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Original Research Article

Assessment of Various Clinical Presentation, Hepatic Abnormalities, and Ultrasonographic Findings in Dengue Fever And its Association with Severity of the Disease

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Abstract

Objectives: The goal of this study is to look at the clinical presentation, hepatic abnormalities, and ultrasonographic findings in dengue fever, dengue hemorrhagic fever, and dengue shock syndrome, and to see how these connect to the severity of the disease.

Material & Methods: Based on their clinical symptoms, 205 hospitalized Dengue fever patients were categorized as DF/DHF/DSS. SGOT, SGPT, PT, APTT, and INR were all monitored in the lab. Abdomen and thorax ultrasonography were performed.

Results: The study analyzed hepatic enzymes, coagulation workup, and ultrasonographic markers in DF/DHF/DSS.

Conclusion: The treating physician may have difficulties when dealing with severe dengue. Thus, utilizing hepatic and ultrasound indicators, early detection of deterioration in clinical condition may be reasonably assessed which will improve the management of dengue sickness and thus reduce mortality and morbidity.

Keywords: dengue, ultrasonography, hepatic enzymes

Introduction

Dengue virus infection is a major and important public health problem in many South East Asian countries and also in more than 100 countries of tropical and subtropical region. [1, 2, 3]Dengue fever ranks as the most important mosquito borne viral disease in the world. The emergence and spread of all four dengue viruses (serotypes) represent a global pandemic. While dengue is a global concern, currently close to75% of the global population exposed to dengue are in the Asia-Pacific region. It is also reported in various literatures that high morbidity and mortality in DF/DHF is due to multiorgan involvement. [4]

People who are infected with the dengue virus are usually asymptomatic (80 percent). Mild symptoms, such as a low-grade temperature, are possible. [5] Dengue infection has been linked to hepatic damage since 1967. [6]

Liver dysfunction in patients with dengue varies from mild injury with elevation of transaminase activity. Hepatomegaly (tender/non tender) to severe hepatocyte injury resulting in jaundice may also occur [1]. Hepatic dysfunction is caused by a direct effect on liver cells or as a consequence of deranged host immune response against the virus. Other factors including race, diabetes, haemoglobinopathies, pre-existing liver damage and the use of hepatotoxic drugs may also play a role. [7]

Ultrasonography (USG) of the chest and abdomen is a cheap, rapid and widely available noninvasive imaging method which can be an important adjunct to clinical profile and early diagnosis of DF prior to obtaining serologic confirmation test results. [8] The ultrasound findings in early milder form of DF include GB (gall bladder) wall thickening, pericholecystic fluid and hepatosplenomegaly. Severe forms of the disease are characterized by fluid collection in the perirenal and pararenal region, hepatic and splenic subcapsular fluid, and more commonly generalized ascites. Ultrasound has two potential uses in the management ofdengue fever. Firstly, as a prognostic indicator, used toassess which patients are at severe risk of entering the critical phase. Secondly, ultrasound is used as means of monitoring for plasma leakage (ascites, pleural effusion and perinephric edema). It is also used to know the presence and degree of plasma leakage at various sites in the body in patients with dengue fever to facilitate early management and hence prevent fatal complications. [9]

Material & Methods:

A hospital based prospective study in Darbhanga Medical College & Hospital, Darbhanga, Bihar for 1 year . By simple random sampling method, 205 patients were selected from OPD of the hospital. The investigators employed a questionnaire to collect data, in which they entered and checked all of the symptoms and lab tests.

Inclusion criteria:

Children who were Dengue Non structural antigen protein 1 [NS1] and/or Immunoglobulin M [IgM] positive only were included in the study.

Exclusion criteria:

Children with other diseases like enteric fever, rickettsial fever, malaria, leptospirosis, septicemia and other viral hemorrhagic fevers.

Ethical committee clearance was taken prior to study. Consent from parents/caretakers of the patients was obtained during the study.

Methodology:

After clinical assessment, the patients were classified as DF/DHF/DSS. Lab investigations included CBC, WBC count, platelet count, hematocrit, SGOT, SGPT, PT, APTT and INR was monitored. Monitoring of hepatic and ultrasonographic parameters was done. Cut off value of prolonged activated partial thromboplastin time (APTT) was 38 second, elevated serum aminotransferase levels (aspartate aminotransferase (AST) or alanine aminotransferase (ALT) were >39 U/L). Liver enzymes and ultrasonographic parameters in DF/DHF/DSS were compared in the study.

Statistical methods:

The results were analyzed using standard normal test and student ‘t’test.

Results:

The mean SGOT and SGPT in DSS were statistically significant in this study. In

DSS, total serum bilirubin was higher than in DHF. The amounts of total protein, albumin, globulin, and ALP were not statistically significant. In all three groups, the coagulation profile was elevated.

Table 1 depicts the mean SGOT/SGPT in DHF and DSS was 132.7 and 89.6, respectively, which was statistically significant.The values of PT/INR/APTT was progressively more in 3 groups. (Table2). Table 3 illustrates total protein, albumin, globulin, and alkaline phosphatase levels in all the 3 groups were not statistically significant, however bilirubin levels were higher in DSS when compared to DHF. Ascites, hepatomegaly, pleural effusion and gall bladder thickening findings in ultrasound were statistically significant in DSS when compared to DHF. (Table 4)

USG revealed statistically significant ascites, pleural effusion, hepatomegaly, and gall bladder thickening in DSS compared to DHF (Table 1, 2, 3, 4).

Table-1: SGOT, SGPT levels in Dengue fever.

	Mean±SD	Mean±SD	Mean±SD	p-value
SGOT(U/L)	103±91.6	132.7±87.1	267.5±161.2	0.0001*
SGPT(U/L)	87.6±36.8	89.6±6.8	254.7±116.0	0.0001*

Table-2: Prothrombin time/INR, Activated partial thromboplastin time in dengue

	DF(N=36)	**DHF**(N=52**)**	**DSS**(N=12)	p-value
APTT(seconds)	37.7±6.8	59.3±8.6	65.9±10.2	0.005*
PT/INR	2.5±0.5	2.7±0.7	2.9±0.9	0.002*

Table-3: Protein, bilirubin and alkaline phosphatase abnormalities in dengue.

	DF(N=36)	**DHF**(N=52)	**DSS**(N=12)	p-value
Total protein (gm/dl)	8.3±0.5	7.8±0.6	8.9±1.2	0.956
Albumin (gm/dl)	6.8±0.5	6.8±0.6	6.3±1.0	0.267
Globulin (gm/dl)	4.1±0.7	3.1±0.7	4.2±0.9	0.248
Bilirubin (mg/dl)	2.1±0.4	2.7±1.6	3.8±2.7	0.005*
Alkaline phosphatase (IU/L)	216.6± 158.8	350.2±234.1	523.7±269.0	0.176

Table-4: Ultrasonographic abnormalities in dengue fever.

Variables	**DF**(N=68)	**DHF**(N=109)	**DSS**(N=28)	p-value
	N (%)	N (%)	N (%)	
Ascites	2(2.94)	39(35.7)	22(78.57)	0.0071*
Hepatomegaly	16(23.52)	31(28.44)	20(71.42)	0.0411*
Splenomegaly	0(0)	19(17.4)	11(39.28)	0.121
Pleural effusion	0(0)	12(11.00)	17(60.71)	0.00009*
GB thickening	0(0)	8(7.33)	10(35.71)	0.000001*

*P<0.05 is statistically significant

Discussion:

Dengue viral infections are one of the most important mosquito borne diseases in the world, caused by four serotypes (DEN1, DEN2, DEN3 and DEN4) of dengue virus. Presently dengue infection is endemic in 112 countries with annually 100 million cases of DF and 50 million cases of DHF occurring globally with an average case fatality rate of around 5%. The manifestations of dengue infections are protean from being asymptomatic to undifferentiated fever, severe dengue infections and unusual complications. Recent studies suggest that there is an upsurge of complicated dengue infections especially in South East and South Asia [10,11].

Dengue fever is a major public health hazard in the world's tropical and subtropical climates. According to the World Health Organization, 50-100 million cases occur annually in more than 100 endemic countries. DF/DHF outbreaks have been documented in several Indian states, including Andhra Pradesh, Karnataka, Kerala, and Maharashtra. Complex immunological mechanisms, T-cell mediated antibodies cross reactivity with vascular endothelium, enhancing antibodies, complement and its products, and numerous soluble mediators including cytokines and chemokines have all been postulated to explain signs and symptoms. Whatever the processes are, they eventually attack vascular endothelium, platelets, and numerous organs, resulting in vasculopathy and coagulopathy, which lead to bleeding and shock [12].

Hepatomegaly is one of the commonest clinical sign of dengue infection. Hepatomegaly is frequent and is commoner in patients with DHF than in those with DF [13]. Association of hepatomegaly with cases of dengue infection has been quite variable, the incidence varying from 43% to 98% whereas in the present study, it was observed in 79% of total cases as shown in the table below. The incidence of hepatomegaly was more in shock cases as compared to non-shock cases. The maximum liver size noted was 9 cm below the right costal margin in our study.

In the present study, mean AST/ALT in DHF and DSS was 132.7 and 89.6, respectively, which was statistically significant. In the study done by Dhrubajyoti et al, the AST was more than ALT in DHF and DSS which was significant. Transaminases levels, particularly AST levels, have been suggested as a potential marker for differentiating dengue from other viral infections during the early febrile phase. [3]

In a research by Bokade et al., bilirubin, serum albumin, and liver enzymes such as ALT, AST, and ALP were all significantly elevated in people who had severe dengue fever. AST was raised in all the three groups and the p value was insignificant and cannot predict the severity and outcome of dengue [15]

Serum ALP levels also showed a similar trend. These enzymes were raised even in the absence of hepatomegaly. All the children with DSS and DHF had elevated enzymes and the mean values were significantly higher than those with DF. [16] The present study revealed that alkaline phosphatase was raised in the DHF and DSS groups. However due to lack of follow up, the trend in the alkaline phosphatase and liver enzymes was not established. Kalenahalli also reported that bilirubin was raised in DHF and DSS cases, whereas globulin was more in DHF and DSS cases compared with DF. [17]

Ultrasonography is a safe, low-cost imaging method that does not utilize ionizing radiation, with high sensitivity to detect early signs of plasma leakage. Particularly pleural effusion may be early identified, up to two days before defervescence, preceding changes in

hematocrit levels. Sonographic findings express the increase in capillary permeability (a sign of plasma leakage) and include cavitary effusion (ascites, pleural and pericardial effusion), and gallbladder wall thickening present in one third of patients affected by the mild presentation, and in 95% of cases with the severe presentation of DHF. Additionally, the presence of fluid in the perirenal space can be visualized. Splenomegaly, hepatomegaly and volumetric increase of the pancreas may also be observed. [18]

In DHF and DSS, ultrasonography revealed ascites, splenomegaly, pleural effusion, and gall bladder thickening. Hepatomegaly, on the other hand, was seen in all three groups. Hepatomegaly is found in all three types of dengue fever, according to Bokade et al. [15]

Pleural effusion and ascites are more common in the DHF and DSS groups, according to Baskar et al and Surangrat et al. [18,19,20]

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