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## Role of gall bladder wall thickening in predicting dengue haemorrhagic fever before it's onset

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### Abstract

**Aim:** The aim of this study is to evaluate role of gall bladder wall thickening in predicting dengue haemorrhagic fever before it's onset.

**Material and Methods:** Abdominal ultrasound was done for all study participants on admission and during treatment via ultrasound machine (GE LOGIQ P9). Ultrasound was done on an empty stomach (fasting for eight hours or more). This investigation aimed to detect plasma leakage in the form of ascites, pleural effusion, and edematous gall bladder wall and also to detect any visceromegaly.

**Conclusion:** Gallbladder wall thickening (GBWT) can be used as an early predictor as well as an important prognostic sign for severe dengue infection and dengue haemorrhagic fever (DHF) especially during an epidemic.

**Keywords:** gall bladder, dengue, haemorrhagic & fever

### Introduction

Dengue fever poses a great economic burden worldwide and specifically in South East Asia. WHO estimated that 50-100 million dengue infections occur worldwide annually, with a 30-fold increase in global incidence observed over the past five years <sup>[1]</sup>.

Almost 75% of the global population exposed to dengue live in the Asia Pacific, and overall expansion in dengue cases have been noted in the past decade <sup>[2, 3]</sup>. The countries with a high incidence are Indonesia, Thailand, Myanmar, Sri Lanka, Bangladesh and India <sup>[4]</sup>.

It is a viral haemorrhagic fever transmitted by *Aedes aegypti* and *Aedes albopictus*. It is caused mainly by dengue virus DENV-2 and DENV-3, although DENV-1 and DENV-4 have also been isolated in recent years <sup>[5-7]</sup>, all of which share little cross immunity. Secondary infection by a different dengue serotype has been confirmed as an important risk factor for the development of dengue haemorrhagic fever (DHF) <sup>[8, 9]</sup>.

Clinically, dengue fever is characterized by high-grade fever, musculoskeletal pain, retro-orbital pain, headache, joint pain, nausea, vomiting, and morbilliform rash <sup>[10]</sup>.

In a small proportion of cases, the virus causes increased vascular permeability that leads to a bleeding diathesis or disseminated intravascular coagulation (DIC) known as dengue haemorrhagic fever (DHF) <sup>[11]</sup>. Clinically many parameters can be used to predict the onset of capillary leakage in DHF, including thrombocytopenia, haemoconcentration, and presence of free fluid in the peritoneal/pleural cavity detected on ultrasound. Dayanand KR, *et al.* reported that the most common ultrasound finding in seropositive is gall bladder wall thickness (86.5%) followed by ascites (41.7%) <sup>[12]</sup>.

Nainggolan L *et al.* also documented that 30 out of 46 patients (65.2%) with plasma leakage had GBWT <sup>[13]</sup>. The purpose of this research is to study correlation between gallbladder wall thickening (GBWT) and severity of dengue disease. Also, to find out whether GBWT can be used as a parameter to predict DHF before it's onset so that it can be reported to treating physician for early therapeutic interventions to reduce morbidity and mortality.

### Materials and Methods

This is a prospective observational study. A total of 90 patients with dengue fever presented to Era's Lucknow medical college and hospital, Lucknow, India, during the peak of the dengue epidemic in 2021. Approval for the study was obtained from the ethical committee of the hospital. Data were collected during this epidemic prospectively. Analysis was done.

**Selection of study participants**

**Inclusion criteria**

Both males and females who had a fever and were confirmed to have dengue fever on the presence of non-structural protein 1 (NS1) or immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies against dengue were included in the study.

**Exclusion criteria**

1. Participants with only dengue IgG antibodies positive (whose presence alone signifies the previous infection) were excluded from the study.
2. Pregnant females
3. Subjects with intrinsic gall bladder disease
4. Subjects with history of congestive cardiac failure or chronic liver disease were also excluded from the study.

**Informed consent**

Consent was taken from all included study participants after explaining to them, the nature and purpose of the research. Clinical history was taken regarding symptoms and recorded. All the data of the patients were recorded.

**Ultrasonography**

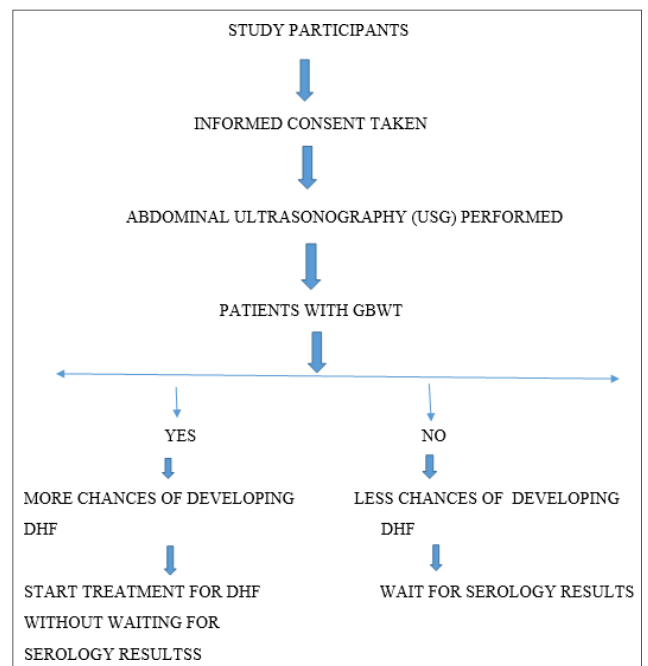
Abdominal ultrasound was done for all study participants on admission and during treatment via ultrasound machine (GE LOGIQ P9).

Ultrasound was done on an empty stomach (fasting for eight hours or more). This investigation aimed to detect plasma leakage in the form of ascites, pleural effusion, and edematous gall bladder wall and also to detect any visceromegaly. GB wall >3mm was classified as GBWT. Hepatomegaly was defined as the right lobe of the liver measuring >15cm in the midclavicular line, and splenomegaly was defined as the spleen measuring >12 cm. Gall bladder wall thickness was estimated by placing callipers over the anterior abdominal wall. All ultrasound examinations were performed by skilled and experienced radiologist. The average values of their findings were used for analysis.



**Fig 2:** Ultrasonography whole abdomen demonstrating thickened and edematous gallbladder wall

**Data analysis**



**Fig 1:** High resolution ultrasonography thorax demonstrating moderate amount of fluid in right pleural space. Pleural Effusion

**Results**

**Table 1a:** Total no. of dengue patients-90

GBWT	+	-	% dengue patients with GBWT
	58	32	

**Table 1b:** Total no. of dengue patients with GBWT - 58

DHF	+	-	% patients with GBWT developing DHF
	53	5	

Total number of patients enrolled were 90. Out of 90 patients, 58 (64.4%) patients were found to be with GBWT, and out them 53 (91.3%) patients developed DHF.

**Table 2:** Gender

Gender		Percentage
Male	53	58.8%
Female	37	41.1%

Out of 90 patients enrolled in the study majority were males (58.8%), rest 41.1% were females.

**Table 3:** Age

Age		
Age group	No. of study participants	Percentage
0-10	1	1.1%
10-20	5	5.5%
20-30	54	60%
30-40	13	14.4%
40-50	8	8.8%
50-60	5	5.5%
60-70	2	2.2%
80-90	2	2.2%
90-100	0	0%

Range of patients enrolled in the study were 5 to 90 years. Majority of the patients were aged between 20-30 years of age (60%).

**Table 4:** USG findings

USG findings		
USG findings	No. of dengue patients presenting with findings	Percentage
Hepatomegaly	35	38.8%
Splenomegaly	20	22.2%
Pleural effusion	15	16.6%
Ascitis	13	14.4%
GBWT	58	64.4%

On the basis of USG findings hepatomegaly is found in 35 (38.8%) patients and splenomegaly is found in 20 (22.2%) patients. Pleural effusion and ascites is found in 15 (16.6%) and 13 (14.4%) patients respectively. GBWT is found in 58 (64.4%) patients.

**Data analysis**

All data collected were entered on SPSS version 24 (IMB Inc., Armonk, USA). Variables like age, gender, diagnosis, serology, ultrasound findings were represented as percentages. Study participants were grouped into two groups: GBWT ≤3mm and GBWT more than 3mm. ap-value of less than 0.005 was considered statistically significant. The sensitivity and specificity of GBWT for the diagnosis of DHF was evaluated to be 91.4% and 96.9%.

**Results**

The results of our study favoured the fact that GBWT is directly related to disease severity. Also, GBWT can be used as a parameter to predict DHF before it’s onset.

**Discussion**

DHF and DSS cause huge morbidity and mortality, however, at the same time, they are preventable. The focus of our study was to establish relationship between GBWT and severity of dengue fever. Also, the study was focused to identify whether GBWT can be used as a predictor of DHF. The results of our study favoured the fact that GBWT is directly related to severity of dengue fever. Also, we could identify GBWT as a parameter to predict DHF before it’s onset, so that treating physician could take necessary steps to prevent morbidity and mortality.

**Dengue classification**

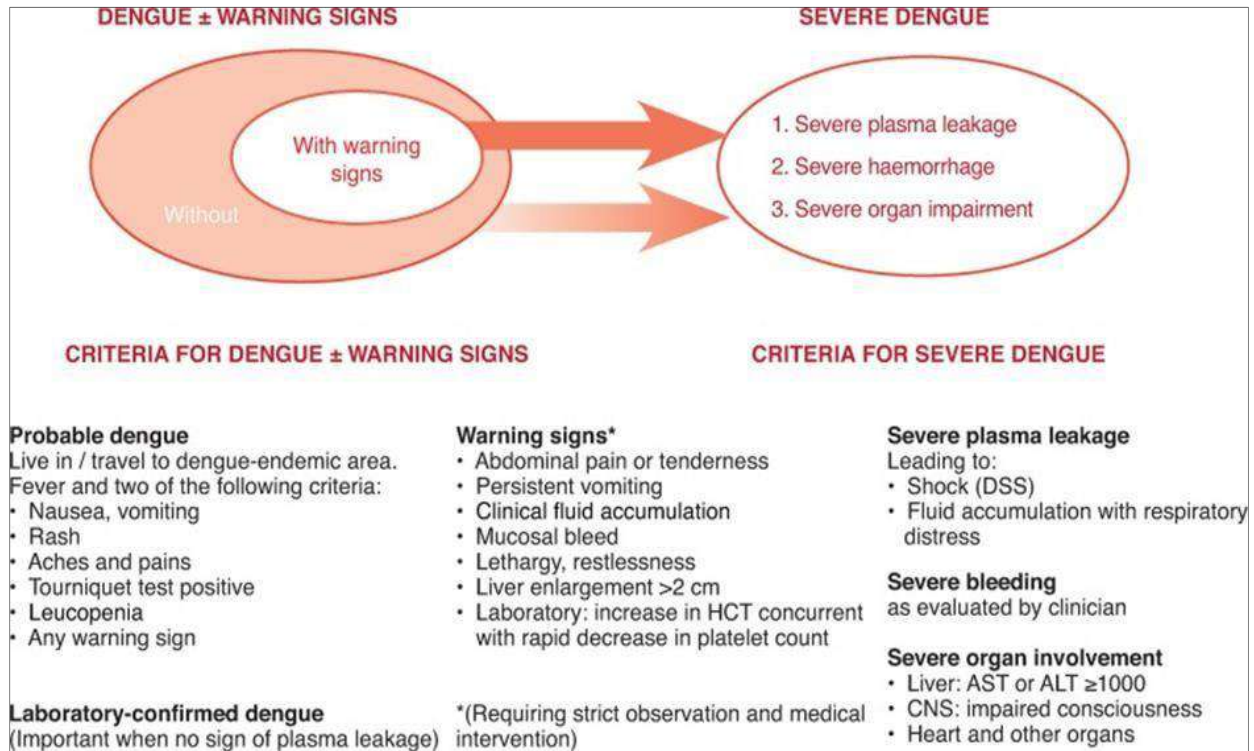
**Table 5:** WHO 1997 dengue classification

Dengue classification criteria	
<b>Dengue fever (DF)</b>	
Acute febrile illness with two or more of the following	Headache
	Retro-orbital pain
	Myalgia
	Leukopenia
	Arthralgia
	Rash
	Supportive serology or occurrence at the same location and time as other confirmed cases of dengue fever
<b>Dengue haemorrhagic fever (DHF)</b>	
All of the following must be present	Fever or history of acute fever, lasting 2-7 days, occasionally biphasic
	Haemorrhagic manifestations: (positive tourniquet test, petechia, ecchymosis, purpura or bleeding from the mucosa, hematemesis/melena)
	Thrombocytopenia (<100000 platelets/mm <sup>3</sup> )
	Evidence of plasma leakage due to increased vascular permeability
<b>Dengue shock syndrome (DSS)</b>	
DHF with hypotension for age or narrow pulse pressure (<20mmHg), plus	Rapid and weak pulse
	Cold clammy skin, restlessness

Source: [14]

**2009 who dengue classification**

**Differentiates features of severe and non-severe dengue**



**Fig 3:** 2009 WHO Dengue Classification (Differentiating Features of Severe and Non-Severe Dengue).

**Conclusions**

Gallbladder wall thickening (GBWT) can be used as an early predictor as well as an important prognostic sign for severe dengue infection and dengue haemorrhagic fever (DHF) especially during an epidemic.

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