Original Article

Prevalence of Hepatic Dysfunction and its Clinical and Biochemical Spectrum in Children Presenting with Dengue Fever

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ABSTRACT

Objective: To determine the prevalence of hepatic dysfunction and it's clinical and biochemical spectrum in children presenting with dengue fever.

Study Design: A prospective cross-sectional study

Place and Duration of Study: This study was conducted at the Khairpur, Medical College and Teaching Hospital, from June 2017 to June 2020.

Materials and Methods: Liver function of the patientswas assessed clinically as well as biochemically.

Results: Hepatic dysfunction was observed 27.5% of patients. 58% were males and 42% were females. 69.5%, 25.2% and 07% had DF (Dengue fever), DHF (Dengue hemorrhagic fever) and DSS (Dengue shock syndrome) with increasing severity of hepatic involvement.

Conclusion: Dengue fever can manifest with hepatic involvement. Children presenting with jaundice, hepatomegaly and elevated transaminases should raise the possibility of dengue infection and its severity.

Key Words: Hepatic dysfunction, Dengue fever,dengue hemorrhagic fever and dengue shock syndrome

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INTRODUCTION

Dengue is a mosquito-borne acute febrile disease (Aedes aegypti*)* with an expanded geographic distribution occurring predominantly in tropical and subtropical areas of the world.[1-2]It has four serotypes called DEN-1, DEN-2, DEN-3 and DEN-4 and belongs to RNA Flavi virus family.[3] It has increased epidemic activity in our country with myriad of clinical and severity presentations. [4]

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The incubation period after the person has been bitten by the mosquito ranges from 3 to 14 days, after which the patient exhibits febrile phase in which dengue viruses may circulate in the peripheral blood. [5] It is followed by a short afebrile and finally a long convalescence phase. [6]

The febrile stage is characterized by constitutional symptoms like fever, malaise, retro-orbital headache, nausea, vomiting, body pains and macular or maculopapular rash.[7-8] Later, the patient may develop bleeding, thrombocytopenia**,** ascites, pleural effusion, hematocrit which signify progression to more sever life-threatening dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS). [9-10] Timely identification of classic dengue fever symptoms and severity is of paramount importance to prevent morbidity and mortality. [11-12]

Dengue fever may present with rare signs and symptoms affecting liver and CNS which indicates bad outcome.[13] The intensity of liver nonfunctioning fluctuates from slight to severe damage. Hepatotoxicity appears to be the result from virus itself, host immune response, metabolic acidosis and/or hypoxia. [14] They may present with mild elevation of transaminases or clinically with jaundice and hepatic failure. [15] The outcome worsens with severity of dengue infection. Recent literature has shown prevalence of hepatic dysfunction to be 14.3%.[16]The study aims to determine the prevalence of hepatic dysfunction in our population as there is paucity of local data. Moreover, data from our study would improve knowledge base of the

clinicians. Therefore, timely diagnosis and quick beginning of suitable sympathetic management would help in preventing adverse outcomes.

MATERIALS AND METHODS

Permission from the ethical review committee of the institute was taken prior to initiation of the study. Informed consent was taken from the parents of each participant of the study in local language for assigning them to sample and using their data in research. Brief history about demographic information was taken.

This was a prospective study which was carried out in the Pediatric Department, Khairpur Medical College and Teaching Hospital. The study duration was between June 2017 and June 2020. A total of 131 reported patients admitted between 2 years and 15 years old were tested in compliance with WHO recommendations and only dengue IgM catch ELISA was serologically confirmed and included in the study. The dengue fever (DF), DHF and DSS were categorized according to the 1997 WHO Classification. Hepatic disorder was labelled as more than 200 U/L patients with Serum Alanin Transaminase (ALT) or Aspartate Transaminase (AST) levels.

Patients having malaria, enteric fever, hepatitis B/C, HIV and malnutrition were excluded by history, examination and investigations. Statistical analysis was done with the help of SPSS version 22. The numerical data was presented as mean and standard deviation and frequency and percentages were calculated for qualitative. The chi-square test was applied to compare the proportions among the groups. P-value ≤ 0.05 was considered as significant level**.**

RESULTS

During the study period, 131 patients were found to have positive serology to dengue virus by ELISA. Among these 76 (58%) were males while the rest were females 55 (42%). Their ages ranged from 2 years to 12 years with a mean age of 6.66±2.01 years. The age distribution showed that the majority of the children were over 6 years of age (55.7%) with 44.3% under 6 years of age.

In our results, DF (Denge Fiever), DHF (Denge hemorrhagic Fiver) and DSS (Dengue Shock syndrome) were observed at 69.5%, 25.2% and 07%. There was 27.5% frequency of hepatic dysfunction (Table 1). All cases presented with fever (100%) and a majority also had an accompanying viral syndrome with body aches and vomiting in patients with dengue fever, dengue hemorrhagic fever and dengue shock syndrome. Hepatomegaly was observed in 63.6% and 100% of children with DHF and DSS compared to 46.1% in DF. Majority of the children with DSS were icteric. Table 2 shows clinical profile liver function test and ultrasound graphic results in different dengue infection groups.

Table No.1: Hepatic Dysfunction with respect to General Characteristics of the Patients (n=234)

Variables	Total n (%)	Hepatic Dysfunction		P-Value
		Yes N=36 N (%)	No N=95 N (%)	
Age (Years)	6.66±2.01	6.25±0.79	6.12±1.14	
≤6	58 (44.3)	15 (25.9)	43 (74.1)	0.43
>6	73 (55.7)	21 (28.8)	52 (71.2)	
Gender				
Male	76 (58)	21 (27.6)	55 (72.4)	0.56
Female	55 (42)	15 (27.3)	40 (72.7)	

Chi-Square Test Applied, P-Value <0.05 Taken As Significant

Table No.2: Clinical and Biochemical Parameters of Dengue Fever (n=234)

Clinical And Biochemical Parameters	Dengue Fever (n=91)	Dengue Hemorrhagic Fever (n=33)	Dengue Shock Syndrome (n=07)
Symptoms			
Fever	91(100%)	33 (100%)	07 (100%)
Body Aches	91(100%)	33 (100%)	07 (100%)
Vomiting	91(100%)	33 (100%)	07 (100%)
Facial Puffiness	33(36.2%)	16 (48.4%)	04 (57.1%)
Maculopapular Rash	51 (56%)	18 (54.5%)	05 (71.4%)
Petechial Spots	49(53.8%)	17 (51.5%)	07 (100%)
Signs			
Jaundice	51 (56%)	19 (57.5%)	06 (85.7%)
Hepatomegaly	42(46.1%)	21 (63.6%)	07 (100%)
Hepatic Tenderness	33(36.2%)	24 (72.7%)	07 (100%)
Hepatic Dysfunction			
Elevated Alt	48(52.7%)	24 (72.7%)	06 (85.7%)
Elevated Ast	39(42.8%)	21 (63.6%)	05 (71.4%)
Elevated Bilirubin	42(46.1%)	19 (57.5%)	05 (71.4%)
Ascites	02(2.19%)	08 (24.2%)	03 (42.8%)
Gall Bladder Wall Thickening >5mm	03(3.29%)	04 (12.1%)	05 (71.4%)

DISCUSSION

Dengue is an important arboviral disease with higher viral load resulting in multiple organ system involvement.[16] It can be attributed to direct viral toxicity or immunogenic response towards the virus. [17] Both hepatocytes and Kupffer cells appear to the prime target of DENV infection manifesting with elevation of liver enzymes and ALF.[18] Hepatic dysfunction in our study was found to be 27.5%. Findings of this study are comparable with other International and local study. It ranges from 36.4-96%.[19-20]In one study by Iqbal et al, he found the overall prevalence to be 12.69%.[21] Jagadish Kumar et al reported hepatic dysfunction to be

17.27%.[22] However, another study indicted the prevalence to be 14.3%.[16]Hepatic dysfunction with respect to age and gender showed that many cases who had it remained in > 6 age group and male gender group, which could be attributed to cultural norms of our society encouraging males to outdoor activities thereby exposing them to being bitten with mosquitoes more than females.

Clinically enlarged liver is the main characteristic feature of dengue contagion. Among 131 cases in this study, 46.1%, 63.6% and 100% had hepatomegaly in children who had DF, DHF and DSS.

The similar finding of hepatomegaly in dengue infection has been seen in children from 43-96%.[23] Mohan, Kulkarni, Jagadish Kumar and Roy et al reported it to be 87%, 90%, 79% and 94%.[22-26]Our study found elevated ALT (52.7%, 72.7% and 85.7%) and AST (42.8%, 63.6% and 71.4%). Similar pattern was seen in a study done by Iqbal et al showing raised ALT (82.7%, 81.2% and 52.6%) and elevated AST (64.2%, 75% and 89.6%) in an aforementioned manner. [16]In comparison, ALT was elevated by 69.4% of DF, 84.6% of DHF and 92% of DSS, and by AST, 88% of DF, 80% of DHF and 96% of DSS, by Jagadish Kumar et al. [22]

Dengue has a wide spectrum of clinical manifestations which requires timely identification and monitoring. Children presenting with classic dengue symptomology should also be evaluated for hepatic biochemical and clinical parameters as they could aid in diagnosis and management of patients. Especially in the pediatric population as liver involvement is more common and severe when compared with adult population. Finally, drugs with the potential to cause or exacerbate liver damage should be avoided.

CONCLUSION

Dengue's liver relationship ranges from jaundice to acute liver failure. Clinical findings of hepatomegaly and jaundice are important. Monitoring biochemical liver profile is important at the time of diagnosis and management as they raise the possibility of dengue infection severity.

Author's Contribution:

Concept & Design of Study:	Kamran Ali Shahani
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Revisiting Critically:	Kamran Ali Shahani, Faiza Shahani
Final Approval of version:	Kamran Ali Shahani

Conflict of Interest: The study has no conflict of interest to declare by any author.

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