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ACALCULOUS CHOLECYSTITIS IN PRIMARY DENGUE FEVER PATIENTS

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ABSTRACT

Dengue Fever (DF) is a mosquito borne viral disease caused by a flavivirus and is endemic in large areas of the south East Asia. The current study is a retrospective analysis of ultrasonographic (USG) features in patients presenting with primary dengue fever. Objective of the study is to investigate the frequency of acute acalculous cholecystitis in primary dengue fever patients and gall bladder edema in dengue fever and its association with platelet count. This study is carried out at Hindu Rao Hospital, Delhi. In this study 50 dengue IgM antibody positive first time affected cases are taken, besides platelets count, Haematocrit analysis and through USG is done in all patients to look for gallbladder edema and cavitory effusion. Patients with history of DM, TB, cirrhosis of liver, viral hepatitis, congestive heart failure, chronic kidney disease, hypoalbuminemia and cholecystitis are excluded from the study. USG has been reported to be a useful diagnostic tool in evaluating patients with DF. The main pathophysiologic change in DF could be increased vascular permeability, causing plasma leakage and serous effusion with high protein content which induces thickening of the gallbladder wall. Acalculous cholecystitis should be suspected in a case of DF presenting with abdominal pain, fever, mild elevation of transaminases and thickened gallbladder wall without stones on USG. In DF patients with acute acalculous cholecystitis, the course of DF could be self limiting and the gall bladder wall could return to normal after several days. Cholecystectomy in DF complicated by acalculous cholecystitis is rarely required. Abdominal USG should be made routine it may usefully support the early clinical diagnosis as PCR (RT-PCR) of dengue virus RNA is accurate method but are too expensive to be done for all patients in developing countries. In our study 66% patients with DF had gall bladder edema. P value was <0.0001 which is statistically significant. Average platelet count was 36,560/ul. Association was more with those patients without any hemorrhagic manifestation. None of the patient required cholecystectomy. In experience, close monitoring of vitals is required and conservative management is sufficient and helpful in patients.

Keywords: Dengue Fever, Flavivirus, Acalculous Cholecystitis, Hypoalbuminemia and Cholecystectomy.

INTRODUCTION

Dengue Fever (DF) is a mosquito-borne viral disease caused by a flavivirus and is endemic in large areas of the Southeast Asia (Halstead, 1980). The incidence of dengue fever and dengue fever with complications has increased thirty folds globally in the last four decades and more than half the world's population (including developed countries) is now threatened with infection from dengue virus (Bennett *et.al.*, 2003). In India, more than 50 outbreaks have been reported by the National Institute of Communicable diseases, New Delhi since 1963. Dengue virus infection manifests with wide range of severity from asymptomatic mild febrile illness to life threatening disease including haemorrhagic manifestations and severe dengue. The clinical picture of classic dengue begins with a high grade fever, intense headache and myalgia, prostration, nausea, vomiting and arthralgia. Various

atypical manifestations of dengue virus infection, including fulminant hepatitis, encephalopathy, cardiomyopathy, acute pancreatitis, and acalculous cholecystitis have been reported during recent years (Sood *et.al.*, 2000, George *et.al.*, 1988 and Nimmannitya *et.al.*, 1987).

Abdominal pain is a commonly reported symptom in dengue fever. The reported causes of abdominal pain in dengue fever include hepatitis, pancreatitis, acalculous cholecystitis and peptic ulcer disease. The clinically overlapping manifestations of dengue virus and bacterial infections make it difficult, if not impossible, to distinguish these infection entities from each other.

Radiographic findings of dengue fever have not yet been clearly elucidated in relation to clinical and serological findings, despite the fact that two-fifths of the world population lives in areas where the virus is endemic.

The current study is a retrospective analysis of ultrasonographic (USG) features in patients presenting with primary dengue fever (during the outbreak of DF) admitted at Hindu Rao Hospital, New Delhi during September to November 2013.

AIMS AND OBJECTIVE

Aim and objective of the study is to investigate the frequency of acute acalculouscholecystitis in primary dengue fever patients and Gallbladder edema in dengue fever and its association with platelet count.

METHODS

The current study is a retrospective study to determine the association between the Dengue infection, platelet count and the presence or absence of gallbladder edema, admitted (during Dengue outbreak) from Sept.2013 to Nov.2013 in Hindu Rao Hospital, Delhi. In this study 50 Dengue IgM antibody positive cases are taken, besides platelets count, haematocrit analysis thorough ultrasonography is done in all patients to look for Gall bladder edema and cavitory effusion.

INCLUSION CRITERIA

1. Indoor patients diagnosed with dengue (positive IgM dengue serology).
2. Patients having manifestations of dengue fever for the first time.

EXCLUSION CRITERIA

1. Patients with history of DM, TB, cirrhosis of liver, viral hepatitis, congestive heart failure, chronic kidney disease and hypoalbuminemia.
2. Patients with past history of dengue.
3. Patients with past history of cholecystitis.

REVIEW OF LITERATURE

Dengue fever is endemic in tropical and subtropical areas. Dengue fever is estimated by the WHO (World Health Organization) to cause about 50-100 million infections per year worldwide. Increased capillary permeability is the main feature of DHF, represented by increased capillary permeability, with leakage of albumin out of the vascular space, leading to cavitory effusion and hemoconcentration with increase in the hematocrit levels described as polyserositis (Vabo *et.al.*, 2004 and Setiawan *et.al.*, 1998) classified into mild and severe, according to the World Health Organization criteria (Organização, 2001). The exact pathogenesis of acute acalculouscholecystitis is obscure but cholestasis and increased bile viscosity from prolonged fasting, spasm of the ampula of vater, infection, endotoxaemia, microangiopathy and ischaemia-reperfusion injury, among other causes have been suggested (Winkler and Gleich, 1998). The pathophysiology in the development of acute acalculouscholecystitis from infection with dengue virus is unknown. Polyserositis is associated to hemorrhagic manifestations and thrombocytopenia.

It is well established in the literature that, typically, the hypotension secondary to this plasma leakage occurs up to 48 hours after defervescence, the moment of fever abatement where the fever decreases to less than 38°C¹². The sonographic signs of plasma leakage, particularly pleural effusion, may be early identified, up to two days before defervescence, preceding changes in hematocrit levels (Srikiatkachorn *et.al.*, 2007).

Despite the nonspecificity of sonographic findings, ultrasonography is useful for the early diagnosis in patients with DHF and for differential diagnosis of other febrile diseases (Setiawan *et.al.*, 1998).

The objective of the present literature review is to describe the main sonographic findings and evaluating the role of ultrasonography in the assessment of patients with suspected dengue hemorrhagic fever.

Frequent sonographic findings in a case of dengue include a thickened gallbladder wall with pericholecystic fluid, ascites, splenomegaly, and pleural effusion which is commonly right-sided (Sood *et.al.*, 2000, George *et.al.*, 1988, Nimmannitya *et.al.*, 1987, Khanna *et.al.*, 2004, Vabo *et.al.*, 2004, Setiawan *et.al.*, 1998, Organização, 2001, Winkler and Gleich, 1998, Srikiatkachorn *et.al.*, 2007, Setiawan *et.al.*, 1998, Venkata, 2005, Thulkar *et.al.*, 2000 and Wu *et.al.*, 2004). Gallbladder edema is found to be more common in cases of secondary dengue and there is a tendency for gallbladder edema to be associated with higher increase of hematocrit and greater severity of illness. In some studies, this finding has been a relevant marker for clinical diagnosis and indicator of severity of DHF in children (Teefey *et.al.*, 1991, Pramuljo and Harun, 1991, Gupta *et.al.*, 2000, Sehgal *et.al.*, 2002).

DISCUSSION

Dengue is the most significant mosquito-borne viral disease in the world today. Approximately 3 billion people worldwide live in areas at risk for transmission of the dengue flavivirus by the *Aedes aegypti* mosquito, and an estimated 100 million people worldwide are infected with the virus each year. Clinical manifestations of the virus include dengue fever without warning signs, dengue fever with warning signs and severe dengue. The classic symptoms of Dengue fever include high fever, headache, musculo-skeletal pain, retro-orbital pain, and rash. Pain in abdomen is considered as one of the warning symptom of dengue.

Laboratory findings include variable degree of Thrombocytopenia, neutropenia followed by lymphocytosis often with atypical lymphocytes. There may be a mild elevation in liver enzymes. Specific diagnosis consists of demonstration of specific IgM antibody which appears in serum by day 5 after onset and persists for 2 to 3 months. It indicates an active or a recent infection (Kuno *et.al.*, 1991 and Dar *et.al.*, 1999) and it can be negative in early cases of primary Dengue Fever. As PCR (RT PCR) of dengue virus RNA has been developed as a sensitive and accurate method but these are too expensive to be done for all patients in developing countries.

Ultrasonography (USG) has been reported to be a useful diagnostic tool in evaluating patients with DHF. It may usefully support the early clinical diagnosis of dengue haemorrhagic fever.

The main pathophysiologic change in DF could be increased vascular permeability, causing plasma leakage and serous effusion with high protein content which induces thickening of the gallbladder wall.

Acalculous cholecystitis should be suspected in a case of DF presenting with abdominal pain, fever, a positive Murphy's sign, mild elevation of transaminases and a thickened gallbladder wall without stones on ultrasonography. In DF patients with acute acalculous cholecystitis, the course of DF could be self-limiting and the gallbladder wall could return to normal after several days. Cholecystectomy in a case of dengue fever complicated by acalculous cholecystitis is rarely required and hence the patient should be closely observed for signs of perforation. Adequate hydration, antipyretics and platelet-transfusion in cases with severe thrombocytopenia may be all they need. There have been numerous studies¹⁴⁻¹⁸ supporting the role of ultrasonography in a case of dengue fever. Abdominal ultrasonography should be made a routine in cases of dengue fever as it may help in the clinical diagnosis as well as early detection of complications as in our case's which enables us to reduce morbidity and recommend close follow up. Our patients were managed conservatively. They improved completely and discharged thereafter. None of the patients needed cholecystectomy. In our experience, close monitoring of vitals is required and conservative management is helpful in these patients.

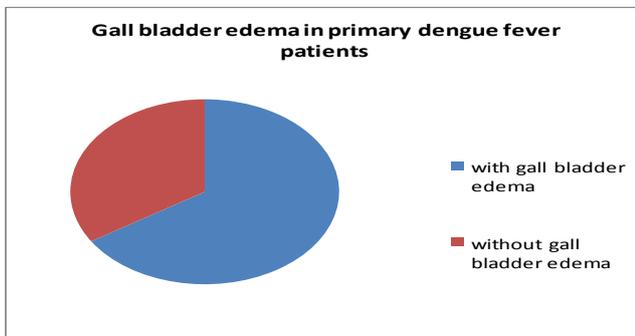


Figure 1: Gallbladder edema in primary dengue fever patients

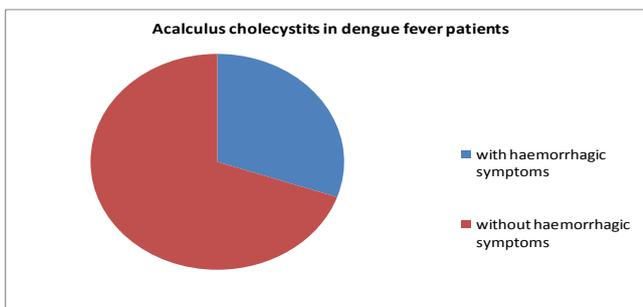


Figure 2: Acalculus cholecystitis in dengue fever patients

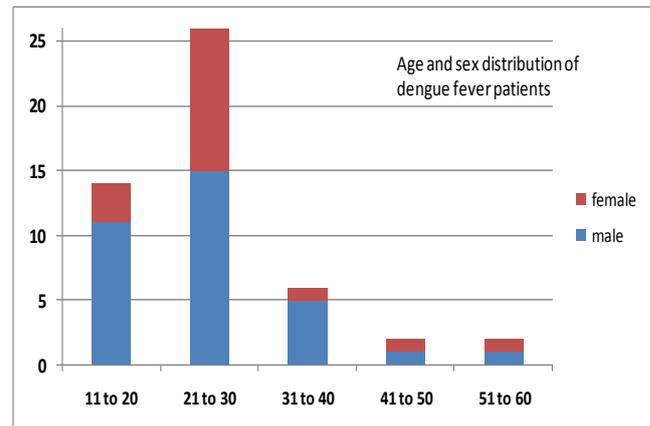


Figure 3: Age and sex distribution of dengue fever patients

CONCLUSION

Dengue epidemics have been occurring in India from time to time²⁵. Gall bladder edema is commonly seen in patients with dengue fever. In our study 66% patients with dengue fever had gall bladder edema. p value was <0.0001 which is statistically significant. Preponderance was seen in the patients between 11 to 30 years suggesting it to be more common in young age group, more in males than in females. Average platelet count at which the results were obtained was 36,560/ul. Association was more with those patients without any haemorrhagic manifestations. None of the patient required any surgical intervention. In our experience timely conservative treatment is sufficient and proper diet. The findings are well above in comparison to previous studies. Thus, prospective study with larger population size and equal age distribution is required for better results.

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