

# Etiology of Abdominal Pain in Dengue Fever<sup>¶</sup>

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## Abstract

Abdominal pain is a commonly reported symptom in DF. The reported causes of abdominal pain in DF include hepatitis, pancreatitis, acalculous cholecystitis and peptic ulcer disease. Till to date, there has been no planned study to evaluate the cause of pain abdomen in DF. This study was planned to evaluate the etiology of abdominal pain in DF.

Patients presenting with fever and pain abdomen to our hospital from July to November 2003 and July to November 2004 were included in the study. A probable diagnosis of DF was made based on the presence of acute febrile illness with two or more of the following manifestations: headache, retro-orbital pain, myalgia, arthralgia, rash, haemorrhagic manifestation and leukopenia. The diagnosis was confirmed by enzyme immunoassay-based serology. DHF was diagnosed based on WHO criteria. The cause of pain abdomen was ascertained by blood tests (amylase, lipase and liver function test), radiology (X-ray abdomen-erect and supine, USG, CECT) and/or endoscopy.

Out of the 100 patients presenting with fever and pain abdomen, 55 patients were diagnosed to have DF. The remaining 45 patients had other causes of fever with pain abdomen. The various causes of pain abdomen diagnosed in patients with DF were: acute hepatitis, acalculus cholecystitis, acute pancreatitis, appendicitis, spontaneous bacterial peritonitis, enteritis, peptic ulcer disease and gastric erosions in 20 (36.4%), 9 (16.4%), 8 (14.5%), 3 (5.45%), 2 (3.63%), 8 (14.54%), 2 (3.63%) and 3 (5.45%) of the patients respectively.

In patients with dengue fever, the etiology of abdominal pain should be aggressively looked into for proper management.

**Keywords:** Dengue fever, abdominal pain, pancreatitis, appendicitis, cholecystitis.

<sup>¶</sup>In DHF endemic countries, abdominal pain is the manifestation of gastrointestinal bleeding and is the alarm clinical signal for impending progression of the severity of the disease to DHF/DSS. As per WHO guidelines\*, abdominal pain is considered as a part of the clinical picture of DF/DHF and not related in most of the cases with other infectious diseases as mentioned by the authors. In epidemic-prone areas, like Delhi, a more comprehensive study based upon confirmed, DHF cases (by virus isolation) with sample size of statistical significance will be required to prove the authors conclusions - Editor.

\*Nimmanitya S. Management of dengue and dengue haemorrhagic fever. In: Monograph on dengue/dengue haemorrhagic fever, 1993, WHO/SEARO, New Delhi, Regional Publication No. 22.

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## Introduction

India is an endemic country for dengue virus infection. Dengue virus infection may be asymptomatic or present as undifferentiated fever: dengue fever (DF) or dengue haemorrhagic fever (DHF)<sup>[1]</sup>. Dengue shock syndrome (DSS) may lead to hypovolemic shock. Abdominal pain is a frequently reported symptom in patients with DF. Pain abdomen is associated strongly with DHF<sup>[2]</sup>. Up to 40% of patients with DHF may have abdominal pain at presentation<sup>[3]</sup>. Pushpawati Singhanian Research Institute is a tertiary care hospital in New Delhi, India. Our hospital being a centre for gastrointestinal problems, we tend to see patients with primary non-gastrointestinal problems coming to us with gastrointestinal complaints. Two patients who had been operated in another hospital with a suspicion of subacute intestinal obstruction were referred to us with post-operative intraperitoneal haemorrhage in July 2003. We diagnosed them to have DHF. This led us to design a study to look into the causes of abdominal pain in DF. The initial results of our study have already been published<sup>[4]</sup>. The study was subsequently continued into the next epidemic of DF in New Delhi.

## Materials and Methods

All patients who presented with fever and pain abdomen from July to November 2003 and July to November 2004, the endemic period for dengue infection, were included in the study. A probable diagnosis of DF was made if the patient presented with an acute febrile illness with two or more of the following manifestations: headache, retro-orbital pain, rash, myalgia, arthralgia, haemorrhagic manifestations and leukopenia<sup>[1]</sup>. The diagnosis was confirmed by looking for the presence of IgM antibodies against dengue virus using the Immunocomb II

Dengue Bispot IgM and IgG test. This test is a solid-phase enzyme immunoassay, based on an immunocapture principle. The sensitivity and specificity of the test is 97.5% and 97.9% respectively. Diagnosis of DHF was made if all of the following were present: (i) fever, or history of acute fever, lasting 2-7 days; (ii) haemorrhagic tendencies, evidenced by at least one of the following: a positive tourniquet test, petechiae, ecchymosis or purpura, bleeding from the mucosa, gastrointestinal tract, injection sites or other locations, haematemesis or melena; (iii) thrombocytopenia (100 000 cells/mm<sup>3</sup> or less); and (iv) evidence of plasma leakage due to increased vascular permeability, manifested by at least one of the following: a rise in the haematocrit equal to or greater than 20% above average for age/sex and population, a drop in haematocrit following volume replacement treatment equal to or greater than 20% of baseline, and signs of plasma leakage such as pleural effusion, ascites and hypoproteinemia. Any patient with DHF and evidence of circulatory failure was diagnosed as dengue shock syndrome.

Blood tests done in all the patients included complete blood count, liver and kidney function tests, lipase and amylase. Patients with deranged liver functions were tested for the presence of hepatitis A (IgM HAV), hepatitis E (IgM HEV), hepatitis B (HBs Ag and IgM HBe) and hepatitis C (anti-HCV) infection. Each patient underwent chest X-ray and abdominal ultrasound. Contrast-enhanced computerized tomography (CECT) and upper gastrointestinal endoscopy were done if the other investigations did not reveal the cause of abdominal pain. The platelet count was done at presentation and at every alternate day in patients with DF and every day in patients with DHF with thrombocytopenia. If the platelet count was less than 20 000 cells/mm<sup>3</sup>, or if there was any evidence of bleeding, diathesis platelets were transfused.



**Table.** *Clinical and laboratory features in patients with dengue fever*

	DF n=30 (%)	DHF n=25 (%)
Fever	30 (100)	25 (100)
Headache	22 (73.3)	18 (72)
Retro-orbital pain	14 (46.6)	16 (64)
Conjunctival suffusion	20 (66.6)	16 (64)
Non-petechial rash	0	12 (48)
Petechial rash	0	13 (52)
Positive tourniquet test	0	25 (100)
Hepatomegaly	7 (23.3)	25 (100)
Tender hepatomegaly	7 (23.3)	13 (52)
Arthralgia	3 (10)	8 (32)
Pain abdomen	30 (100)	25 (100)
Haemoconcentration $\geq 20\%$	0	5 (20)
Thrombocytopenia (normal, $1.5\text{--}3.5 \times 10^6/\text{mm}^3$ )	6 (20)	25 (100)
Leukopenia (normal, $4\text{--}11 \times 10^3/\text{mm}^3$ )	3 (10)	5 (20)
Hyperbilirubinemia (normal, $<1.5 \text{ mg/dl}$ )	7 (23.3)	13 (52)
AST/ALT >twice (normal, 20–40 u/l)	12 (40)	18 (72)
AST/ALT >ten times (normal, 20–40 u/l)	7 (23.3)	13 (52)
Deranged prothrombin time	7 (23.3)	13 (52)
Pleural effusion	0	17 (68)
Ascites	0	18 (72)
Amylase/lipase > three times normal	2 (6.6)	6 (24)

## Results

There were 100 patients who presented with fever and abdominal pain. Fifty-five of these patients had DF. The diagnosis in the rest of

the 45 patients presenting with abdominal pain and fever were acute viral hepatitis in 20 (hepatitis A – 7 patients, hepatitis E – 11 patients, hepatitis B – 2 patients), acute calculous cholecystitis in 4, amoebic liver abscess in 6, typhoid fever in 5, surgical obstructive jaundice due to gall bladder cancer and cholangitis in 3, pyelonephritis in 3 and acute pancreatitis in 4 patients. Among the 55 patients with DF, there were 35 male and 20 female patients. The mean age of the patients was 35.5 years (range 20–67 years). The clinical and laboratory findings are shown in the Table. There were 30 patients with DF and 25 patients with DHF. Sixteen patients had grade I DHF and nine had grade II DHF. All the patients with DF and DHF had temperature ranging from 102 °F to 104 °F. The mean duration of fever was 5 days. Sixteen out of 55 (29%) patients had backache and severe myalgia suggestive of break-bone (camel back) fever. The non-petechial rash started from the trunk and spread in a centrifugal manner. This rash had a sandpaper feel. Twenty patients (36.36%) with pain abdomen had tender hepatomegaly, hyperbilirubinemia and AST/ALT levels >10 times, suggestive of acute hepatitis. Two of the 20 patients went on to develop acute liver failure. These two patients were managed in the intensive care unit (ICU) and they recovered. All these patients were serologically negative for hepatitis A, hepatitis E, hepatitis B and hepatitis C infection. Nine (16.36%) patients with pain in the right upper quadrant had a positive Murphy's sign and the ultrasound showed thickened gall bladder wall with pericholecystic fluid without evidence of cholelithiasis, suggesting acute acalculous cholecystitis. None of these patients had diabetes mellitus. Eight (14.54%) patients had epigastric pain radiating to the back with elevated amylase and lipase levels suggestive of acute pancreatitis. The ultrasound supported the diagnosis of acute pancreatitis in five patients. CECT established the diagnosis of



pancreatitis in three patients. None of these eight patients had gall stones or were alcohol consumers. Three patients (5.45%) had acute appendicitis clinically, which was confirmed on CECT. One patient underwent uneventful surgery. The other two patients were managed conservatively. Eight patients (14.54%) presented with abdominal pain and diarrhoea suggestive of enteritis. In the rest of the five patients upper gastrointestinal endoscopy (UGIE) was done. Three (5.45%) patients had gastric erosions and two (3.63%) had gastric ulcers. Two patients with normal UGIE underwent CECT which did not reveal any cause of abdominal pain. Both these patients had ascites and underwent diagnostic ascitic tap after correction of platelet count. Both patients had an ascitic fluid cell count of more than 500 neutrophils, suggestive of spontaneous bacterial peritonitis. Ascitic fluid culture grew *E. coli* in one patient. The second culture was sterile. Both patients became symptom-free after five days of intravenous cefotaxime in the dose of 2 g twice a day.

## Discussion

Abdominal pain is a common feature in patients with dengue fever<sup>[5,6]</sup>. This is the first study which looked into the various causes of abdominal pain in DF. In our series we could establish the cause in all the patients. There is a possibility of a selection bias as the inclusion criteria included patients with abdominal pain. Also, it is difficult

to say if gastric erosions and ulcers were in fact the cause of abdominal pain in five patients in whom no other cause of abdominal pain could be found. Hepatic involvement is commonly seen in DF<sup>[7,8]</sup>. Fifty-four per cent (30/55) patients had elevated AST/ALT in the present series. Acute hepatitis was diagnosed in 20 patients. As reported earlier, liver involvement was more common in DHF as compared to DF<sup>[8]</sup>. Thickened GB wall on USG has been reported in up to 59% of patients with DF<sup>[9]</sup>. In the absence of clinical signs this does not imply acute cholecystitis. Acute acalculus cholecystitis has been rarely reported in DF<sup>[5]</sup>. Diagnosis of acute acalculus cholecystitis was made in 16.36% of patients with DF on the basis of clinical and USG findings. All the 9 patients improved on conservative treatment. We found acute pancreatitis in 14.54% patients with DF and abdominal pain. All these patients had mild acute pancreatitis. Pancreatitis has been earlier reported in DF<sup>[10]</sup>. Mild acute pancreatitis was found in 29% of patients with DF in one series<sup>[11]</sup>. It is unlikely that appendicitis in the three patients was an incidental finding. Appendicitis has not been previously reported in DF. This is also the first report of spontaneous bacterial peritonitis in DF.

## Conclusion

If carefully looked into, the etiology of abdominal pain in DF can be found and appropriately managed.

## References

- [1] World Health Organization. *Dengue haemorrhagic fever: diagnosis, treatment, prevention and control*. 2<sup>nd</sup> ed. Geneva, 1997. <http://www.who.int/csr/resources/publications/dengue/itoviii.pdf>
- [2] Casali CG, Pereira MR, Santos LM, Passos MN, Fortes Bde P, Ortiz Valencia LI, Alexandre Ade J

and Medronho Rde A. The epidemic of dengue and hemorrhagic dengue fever in the city of Rio de Janeiro, 2001/2002. *Rev Soc Bras Med Trop*. 2004; 37(4): 296-299. (Article in Portuguese).

- [3] Richards AL, Bagus R, Baso SM, Follows GA, Tan R, Graham RR, Sandjaja B, Corwin AL and Punjabi N. The first reported outbreak of dengue hemorrhagic fever in Irian Jaya, Indonesia. *Am J Trop Med Hyg*. 1997; 57(1): 49-55.



- [4] Khanna S, Vij JC, Kumar A, Singal D and Tandon R. Dengue fever is a differential diagnosis in patients with fever and abdominal pain in an endemic area. *Ann Trop Med Parasitol*. 2004; 98(7): 757-760.
- [5] Mendez A and Gonzalez G. Dengue haemorrhagic fever in children: ten years of clinical experience. *Biomedica*. 2003; 23(2): 180-193.
- [6] Wang JY, Tseng CC, Lee CS and Cheng KP. Clinical and upper gastroendoscopic features of patients with dengue virus infection. *J Gastroenterol Hepatol*. 1990; 5(6): 700-701.
- [7] Kalayanaroj S and Nimmanitya S. Clinical presentations of dengue hemorrhagic fever in infants compared to children. *J Med Assoc Thai*. 2003; 86 (Suppl 3): S673-S680.
- [8] Wahid SF, Sansui S, Zawawi MM and Ali RA. A comparison of the pattern of liver involvement in dengue hemorrhagic fever with classic dengue fever. *Southeast Asian J Trop Med Public Health*. 2000; 31(2): 259-263.
- [9] Wu KL, Changchien CS, Kuo CH, Chiu KW, Lu SN, Kuo CM, Chiu YC, Chou YP and Chuah SK. Early abdominal sonographic findings in patients with dengue fever. *J Clin Ultrasound*. 2004; 32(8): 386-388.
- [10] Jusuf H, Sudjana P, Djumhana A and Abdurachman SA. DHF with complication of acute pancreatitis related hyperglycemia: a case report. *Southeast Asian J Trop Med Public Health*. 1998; 29(2): 367-369.
- [11] Setiawan MW, Samsi TK, Wulur H, Sugianto D and Pool TN. Epigastric pain and sonographic assessment of the pancreas in dengue hemorrhagic fever. *J Clin Ultrasound*. 1998; 26(5): 257-259.

