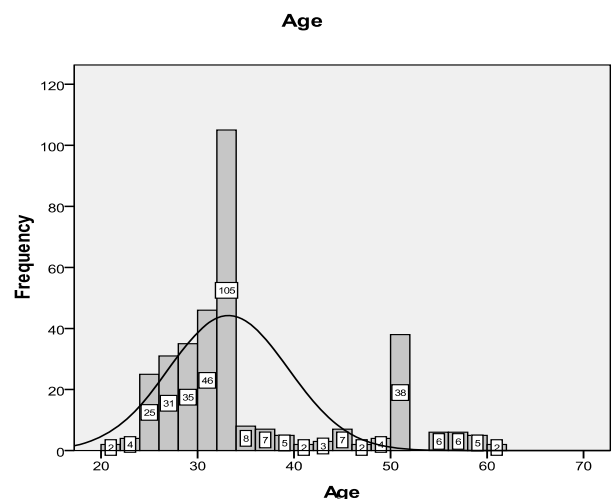


Figure-2. Frequency distribution of age (years)

Severity	Frequency (n)	Percentage (%)
Mild	80	23.3%
Moderate	246	71.7%
Severe	17	5.0%
Total	343	100%

**Table-I. Frequency distribution of severity of liver enzyme derangement (n=343)**

Severity of Liver Enzyme Derangement					
Gen-der	Mild (n=80)	Moderate (n=246)	Severe (n=17)	Total	P-Value
Male	80	126	17	223	0.000
Female	0	120	0	120	
Total	80	246	17	343	

**Table-II. Distribution of severity of liver enzyme derangement according to gender (n=343)**

Severity of Liver Enzyme Derangement					
Dura-tion of Fever	Mild (n=80)	Moderate (n=246)	Severe (n=17)	Total	P-Value
5-8 Days	80	210	0	290	0.000
9-12 Days	0	36	17	53	
Total	80	246	17	343	

**Table-III. Distribution of severity of liver enzyme derangement according to duration of fever (n=343)**

## DISCUSSION

Dengue is a mosquito-borne viral infection of humans which affects up to 100 million people across the tropical world.<sup>18</sup> There are four serotypes of the virus and spectrum of disease ranges from asymptomatic infection to acute Dengue hemorrhagic fever with complications.<sup>19</sup> Acute Dengue hemorrhage fever begins as a febrile illness categorized by high grade fever, bone pains, headache and other non-specific symptoms difficult to distinguish from any other viral illness.<sup>20-22</sup> More severe cases develop circulatory collapse due to increased vascular permeability, multiple organ failure. Dengue shock syndrome, bleeding due to thrombocytopenia and deranged hemostasis. No specific antiviral therapy is available. In recent years, there has been a marked increase in cases of Dengue fever in South-East Asia in adult population with Dengue fever requiring hospitalization, thus increasing the economic burden.<sup>23</sup> To combat the

problem, it is required to study the clinical profile and evolution of different laboratory parameters in this infection. Dengue virus directly affects the reticuloendothelial system of the host. Hepatic dysfunction is thus a well recognized feature of Dengue infections.<sup>24-26</sup> Injury to liver cells could result both from direct effect of the virus or due to unregulated immune response of the host;<sup>27</sup> hence liver function tests are of significance for timely diagnosis and assessment of severity of Dengue fever. It was observed in this study that mortality and complications of acute Dengue fever significantly correlated with liver dysfunction and raised aminotransferases. ALT was higher in patients with septicemia, hepatica and renal failure and in patients who died, AST was significantly raised in patients with DHF, DSS, septicemia, hepatic and respiratory failure, also in patients with encephalopathy. Raised aminotransferase were also reported by Souza et al and Chhina RS et al.<sup>28,29</sup>

## CONCLUSION

AST and ALT were statistically higher in patients with worse outcome thus can lead to early recognition of high risk cases.

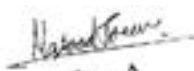


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**AUTHORSHIP AND CONTRIBUTION DECLARATION**

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Masood Tareen	Contributions to conception and design, acquisition of data, analysis and interpretation of data.	
2	Riaz Hussain Awan	Drafting of the article and shares its expert research opinion and experience in finalizing the manuscript.	
3	Seema Nayab	Contributed in conception and interpretation of data and give his expert view for manuscript designing.	
4	Khadim Hussain Awan	Collection and acquisition of data, analysis and interpretation of data and make it suitable for final revision and a corresponding author.	