



## Research Article

# Breakbone Fever- Sonological Manifestations of Dengue

Authors

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### Abstract

**Background:** Dengue fever is a major cause of illness and death worldwide. The disease is caused by dengue virus which gets transmitted to humans by the bites of infected mosquitoes, *Aedes (Ae.) aegypti* and *Ae. albopictus*<sup>[1]</sup>. The disease represents a global health issue as it is endemic in around 100 countries, most of which are in tropical and sub-tropical areas.

**Objectives:** To determine importance of ultrasonography in the early diagnosis, severity grading and prognostic management of patient suffering from dengue To evaluate the typical sonographic features seen in patients suffering from dengue fever. To correlate ultrasound findings with platelet counts and to predict severity of dengue fever based on these findings.

**Materials and Methods:** This is a retrospective study done in KIMS hospital Bangalore from June 2015 to January 2016 involving 140 patients with clinical suspicion of dengue fever. Ultrasound of abdomen, pelvis and thorax was done using GE Voluson Pro750 and Philips HD7 machines. The typical edematous GB wall thickening resembling onion peel was an important criteria in our Ultrasound study (Sachar and sunders sign). The serology markers were NS1Ag, IgG and IgM. Platelet count values were graded as severe (less than 50,000) and mild (50,000 – 100,000).

**Results:** Sonography was conducted on 140 patients of whom 110 were seropositive for dengue. With the exclusion of 30 seronegative cases the total number of patients included in our study was 110 cases ranging from 1-90 years of which 64(58%) were males and 46(42%) were female. The majority of patients in the study ranged from 20 to 40 years. All 110 (100%) patients presented with fever, 93 (85%) had generalized body ache, 68(62%) had nausea and vomiting and 25(23%) had generalized skin rash.

Sonographic correlation in 55 patients with platelet count less than 50000, demonstrated gall bladder wall thickening in 52 patients (94%), ascites in 48(87%), pleural effusion in 39 patients (71%), splenomegaly in 14(25%) and hepatomegaly in 11(20%). The 36 patients with platelet count 50000 to 100000/mL, demonstrated gall bladder wall thickening in 29(81%), ascites in 22(61%), pleural effusion in 15(42%), with sonography. In this study, platelet counts were reduced in all 140 cases and dengue serology was positive in 110. Platelet counts below 50000/mL was noted in 55(50%) and 50000 to 100000mL in 36(33%) patients.

**Conclusion:** In a dengue epidemic ultrasound findings of gall bladder edema with or without ascites, pleural effusion and ascites should definitely suggest a provisional diagnosis of dengue fever prior to confirmatory serology reports. This helps in early management of patients there by reducing morbidity and mortality associated with dengue fever.

**Keywords:** Dengue fever, gall bladder wall edema, ascites, pleural effusion, hepatomegaly, splenomegaly, platelet count.

## Introduction

Dengue fever is a major cause of illness and death worldwide. The disease is caused by dengue virus which gets transmitted to humans by the bites of infected mosquitoes, *Aedes (Ae.) aegypti* and *Ae. albopictus*<sup>[1]</sup>. The disease represents a global health issue as it is endemic in around 100 countries, most of which are in tropical and sub-tropical areas. Over the last decades, the incidence rate and the geographic distribution of dengue have rapidly increased (almost 30-fold). Data from the World Health Organization (WHO) estimates up to 100 million cases of dengue fever each year. Changes in dengue epidemiology and the increase in incidence rates (with and without co-morbidities) have led the WHO to propose a new dengue classification system according to disease severity<sup>[2]</sup>.

## Objectives

The purpose of our study is to determine importance of ultrasonography in the early diagnosis, severity grading and management of patients suffering from dengue as serology takes approximately 7 to 10 days to give a positive result.

## Material and Methods

This is a retrospective study done in KIMS hospital Bangalore from June 2015 to January 2016 involving 140 patients with clinical suspicion of dengue fever.

All patients of any age of both sexes presenting with clinical suspicion of dengue fever were included in the study. Patients with negative dengue serology and those associated with other medical conditions like chronic heart disease and chronic renal disease were excluded.

A detailed history of all patients included in the study was taken along with thorough clinical examination and laboratory investigation findings were recorded as per proforma. Based on the platelet count patients were categorically split into two groups. One group with <50000/mL and another with >50000mL.

Ultrasound abdomen and thorax was performed in all 140 cases with ultrasound machine (GE Voluson

Pro750 and Philips HD7 machines) using 3.5 and 5 MHz probes. Ultrasound examination findings gall bladder wall edema, ascites, pleural effusion, splenomegaly and hepatomegaly were noted in all patients. Gall bladder wall edema was measured between two layers of anterior wall of gall bladder. Both the pleural spaces were evaluated through an intercostal approach. Liver measuring more than 15 cms was taken as hepatomegaly, spleen of long axis more than 12 cms and short axis more than 5 cms was taken as splenomegaly.

The serological tests for dengue fever was performed using dengue card test includes NSag1 (nonstructural antigen test), IgM and IgG in all patients. IgM and IgG are antibodies against dengue virus in human plasma.

## Observation

**Table 1** Significance relation between platelets and associated parameters

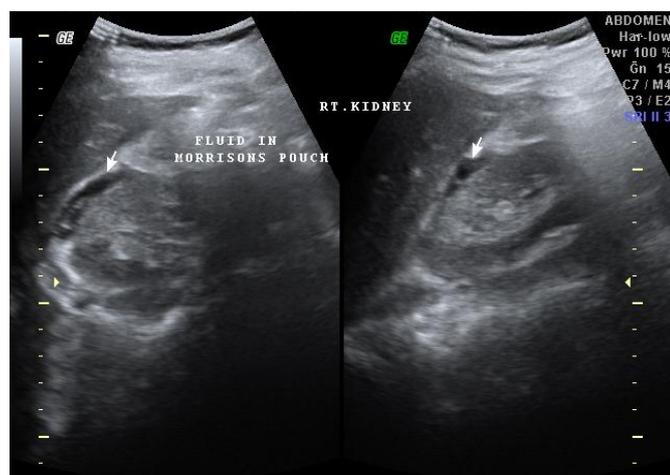
Ultrasound findings	No	Platelets counts	
		<50000 (n=55)	50000-100000 (n=36)
GBE	86	52(94.0%) (P=0.0012)	29(83.0%) (P=0.0016)
PE	56	39(71.0%) (P=0.003)	15(42.0%) (P=0.081)
ASCITES	73	48(87.0%) (P=0.0012)	22(61.0%) (P=0.006)
HPM	18	11(20.0%) (P=0.061)	05(13. %) (P=0.231)
SPM	20	14(25.0%) (P=0.041)	04(11.0%) (P=0.421)
Normal	13	0(0.00%)	02(6.0%) (0.741)



**Fig. 1** Ultrasound image showing gall bladder wall edema



**Fig. 2** Ultrasound image showing left pleural effusion.



**Fig. 3** Ultrasound image showing ascites.

## Results

Ultrasonography was conducted on 140 patients of which 110 were seropositive for dengue. 30 seronegative cases were excluded. Total number of patients included in our study was 110 cases of which 64(58%) were males and 46 (42%) cases were female. The age range of patients varied from 1 to 90 years. Majority of our cases were in the age group of 20 to 40 years. All 110 (100%) patients presented with fever for 3 to 5 days, 93 (85%) patients had generalized body ache, 68(62%) patients had nausea and vomiting and 25(23%) patients had skin rash.

Ultrasound findings in 110 sero- positive cases included edematous gall bladder wall thickening in 86 patients(78%), ascites in 73 patients (66%), pleural effusion in 56 patients (51%), splenomegaly in 20 patients (20%) and hepatomegaly in 18patients (16%) .

Platelet count values versus ultrasound finding:

1) Severe dengue with platelet count less than 50000/mL was present in 55 cases of which gall bladder wall thickening was seen in 52 patients (94%), ascites in 48(87%), pleural effusion in 39 patients (71%), splenomegaly in 14 patients (25%) and hepatomegaly in 11patients (20%).

2) Mild dengue with platelet count 50000 to 100000/mL was present in 36 patients of which gall bladder wall thickening in 29 patients (81%), ascites in 22(61%), pleural effusion in 15patients (42%), splenomegaly in 4patients (11%) and hepatomegaly in 5 patients (20%) were present on ultrasound.

In our study platelet counts were reduced in all 140 cases but dengue serology was positive in 110 cases. Platelet count was below 50000 in 55 (50%) and 50000 to 100000/mL in 36 (33%) patients.

## Discussion

Dengue fever is caused by infection with dengue virus (DENV). The DENV is a vector-borne virus transmitted to humans primarily by two mosquito species, *Ae. aegypti* or *Ae. albopictus*. DENV is a single positive-stranded RNA virus belonging to Flavivirus genus of the *Flaviviridae* family and has 4 major serotypes (DENV 1–4) that are antigenically distinct from each other. Each DENV serotype is phylogenetically distinct suggesting that each serotype could be considered a separate virus<sup>[3]</sup>. Mosquitoes transmit the virus by feeding on blood of infected persons. At first, the virus infects and replicates in the mid-gut epithelium of the mosquito and then spreads to other organs until it reaches the salivary glands after 10–14 days where it can be inoculated to another person during subsequent blood meal. Vertical transmission of DENV in mosquitoes, i.e. from mosquito to larvae has been reported by a number of research groups. Clinically, dengue infection has a broad spectrum of features. The vast majority of cases are asymptomatic and passes unnoticed. Typically, the symptoms start to be prominent after an incubation period of 3–10 days<sup>[4]</sup>. The severity of the clinical manifestations varies from mild symptoms to severe life threatening symptoms in the case of dengue

hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [5].

Dengue fever mostly occurs in children and young adults<sup>[6]</sup>. Clinical features vary with the age of the patient although clinically occult infection occurs in about 80%<sup>[7]</sup>. There are four presentations

- Non-specific febrile illness
- Classical dengue fever
- Dengue haemorrhagic fever
- Dengue haemorrhagic fever with dengue shock syndrome, encephalopathy and liver failure

**Non-specific febrile illness:** A maculo-papular rash occurs mostly in young children. Upper respiratory features, especially pharyngitis, are common<sup>[8]</sup>.

**Classical dengue fever (DF)** is primarily a disease of older children and adults. It begins abruptly followed by three phases – febrile, critical and recovery. The fever may be biphasic lasting 3 to 7 days and accompanied by a variety of symptoms including severe headache, retro-orbital pain, fatigue, nausea, vomiting, generalised aches, arthralgia and myalgia, hence the term “break bone fever”<sup>[7]</sup>.

Dengue haemorrhagic fever (DHF) is primarily a disease of children under 15 years in hyperendemic areas. It usually follows a secondary dengue infection and is characterized by high fever, haemorrhages, circulatory failure and hepatomegaly<sup>[9]</sup>.

**Dengue shock syndrome (DSS)** is associated with almost 50% mortality. Warning signs include sustained abdominal pain, vomiting, irritability or somnolence, a fall in body temperature and decrease in platelet count<sup>[8]</sup>.

Typically, leucopenia and thrombocytopenia occur as early as the second day of fever. After the onset of illness, the virus can be detected in serum, plasma, circulating blood cells and other tissues for 4–5 days. During the early stages of the disease, virus isolation, nucleic acid or antigen detection can be used to diagnose the infection. At the end of the acute phase of infection, serology is the method of choice for diagnosis. These antibodies are

detectable in 50% of patients by days 3-5 after onset of illness, increasing to 80% by day 5 and 99% by day 10<sup>[10]</sup>.

Thrombocytopenia has always been one of the criteria used by WHO guidelines as a potential indicator of clinical severity. In the most recent 2009 WHO guidelines, the definitions generally describe a rapid decline in platelet count or a platelet count less than 150,000 per microliter of blood. Most clinical guidelines recommend that platelet transfusions be given to patients who develop serious hemorrhagic manifestations or have very low platelet counts, platelet counts falling below  $10\text{--}20 \times 10^9 \text{ L}^{-1}$  without hemorrhage or  $50 \times 10^9 \text{ L}^{-1}$  with bleeding or hemorrhage<sup>[11]</sup>.

Serology is the mainstay in the diagnosis of dengue fever. Hemagglutination inhibition antibodies usually appear at detectable levels by day 5-6 of febrile illness. Ultrasound findings in early, milder form of dengue fever include GB wall thickening, minimal ascites, pleural effusion and hepatosplenomegaly.

There is no specific therapy. Uncomplicated dengue infection usually resolves spontaneously. Patients with life threatening complications should be managed in hospital with supportive treatment. Fluid replacement and close monitoring of fluid and electrolytes balance are vital. Isotonic solutions (e.g. 0.9% saline, Ringer’s lactate or Hartmann’s solution) should be used<sup>[12]</sup>.

Ultrasonography was conducted on 140 patients of whom 110 were seropositive for dengue. 30 seronegative cases were excluded. Total number of patients included in our study was 110 cases of which 64 (58%) were males and 46 (42%) cases were female. The age ranged of patients varied from 1 to 90 years. Majority of our cases were fallen in the age group of 20 to 40 years with male predominance. These findings were correlating well with study done by Santosh et al<sup>[13]</sup> and shruti et al<sup>[14]</sup> studies.

Commonest ultrasound findings in seropositive dengue patient with platelet count less than 50000 were gall bladder wall edema, ascites and pleural effusion (Figure 1,2,3). These findings were

correlating well with venkatsai<sup>[15]</sup> et al study. In their study they concluded that ultrasound of the abdomen is important adjunct to clinical profile in diagnosing dengue fever and may help to direct further confirmatory investigations. Further diagnosis can be made early in the course of disease compared with other modes of diagnosis. During epidemic the ultrasound findings of gall bladder edema with or without polyserositis in febrile patients should suggest the possibility dengue fever. Study did by Santosh et al<sup>[13]</sup> showed that gall bladder wall edema, pleural effusion, ascites and hepatosplenomegaly should strongly favor the diagnosis of dengue fever in patient presenting with fever and associated symptoms particularly during epidemic.

In our study gall bladder wall edema was present in 94% of cases with platelet count less than 50000/mL. This suggests gall bladder wall edema was an important ultrasound marker in severe dengue. This findings were correlating well with shashidhar et al study<sup>[16]</sup>.

In our study Gall bladder wall edema, ascites and pleural effusion were not significant in patients with platelet counts 100000 to 150000/mL. [31%].

Gall bladder wall edema was nonspecific in the study done by Omprakash, Bhangdia et al<sup>[17]</sup> and Ventak, Sai, et al<sup>[15]</sup> study. In our study dengue seropositive patients with platelet count less than 50000/mL showed all the ultrasound features of dengue fever. This indicates that in severe dengue the referring / treating physician can begin treatment before seropositive laboratory findings.

In our study dengue seropositive patients with platelet count less than 50000 showed all the ultrasound features of dengue fever (Table 1). This indicates severe dengue and referring / treating physician can plan / tailor treatment at earliest before arrival of laboratory parameters.

### Conclusion

During epidemics of dengue patient presenting with acute onset high grade fever with associated symptoms on ultrasound if gall bladder wall edema, ascites and pleural effusion were present then

strongly suggests diagnosis of dengue fever. Ultrasonography is simple noninvasive and non-ionizing modality which helps in the early diagnosis of dengue fever prior to serological confirmations. There by helps in planning and early initiation of management of patients. Finally helps in reducing morbidity and mortality associated with dengue fever. If all mentioned ultrasound findings of dengue were present then platelet count would be less than 50000. ultrasound findings plays additional role to clinical and laboratory parameters.

From this study we arrive at a conclusion that when ultrasound is used as the initial modality of choice of investigation for a patient with suspected dengue fever, the findings of gall bladder wall edema, ascites and pleural effusion may aid in the early management.

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