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DENGUE FEVER;
HEPATIC INVOLVEMENT IN CHILDREN UPTO 12 YEARS OF AGE

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ABSTRACT… Introduction: Dengue can indicate a diverse clinical spectrum. The intensity of hepatic involvement in patients, with dengue infection varies from soft injury to severe injury by means of jaundice and liver cell failure. Even if liver is not a most important objective limb, liver involvement is a renowned aspect. **Objectives:** The objective of this study was to assess liver involvement in dengue patients upto 12 years of age. **Study Design:** The study was Prospective observational. **Place and Duration of Study:** Study was conducted in children ward, Paediatric Department, Holy Family Hospital Rawalpindi from August 2014 to October 2015. **Methods:** Upto 12 years of age, all suspected dengue children patients were screened and solitary serologically established cases by dengue IgM capture ELISA were incorporated in the study after taking written permission from the parents of the patients. Patients were categorized according to GCP dengue guidelines into dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). **Results:** Among 146 children, 78 were in the group of DF, 35 were in the group of DHF and 33 were in the group of DSS. Most children (70 %) were above 5 years. Fever was the leading illness followed by body aches, hepatomegly, rashes, edema, headache, petechiae, hepatic tenderness, pain in abdomen, vomiting, mucosal bleed and jaundice. Children with DSS have more liver involvement. Hepatomegaly and thickening of gall bladder was maximum in children with DSS and can be an indication of severe illness. Serum bilirubin, serum albumin, liver enzymes like ALT, AST and ALP were considerably elevated in children with DSS as compare to other two groups. 32 patients out of 33 with DSS had liver involvement. **Conclusion:** Dengue fever has become a main health issues at the moment in Pakistan. Hepatic association in dengue in children has high fatality rate and spectrum varies from jaundice to rise of liver enzymes.

Key words: Dengue in children, hepatomegaly, hepatic dysfunction.

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INTRODUCTION

Dengue fever is due to arthropod born viruses.[1] It is mainly frequent mosquito born, arboviral disease in various tropical and sub-tropical areas of world. The occurrence has increased 30-fold with growing geographic growth to new countries and in the current decade from city to rural settings.[2]

According to world health organization (WHO) approximately 50-100 million infections take place yearly and mostly among children.[3] Dengue virus is widespread and it hits the highest point in post monsoon phase and floods make the state terrible in Pakistan.[4] Evidence suggests that in Pakistan, overall weight of disease and its severity is on the rise.[5] unexpected manifestations linking hepatic and vital nervous system in dengue illness has reported.[6,7] The extent of liver involvement with dengue infection in children vary from soft injury with rise of transaminases to severe injury with jaundice and liver cell breakdown.[8-11] Frequency of liver involvement is more in dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF).[6,8-14] Before time identification and timely initiations of suitable supportive treatment can reduce the morbidity and death. A large amount of the statistics reported on irregular hepatic functions in dengue fever are retrospective.[6,10,12,13] This prospective observational study was intended to assess the spectrum of hepatic involvement in children with dengue infection.

OBJECTIVE

To evaluate hepatic involvement in dengue fever in children.

MATERIALS AND METHODS

This study was conducted in children ward, Paediatric Department, Holy Family Hospital and Rawalpindi Medical College from August 2014 to October 2015. All suspected dengue patients from Dengue Emergency upto 12 years of age were screened and only serologically confirmed cases by dengue IgM capture ELISA were included in study after obtaining written informed consent from the parents of the patients. Dengue Expert Advisory Group (DEAG) Good Clinical Practice Guidelines for the management of dengue Infection referred as GCP dengue guidelines 2012 were applied for grouping of patients into dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[15]

Complete history was taken. Detailed medical assessment was carried out in each case. Data was collected in a pre written Performa.

Those children who had recognized hematological disorder, like pre existing liver diseases, malaria, hepatitis A and B, typhoid and those whose consent could not be obtained were excluded from study. Investigation which includes, total count (TC), dengue NS1 Ag, IgM ELISA, hemoglobin (Hb), differential leukocyte count (DLC), platelet count, Hematocrite (HCT), peripheral blood smear, serum bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (AP), serum albumin, prothrombin time (PT), activated partial thromboplastin time (APTT), INR, ultrasound abdomen and chest X-ray were done.

The data was entered and analyzed with SPSS 22. Categorical variables were expressed in actual numbers and percentages and Continuous variables were expressed as mean $\pm$ standard deviation. Categorical variables were compared across groups by performing One Way-ANOVA test. P value <0.05 was considered statistically significant.

RESULTS

The study group included 146 children, 92 were male and 54 were female. Minimum age of patient was 3 months and maximum age was 12 years with mean age 6.2 $\pm$ 1.2 years, satisfying the GCP criteria for dengue fever exclusive of malaria, enteric fever, Hepatitis A and Hepatitis B.[16] Out of 146 children that were enrolled, 78 were in the group of DF, 35 were in the group of DHF and 33 were in the group of DSS. The majority (78%) were above 5 years. Fever (100%) was the chief complaint in all cases followed by body aches (58.22%), hepatomegly (49.32%), rashes (42.47%), edema (41.78%), headache (31.5%), petechiae (28.1%), hepatic tenderness (28.08%), pain in abdomen (26%), vomiting (23.97%), mucosal bleed (16.44%) and jaundice (7.53%). Out of 146 children, 72 (49.32 %) had hepatomegaly, noticed more in DSS and DHF (93.93% and 85.7%) than in DF (14.1%) group ($P>0.001$). Hepatic tenderness has been observed in 41 (28.08%) children which was noticed more in DSS and DHF (54.54% and 54.28%) than in DF (5.12%) children ($P>0.001$). Distribution of study subjects according to clinical presentation is given in Table-I and details of Signs and Symptoms in all three groups are given in Table-II.

Clinical Presentation	Frequency	Percentage (%)
Fever	146	100
Edema	61	41.78
Headache	46	31.5
Vomiting	35	23.97
Abdominal Pain	38	26
Bodyache	85	58.22
Mucosal bleed	24	16.44
Petechiae	41	28.1
Rash	62	42.47
Jaundice	11	7.53
Hepatomegaly	72	49.32
Hepatic tenderness	41	28.08

Table-I. Distribution of study subjects according to clinical presentation

Symptoms	DF (n=78) (53.4%)		DHF (n=35) (24 %)		DSS (n=33) (22.6%)	
	freq	%	freq	%	freq	%
Fever	78	100	35	100	33	100
Edema	19	24.36	25	71.4	17	51.5
Headache	33	42.3	6	17.14	7	21.2
Vomiting	5	6.4	7	20	23	69.7
Abdominal Pain	5	6.4	9	25.7	24	72.7
Body ache	46	58.97	24	68.57	15	45.45
Mucosal bleed	2	2.56	11	31.43	11	33.33
Petechiae	16	20.5	13	37.14	12	36.36
Rash	38	48.7	10	28.57	14	42.42
Jaundice	1	1.28	2	5.71	8	24.24
Hepatomegaly	11	14.1	30	85.7	31	93.93
Hepatic tenderness	4	5.12	19	54.28	18	54.54

Table-II. Details of symptoms and sings in all three groups

Parameters	DF (n=78)		DHF (n=35)		DSS (n=33)	
	freq	%	freq	%	freq	%
Jaundice	1	1.28	2	5.71	8	24.24
Hepatomegaly	11	14.1	30	85.7	31	93.93
Hyperbilirubinemia	1	1.28	2	5.71	8	24.24
Hypoalbuminemia	7	8.97	23	65.7	20	60.6
Elevated ALT	58	74.36	30	85.7	30	90.9
Elevated AST	68	87.18	32	91.4	32	96.97
Elevated ALP	36	46.15	28	80	28	84.85
Prolonged PT	5	6.14	11	31.43	13	39.39
INR	2	2.56	9	25.7	15	45.45
Gall bladder thickness	4	5.13	7	20	19	57.58

Table-III. Hepatic involvement in all three groups

Hepatic Involvement in all three groups is given in Table-III. Jaundice was present in 24.24% patients of DSS, 5.71% patients of DHF and 1.28% patients of DF. Hepatomegaly was present 93.93% in group DSS, which was statistically significant when compared with group DHF (85.7%) and group DF (14.1%). Hypoalbuminemia was present 65.7% in group DHF, 60.6% in group DSS and 8.97% in group DF. ALT levels were observed raised in 90.9%, 85.7% and 74.36% in group DSS, DHF and DF respectively which is statistically significant with p value 0.008. AST levels were observed raised in 96.97% in group DSS, 91.4% in group DHF and 87.18% in group DF but the difference has no statistical significance. Alkaline phosphates levels were raised in 46.15% cases with DF, 80% cases with DHF and 84.85% cases of DSS and the difference was statistically significant with p value <0.001. Coagulation abnormalities occurred in more numbers in group DSS as compared to other two groups. PT was prolonged in 39.39% and INR was deranged in 45.45% in group DSS which was clinically significant. Thickening of gall bladder occurred in 57.58% in group DSS, 20% in group DHF and 5.13% in group DF and the difference was statistically significant. Out of 33 patients with DSS, 32 had hepatic dysfunction.

DISCUSSION

An attempt has been made to learn the profile of hepatic involvement in patients with dengue infection. Presentation of dengue virus infection varies from asymptomatic patients to patients with undifferentiated elevated fever. Bulk of the patients were male in our study that is similar finding in other studies published in India.[16,17] This could be explained that male children have their involvement in outdoor activities during day timings which lead to more exposure.

Hepatic involvement in dengue infections is often demonstrated clinically by hepatomegaly or biochemically by increase in liver enzymes. In our study hepatic dysfunction is more common in patients with DSS. The degree of liver function tests derangement was observed more in DSS as compared to other two groups.

In our study hepatomegaly is a common clinical signs (93.93% of patients with DSS) and thickening of gall bladder wall is common radiological sign (57.58% of children with DSS) and can indicate presence of severe disease ($P<0.001$). Similar involvement of hepatomegaly in dengue has been identified in a study by Kalenahalli.[18] Some recent studies suggested that hepatomegaly is present in 50–100% of cases,[9,10,19-24] as others document a moderate rate of hepatomegaly.[11,25,26] Most studies observed high level of hepatomegaly in DSS.

Elevated enzymes are sensitive indicators of liver damage in dengue patients, as has been identified in numerous studies.[9,10,11,19,23] Our data suggests that serum bilirubin, serum albumin and liver enzymes (ALT, AST, ALP) were considerably elevated in patients with DSS as compare to other two groups. P value is significant for all parameters except for AST. All three groups have elevated AST, P value cannot predict sternness of dengue being insignificant. Most of the children have meek or modest rise of these transaminases and some of them have rise by 10-fold or greater. AST level is usually higher than ALT in children with dengue during the first week of infection, with a decrease to standard levels within three weeks. Similar findings has been identified in a study by Gandhi .[27] A number of authors have published that the levels of serum AST are more than serum ALT, which is dissimilar to the normal finding of viral hepatitis.[28] Overall, the studies have shown uniformity, with high level of liver enzymes being a frequent feature of dengue disease and as such possibly represent a discriminating factor in differentiating dengue from other febrile diseases.

CONCLUSION

Dengue fever is becoming one of the major health issues at the moment in Pakistan. Hepatic association in dengue in children has high fatality rate and spectrum varies from jaundice to rise of liver enzymes. Clinical signs along with symptoms make it complex to differentiate liver dysfunction in dengue from other common causes such as viral hepatitis. Elevated indicator of doubt is significant for diagnosis of these patients for improving outcome of the disease. Incidence of hepatomegaly, jaundice and fever in widespread areas should stimulate the doubt of dengue hepatitis.

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