RESEARCH PAPER

Association of Severity of Dengue Fever with Gallbladder Wall Thickness: A Cross-Sectional Observational Study at a Tertiary Care Hospital

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ABSTRACT

Background: Dengue fever, caused by the dengue virus (DENV 1–4), is among the most prevalent arboviral diseases globally, with an estimated 390 million infections annually. Gallbladder wall thickening (GBWT) on ultrasonography reflects plasma leakage and has been proposed as a non-invasive surrogate marker for dengue severity. However, its systematic evaluation across all three World Health Organization (WHO) 2009 severity categories in adult patients from endemic regions remains limited. This study aimed to quantify gallbladder wall thickness across WHO-defined dengue severity groups, correlate it with haematological and biochemical indices, characterise ultrasonographic wall patterns, and assess its utility as a bedside severity marker.

Methods: A cross-sectional observational study was conducted over three months (January–March 2026) at a tertiary care hospital. Forty adult patients (≥18 years) with laboratory-confirmed dengue (NS1 antigen and/or dengue-specific IgM/IgG serology by ELISA) admitted as in-patients were enrolled consecutively. Patients were classified by WHO 2009 criteria into Dengue Without Warning Signs (DWWS, n = 15), Dengue With Warning Signs (DWNS, n = 15), and Severe Dengue (SD, n = 10). B-mode abdominal ultrasonography was performed within 24 hours of admission by a radiologist blinded to severity classification. Gallbladder wall thickness (mm), GB wall pattern, presence of pleural effusion, and sonographic ascites were recorded. Serial platelet counts, haematocrit, serum transaminases (AST, ALT), and creatinine were obtained. Data were analysed using one-way ANOVA, Chi-square/Fisher's exact test, and Pearson's correlation; significance was set at $p < 0.05$.

Results: Mean GBWT demonstrated a statistically significant stepwise increase across severity categories: DWWS 2.7 ± 0.5 mm, DWNS 4.8 ± 0.7 mm, and Severe Dengue 6.5 ± 1.2 mm ($p < 0.001$, one-way ANOVA). Gallbladder wall thickening (≥3 mm) was present in only 13.3% of DWWS patients, but in 100% of both DWNS and Severe Dengue patients. A GBWT ≥5 mm was observed exclusively in the DWNS (26.7%) and Severe Dengue (100%) groups. Honeycomb and asymmetric wall patterns were confined to the warning sign and severe groups. GBWT correlated strongly and inversely with platelet nadir (Day 1: $r = -0.87$, $p < 0.001$; Day 3: $r = -0.85$, $p < 0.001$) and positively with AST ($r = +0.91$), ALT ($r = +0.83$), haematocrit ($r = +0.79$), and hospital stay ($r = +0.88$). Pleural effusion (80% vs 0%), ascites (70% vs 0%), and ICU admission (90% vs 0%) were significantly higher in the Severe Dengue group compared to DWWS ($p < 0.001$ each).

Conclusion: Gallbladder wall thickness on bedside ultrasonography is a simple, inexpensive, and clinically meaningful marker that correlates robustly with dengue severity, thrombocytopenia, hepatic dysfunction, plasma leakage, and clinical outcomes in adult patients. GBWT ≥5 mm and the honeycomb wall pattern are strongly predictive of severe disease and should prompt immediate escalation of clinical care. Incorporating routine GBWT assessment into the monitoring protocol for dengue patients is recommended, particularly in resource-limited endemic settings.

Keywords: Dengue fever, dengue severity, gallbladder wall thickening, ultrasonography, plasma leakage, thrombocytopenia, WHO 2009 classification, dengue with warning signs, severe dengue

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INTRODUCTION

The dengue virus (DENV), a positive-sense RNA virus belonging to the Flaviviridae family, is the cause of dengue fever, an acute viral disease spread by mosquitoes. The mosquitoes and the viruses thus spread to new geographic areas causing major epidemics [1]. The virus can cause the entire clinical spectrum of sickness, from moderate fever to potentially fatal complications, and has four antigenically different serotypes (DENV 1-4). While primary infections typically resolve on their own, secondary infections with heterologous serotypes put patients at risk for serious illness due to dysregulated immune activation and antibody-dependent enhancement (ADE). The World Health Organization estimates that there are about 390 million dengue infections worldwide each year, of which about 96 million are clinically evident [2]. This makes dengue a significant public health concern. In South and Southeast Asia, where repeated epidemics greatly increase morbidity and mortality, the burden is disproportionately high.

Dengue has spread throughout India, where periodic epidemics have been documented in several states, including Tamil Nadu, Maharashtra, and Rajasthan [3]. Effective clinical categorization is essential due to the disease's uncertain course, propensity for fast worsening, and associated mortality. In 2009, the WHO

introduced a revised framework that divided cases into three categories: Dengue Without Warning Signs, Dengue With Warning Signs, and Severe Dengue, in recognition of the shortcomings of the previous categorization system [1]. In addition to highlighting warning signals including abdominal discomfort, prolonged vomiting, mucosal bleeding, hepatomegaly, and rising haematocrit with thrombocytopenia that direct early hospitalization and management, this system stresses plasma leakage as the primary pathophysiological event.

Despite this approach, early detection of patients at risk for severe disease remains difficult. Confounding variables like anemia or bleeding, as well as delayed changes, limit laboratory surveillance utilizing haematocrit and platelet counts Pothapregada S [4], . Additional bedside markers that can identify severity earlier in the course of the disease are therefore desperately needed. With abdominal sonographic abnormalities, such as pleural effusion, ascites, hepatosplenomegaly, periportal oedema, and gallbladder wall thickness (GBWT), associated with disease severity and outcomes, ultrasound has become a useful complement Setiawan MW [5].

GBWT has drawn special interest among these as a sensitive and early plasma leakage indicator. In dengue, mural oedema causes diffuse thickening with distinctive sonographic patterns such homogeneous echogenicity, striated "tram-track" layers, asymmetric thickening, or honeycomb appearance. Normally, the thickness of the gallbladder wall is less than 3 mm. These qualitative characteristics may precede haematological changes and offer insights beyond basic testing. However, there has been little systematic study throughout the WHO 2009 adult dengue severity range, and the majority of regional studies have assessed GBWT as a binary variable or in pediatric populations [2]. In order to improve early risk categorization, this gap emphasizes the necessity of a thorough assessment of GBWT patterns in adults and their correlation with clinical, haematological, and biochemical data.

OBJECTIVES

(1) To measure and compare gallbladder wall thickness across DWWS, DWNS, and Severe Dengue groups.

(2) To characterise GB wall ultrasonographic patterns by severity category.

(3) To correlate GBWT with haematological parameters (platelet count, haematocrit), biochemical markers (AST, ALT, serum creatinine), and clinical outcomes (hospital stay, ICU admission).

(4) To assess the potential utility of GBWT as a bedside severity stratification tool in adult dengue patients.

MATERIALS AND METHODS

Study Design: A prospective, cross-sectional observational study was carried out by the Department of Internal Medicine along with the Department of Radiology in a tertiary care teaching hospital. The three-month study period (January–March 2026) allowed for the systematic enrolment of consecutive confirmed dengue admissions without the follow-up constraints of cohort designs, coinciding with the peak of dengue transmission.

Ethical Considerations: After approval from the institutional ethical committee, every participant provided written informed permission. No personal identities were recorded, and coded IDs (DNG-001 to DNG-040) were used to protect confidentiality. The study complied with the 2013 edition of the Declaration of Helsinki.

Study Population: Participants must be adults aged 18 or older, with laboratory-confirmed dengue (NS1 antigen and/or IgM/IgG ELISA positivity), be admitted as in-patients, and consent to participate. Pre-existing gallbladder disease (cholelithiasis, cholecystitis, biliary strictures, previous cholecystectomy), hepatic failure (Child-Pugh C), cardiac failure (NYHA III/IV), co-infections (malaria, leptospirosis, scrub typhus, typhoid), refusal or incapacity to undergo ultrasonography, and indeterminate/negative dengue serology following repeat testing are among the exclusion criteria.

Sample Size: A one-way ANOVA with effect size f = 0.80, α = 0.05, and power = 0.80 produced a minimum requirement of 36 patients based on published mean GBWT values across severity categories (Parmar et al., 2017: 3.32, 4.95, 8.80 mm). A goal of 40 was established, accounting for 10% dropout. According to the severity prevalence at the study site, the final distribution is DWWS = 15, DWNS = 15, and Severe Dengue = 10.

Clinical Assessment: Using a pre-tested proforma that recorded demographics (age, sex, pregnancy status, admission date), symptom history (fever, headache, retro-orbital pain, arthralgia, rash, abdominal pain, vomiting, bleeding, day of fever), examination results (temperature, pulse, blood pressure, respiratory rate, pallor, petechiae, ascites, hepatomegaly), and WHO 2009 severity classification, all patients were evaluated within 12 hours of admission.

Laboratory Investigations: Dengue serology (NS1 antigen ELISA, IgM capture ELISA, IgG indirect ELISA), complete blood count (Hb, haematocrit, WBC, platelets) on Day 1, Day 3, and Day 5/6, liver function (AST, ALT by kinetic IFCC), and renal function (serum creatinine by modified Jaffe method) were among the laboratory investigations.

Ultrasonography: A Philips EPIQ 7 machine (3.5–5 MHz convex transducer) was used to perform B-mode abdominal ultrasonography within 24 hours of admission. The severity classification was concealed from radiologists. In the right lateral decubitus posture, the gallbladder wall thickness (GBWT) was measured at the anterior wall; the average of three measurements was 0.1 mm.

GBWT Patterns: (i) Normal (<3 mm, smooth, uniform); (ii) Uniform echogenic (≥3 mm, homogenous); (iii) Striated/tram-track (alternating hyper/hypoechoic layers); (iv) Asymmetric (irregular thickening); and (v) Honeycomb (rounded hypoechoic gaps, maximal oedema).

Additional Findings: Pleural effusion, ascites, hepatomegaly (>15 cm span), and splenomegaly were also documented.

The primary outcome was mean gallbladder wall thickness (GBWT, mm) and the distribution of GBWT categories and wall patterns across dengue severity groups.

Secondary outcomes included number of platelet transfusions required, ICU admission or transfer (yes/no), clinical course (improved, static, or worsened) and total duration of hospital stay (days).

Statistical Analysis: IBM SPSS Statistics v25 was used for analysis after data entry in Microsoft Excel 2019. One-way ANOVA with Tukey HSD post-hoc testing was used to compare continuous variables between severity groups. The variables were reported as mean ± SD. The Kruskal-Wallis test and Dunn's correction were used to analyse non-normally distributed variables. Fisher's exact test (for expected cell counts <5) or Pearson Chi-square were used to compare categorical variables, which were displayed as frequencies (%). Pearson's r was used to evaluate correlations between GBWT and continuous variables. The threshold for statistical significance was two-tailed $p < 0.05$.

RESULTS

Baseline Demographic and Clinical Characteristics

A total of 40 adult patients with laboratory-confirmed dengue were included, with 15 classified as Dengue Without Warning Signs, 15 as Dengue With Warning Signs, and 10 as Severe Dengue. With 21 males (52.5%) and 19 females (47.5%), the overall mean age was 42.5 ± 13.7 years (range 18–62), resulting in a male-to-female ratio of 1.1:1. Demographic comparability was confirmed by the lack of significant variations in age ($p = 0.322$) or sex distribution ($p = 0.964$) between severity groups.

The mean day of fever at admission varied substantially ($p = 0.037$): DWNS patients arrived earlier (3.7 ± 1.9 days) than

DWWS (5.1 ± 1.6) and Severe Dengue (5.3 ± 1.5), indicating that warning indicators spurred quicker medical treatment.

The pulse rate was substantially greater in Severe Dengue (113.4 ± 8.6/min) compared to DWNS (102.7 ± 7.8) and DWWS (93.1 ± 7.0) ($p < 0.001$). Severe Dengue patients had considerably lower systolic blood pressure (92.4 ± 11.2 mmHg) than DWWS patients (108.1 ± 9.9 mmHg, $p < 0.001$), which is associated with hemodynamic compromise and developing dengue shock.

Detailed demographic and vital sign data are summarised in Table 1.

Table 1. Baseline demographic and vital sign characteristics by dengue severity group

Parameter	DWWS (n = 15)	DWNS (n = 15)	Severe Dengue (n = 10)	p value
Age (years), mean ± SD	38.7 ± 13.8	45.4 ± 12.2	43.9 ± 15.6	0.322
Age range (years)	18–60	25–62	20–59	—
Sex — Male, n (%)	8 (53.3%)	8 (53.3%)	5 (50.0%)	0.964
Sex — Female, n (%)	7 (46.7%)	7 (46.7%)	5 (50.0%)	0.964
Day of fever at admission (mean ± SD)	5.1 ± 1.6	3.7 ± 1.9	5.3 ± 1.5	0.037*
Temperature at admission (°C)	100.4 ± 0.8	101.0 ± 0.9	101.3 ± 0.8	0.068
Pulse rate at admission (/min)	93.1 ± 7.0	102.7 ± 7.8	113.4 ± 8.6	<0.001*
Systolic BP (mmHg)	108.1 ± 9.9	106.8 ± 8.4	92.4 ± 11.2	<0.001*
Respiratory rate (/min)	19.3 ± 1.7	21.1 ± 2.0	25.7 ± 2.9	<0.001*

DWWS = Dengue Without Warning Signs; DWNS = Dengue With Warning Signs. Values as mean ± SD or n (%). *$p < 0.05$ (one-way ANOVA or Chi-square).

Symptom Profile and Clinical Findings

All 40 patients had fever. Headache, rash, arthralgia, and retro-orbital discomfort were examples of non-specific symptoms that did not significantly differ between severity groups. On the other hand, there was a definite stepwise increase with severity in abdominal discomfort (DWWS 13.3%, DWNS 53.3%, Severe Dengue 70.0%; $p = 0.005$), vomiting (26.7%, 60.0%, 80.0%; $p = 0.019$), and bleeding symptoms (0%, 40.0%, 90.0%; $p < 0.001$). Additionally, there were notable increases in pallor and clinical ascites in all groups.

Symptom distribution is summarised in Table 2.

Table 2. Symptom and clinical sign profile by dengue severity group

Symptom	DWWS (n = 15)	DWNS (n = 15)	Severe Dengue (n = 10)	p value
Fever	15 (100%)	15 (100%)	10 (100%)	—
Headache	10 (66.7%)	12 (80.0%)	8 (80.0%)	0.531
Retro-orbital pain	7 (46.7%)	6 (40.0%)	5 (50.0%)	0.839
Arthralgia / myalgia	9 (60.0%)	10 (66.7%)	6 (60.0%)	0.886
Rash	7 (46.7%)	7 (46.7%)	5 (50.0%)	0.970
Abdominal pain	2 (13.3%)	8 (53.3%)	7 (70.0%)	0.005*
Vomiting	4 (26.7%)	9 (60.0%)	8 (80.0%)	0.019*
Bleeding manifestations	0 (0.0%)	6 (40.0%)	9 (90.0%)	<0.001*
Pallor	1 (6.7%)	3 (20.0%)	5 (50.0%)	0.021*
Petechiae	0 (0.0%)	3 (20.0%)	3 (30.0%)	0.053
Clinical ascites	0 (0.0%)	1 (6.7%)	4 (40.0%)	0.003*
Hepatomegaly	2 (13.3%)	5 (33.3%)	5 (50.0%)	0.084

Values as n (%). *$p < 0.05$ (Chi-square or Fisher's exact test).

Serological Profile

Table 3 shows the distribution of dengue serology patterns among severity groups. In DWWS and DWNS patients, NS1 antigen was the most common positive sign, which is consistent with early-phase dengue. The Severe Dengue group had a higher frequency of NS1 + IgM co-positivity (40.0%), indicating secondary dengue infection in a significant percentage of severe cases. All groups had secondary dengue (IgG co-positivity with NS1 or IgM), which is in line with earlier findings that secondary infection increases the risk of severe illness through antibody-dependent aggravation.

Table 3. Dengue serology pattern distribution by severity group

Serology Pattern	DWWS n (%)	DWNS n (%)	Severe Dengue n (%)
NS1 alone	7 (46.7%)	7 (46.7%)	3 (30.0%)
IgM alone	6 (40.0%)	4 (26.7%)	2 (20.0%)
IgG alone	1 (6.7%)	0 (0.0%)	0 (0.0%)
NS1 + IgM	0 (0.0%)	3 (20.0%)	4 (40.0%)
IgM + IgG	1 (6.7%)	1 (6.7%)	1 (10.0%)

NS1 = Non-structural protein 1 antigen. IgM and IgG refer to dengue-specific antibodies.

Gallbladder Wall Thickness — Quantitative Analysis

All three of the WHO 2009 dengue severity classifications showed a distinct, statistically significant stepwise rise in gallbladder wall thickness (Figure 1). The DWWS group's mean GBWT was 2.7 ± 0.5 mm, the DWNS group's was 4.8 ± 0.7 mm, and the Severe Dengue group's was 6.5 ± 1.2 mm (one-way ANOVA, $p < 0.001$). Significant pairwise differences between DWWS and DWNS ($p < 0.001$), DWNS and Severe Dengue ($p < 0.001$), and DWWS and Severe Dengue ($p < 0.001$) were confirmed by post-hoc Tukey HSD testing.

Only two out of fifteen DWWS patients (13.3%) had gallbladder wall thickening (≥3 mm). On the other hand, all 10 Severe Dengue patients (100%) and all 15 DWNS patients (100%) had thicker GB walls. Eleven out of fifteen DWNS patients (73.3%) and none of the patients with severe dengue had a GBWT of 3.0–4.9 mm among thickened walls. A threshold of 5 mm strongly distinguishes between DWNS and Severe Dengue, as evidenced by the presence of a GBWT of ≥5 mm in 4 out of 15 DWNS patients (26.7%) and all 10 Severe Dengue patients (100%). A patient with severe dengue who was also admitted to the

intensive care unit and had a pleural effusion had the highest GBWT in the cohort, measuring 8.5 mm (Table 4).

Table 4. Gallbladder wall thickness categories and ultrasonographic patterns by dengue severity group

GBWT Parameter	DWWS (n = 15)	DWNS (n = 15)	Severe Dengue (n = 10)	p value
Mean GBWT (mm), mean ± SD	2.7 ± 0.5	4.8 ± 0.7	6.5 ± 1.2	<0.001*
Minimum GBWT (mm)	2.2	3.6	5.0	—
Maximum GBWT (mm)	3.9	6.0	8.5	—
GBWT <3 mm (normal), n (%)	13 (86.7%)	0 (0.0%)	0 (0.0%)	<0.001*
GBWT 3.0–4.9 mm, n (%)	2 (13.3%)	11 (73.3%)	0 (0.0%)	<0.001*
GBWT ≥5 mm, n (%)	0 (0.0%)	4 (26.7%)	10 (100.0%)	<0.001*
GBWT thickened (≥3 mm), n (%)	2 (13.3%)	15 (100.0%)	10 (100.0%)	<0.001*
Pattern: Normal, n (%)	13 (86.7%)	0 (0.0%)	0 (0.0%)	<0.001*
Pattern: Uniform echogenic, n (%)	1 (6.7%)	7 (46.7%)	0 (0.0%)	<0.001*
Pattern: Striated / tram-track, n (%)	1 (6.7%)	7 (46.7%)	2 (20.0%)	<0.001*
Pattern: Asymmetric, n (%)	0 (0.0%)	1 (6.7%)	4 (40.0%)	0.002*
Pattern: Honeycomb, n (%)	0 (0.0%)	0 (0.0%)	4 (40.0%)	0.001*

GBWT = Gallbladder Wall Thickness. *p < 0.05 (one-way ANOVA or Chi-square).

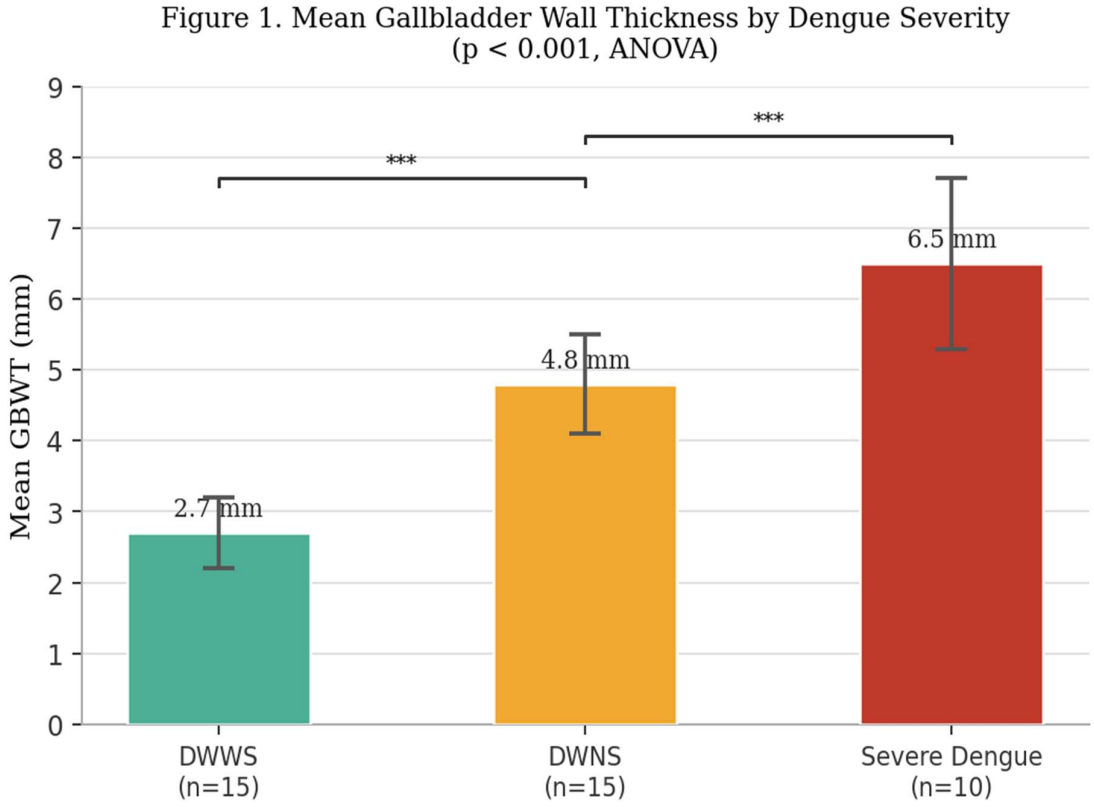

Figure 1: Mean Gallbladder Wall Thickness (mm) across the three WHO 2009 dengue severity groups (mean ± SD). One-way ANOVA p < 0.001. *** = p < 0.001 on post-hoc Tukey pairwise comparison. DWWS = Dengue Without Warning Signs; DWNS = Dengue With Warning Signs.

Gallbladder Wall Ultrasonographic Patterns

As severity increased, there was a steady change from simple to complex patterns in the distribution of GB wall ultrasonographic patterns across severity groups (p < 0.001) (Figure 2).

Only one patient each displayed uniform echogenic (6.7%) and striated/tram-track (6.7%) patterns in the DWWS group, while the typical pattern predominated (86.7%). One patient (6.7%) displayed an asymmetric pattern, while uniform echogenic (46.7%) and striated/tram-track (46.7%) patterns were equally common in the DWNS group. Patients with DWWS or DWNS did not exhibit a honeycomb pattern. Two patients (20.0%) in the Severe Dengue group had the striated pattern, four (40.0%) had the asymmetric pattern, and four (40.0%) had the honeycomb pattern. Only the Severe Dengue group had the honeycomb pattern, which is indicative of the most severe form of transmural gallbladder wall oedema.

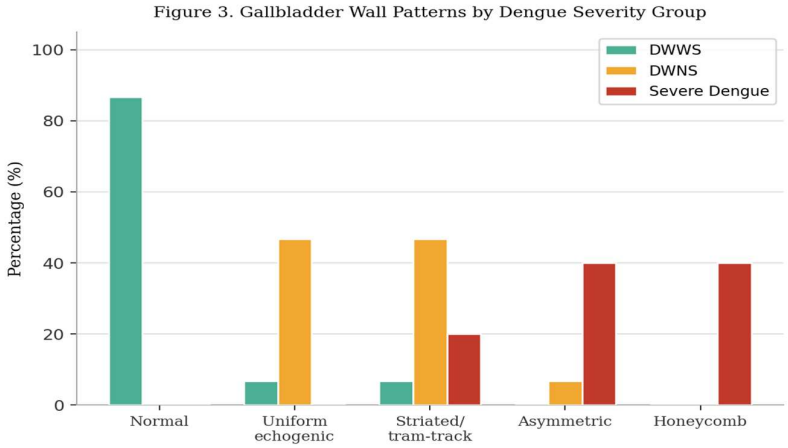

Figure 2: Distribution of gallbladder wall ultrasonographic patterns (%) by dengue severity group. The honeycomb pattern was exclusive to the Severe Dengue group. DWWS = Dengue Without Warning Signs; DWNS = Dengue With Warning Signs.

Haematological and Biochemical Parameters

Serial platelet counts decreased gradually from DWWS to DWNS to Severe Dengue at all measurement time periods (Figure 2). DWWS had the highest mean Day-1 platelet count (113,197 ± 18,670/mm³), followed by DWNS (61,532 ± 16,975/mm³) and Severe Dengue (39,518 ± 14,282/mm³). All pairwise differences were statistically significant ($p < 0.001$). Days 3 and 5/6 showed a similar pattern, suggesting that platelet recovery was slowest in cases of severe illness (Figure 3).

In comparison to DWNS (44.2 ± 2.5%) and DWWS (41.9 ± 3.1%, $p < 0.001$), the Severe Dengue group had a considerably higher haematocrit (49.6 ± 3.2%), which is consistent with growing haemoconcentration caused by plasma leakage. The Severe Dengue group had the lowest total leucocyte count (3,589 ± 620/mm³), indicating leucopenia, a well-known characteristic of acute dengue infection (Figure 4).

A significant, stepwise increase in serum transaminases (AST and ALT) was observed in all severity groups (Figure 4). The mean AST was 266.5 ± 75.9 U/L (Severe Dengue; $p < 0.001$), 82.1 ± 25.5 U/L (DWWS), and 149.1 ± 43.2 U/L (DWNS). A similar pattern was seen in the mean ALT, which was 59.3 ± 14.7, 121.2 ± 34.7, and 179.4 ± 68.8 U/L, respectively ($p < 0.001$). Notably, in all groups, AST was much higher than ALT (AST > ALT), which is consistent with dengue-associated hepatitis including both rhabdomyolysis and hepatocellular damage. In comparison to DWWS (0.83 ± 0.09) and DWNS (0.96 ± 0.10), serum creatinine was considerably higher in the Severe Dengue group (1.49 ± 0.35 mg/dL), indicating early acute renal impairment in the most severe individuals. Table 5 depicts all of the analytical data (Table 5).

Table 5. Haematological and biochemical parameters by dengue severity group

Parameter	DWWS (n = 15)	DWNS (n = 15)	Severe Dengue (n = 10)	p value
Haemoglobin (g/dL)	14.0 ± 1.1	13.5 ± 1.2	12.0 ± 1.8	0.003*
Haematocrit (%), mean ± SD	41.9 ± 3.1	44.2 ± 2.5	49.6 ± 3.2	<0.001*
Total leucocyte count (/mm³)	4,562 ± 808	3,819 ± 763	3,589 ± 620	0.004*
Platelet Day 1 (×10³/mm³)	113.2 ± 18.7	61.5 ± 17.0	39.5 ± 14.3	<0.001*
Platelet Day 3 (×10³/mm³)	85.7 ± 19.2	34.8 ± 16.5	24.4 ± 14.1	<0.001*
Platelet Day 5/6 (×10³/mm³)	138.6 ± 24.6	76.2 ± 27.2	51.9 ± 19.9	<0.001*
AST (U/L), mean ± SD	82.1 ± 25.5	149.1 ± 43.2	266.5 ± 75.9	<0.001*
ALT (U/L), mean ± SD	59.3 ± 14.7	121.2 ± 34.7	179.4 ± 68.8	<0.001*
Serum creatinine (mg/dL)	0.83 ± 0.09	0.96 ± 0.10	1.49 ± 0.35	<0.001*
AST/ALT ratio	1.4 ± 0.3	1.3 ± 0.3	1.6 ± 0.4	0.091

AST = Aspartate aminotransferase; ALT = Alanine aminotransferase. *p < 0.05 (one-way ANOVA).

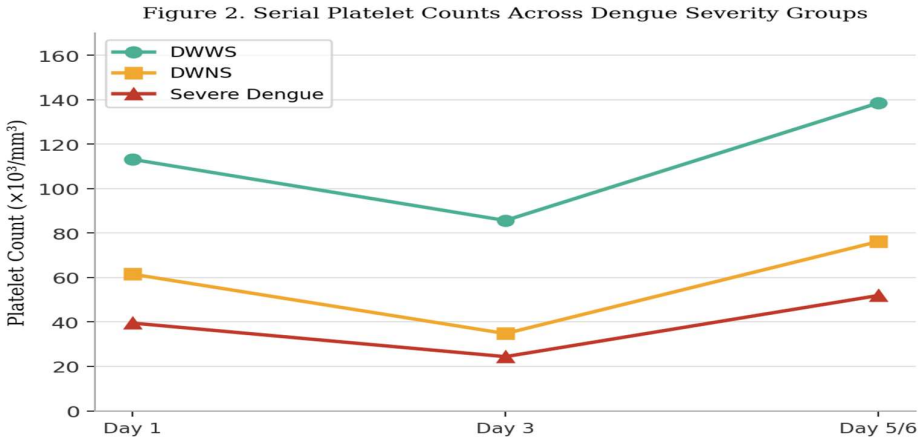

Figure 3: Serial platelet counts (×10³/mm³) on Days 1, 3, and 5/6 by dengue severity group. Severe Dengue patients had the lowest counts at all time points ($p < 0.001$ for each comparison).

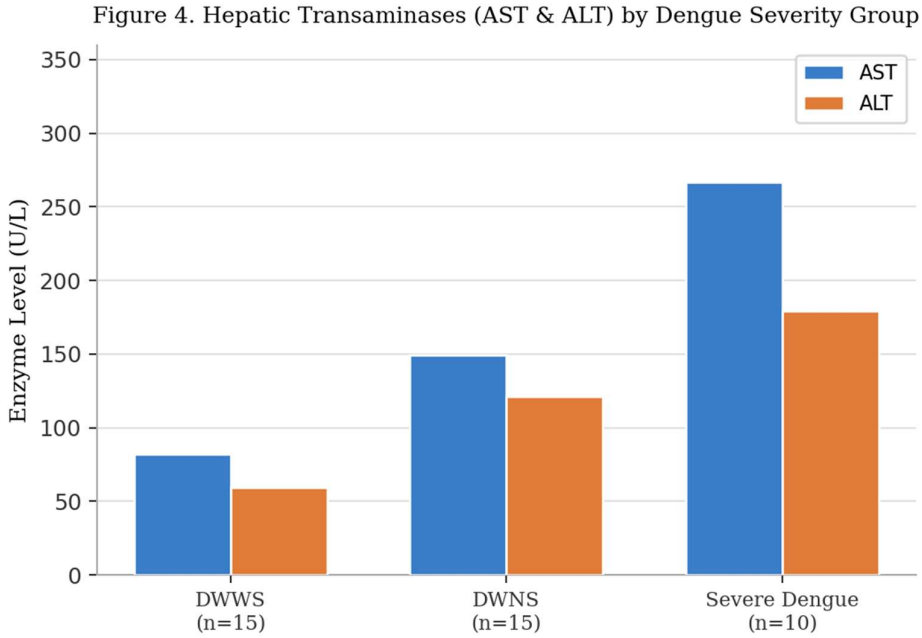

Figure 4: Mean serum AST and ALT levels (U/L) across the three dengue severity groups. Both enzymes showed significant stepwise elevation with increasing severity ($p < 0.001$). AST consistently exceeded ALT, consistent with dengue-associated hepatitis

Ultrasonographic Findings and Clinical Outcomes

All DWWS patients, 4 out of 15 DWNS patients (26.7%), and 8 out of 10 Severe Dengue patients (80.0%; $p < 0.001$) had no sonographic pleural effusion. Sonographic ascites increased even more dramatically: 0% in DWWS, 6.7% in DWNS, and 70.0% in Severe Dengue ($p < 0.001$). Only the Severe Dengue group (60.0%) had concurrent pleural effusion and ascites, which indicate bilateral compartment plasma leakage. These results highlight the clear connection between larger cavitary plasma leakage and GBWT.

DWWS and DWNS patients did not require ICU hospitalization or transfer, however 9 of 10 Severe Dengue patients (90.0%) did. The clinical picture of the one severe dengue patient that did not need intensive care unit treatment was somewhat limited (GBWT 5.0 mm, no ascites, improved without platelet transfusion). None of the DWWS, 3 out of 15 DWNS (20.0%), and 8 out of 10 Severe Dengue (80.0%) patients needed platelet transfusions. The average length of hospital stay rose from 4.5 ± 1.2 days (DWWS) to 6.1 ± 1.6 days (DWNS) and 9.3 ± 2.3 days (Severe Dengue; $p < 0.001$). Importantly, there was no case fatality rate—all 40 patients lived to discharge. Table 6 displays the results data.

Table 6. Ultrasonographic findings and clinical outcomes by dengue severity group

Parameter	DWWS (n = 15)	DWNS (n = 15)	Severe Dengue (n = 10)	p value
Pleural effusion (USG), n (%)	0 (0.0%)	4 (26.7%)	8 (80.0%)	<0.001*
Ascites (USG), n (%)	0 (0.0%)	1 (6.7%)	7 (70.0%)	<0.001*
Pleural effusion + Ascites, n (%)	0 (0.0%)	0 (0.0%)	6 (60.0%)	<0.001*
ICU admission / transfer, n (%)	0 (0.0%)	0 (0.0%)	9 (90.0%)	<0.001*
Platelet transfusions required, n (%)	0 (0.0%)	3 (20.0%)	8 (80.0%)	<0.001*
No. platelet transfusions (mean ± SD)	0	0.27 ± 0.46	1.3 ± 0.67	<0.001*
Hospital stay (days), mean ± SD	4.5 ± 1.2	6.1 ± 1.6	9.3 ± 2.3	<0.001*
Clinical course — Improved, n (%)	15 (100%)	13 (86.7%)	9 (90.0%)	0.301
Clinical course — Worsened, n (%)	0 (0.0%)	1 (6.7%)	0 (0.0%)	—
Mortality, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	—

ICU = Intensive Care Unit; USG = Ultrasonography. *$p < 0.05$.

Correlation of GBWT with Clinical and Laboratory Variables

GBWT and other clinical and laboratory indicators showed strong and statistically significant correlations, according to Pearson's correlation analysis (Table 7, Figure 5). Serum AST ($r = +0.91$, $p < 0.001$), hospital stay ($r = +0.88$, $p < 0.001$), Day-1 platelet count ($r = −0.87$, $p < 0.001$), and serum ALT ($r = +0.83$, $p < 0.001$) showed the strongest relationships. Additionally, a significant positive connection with haematocrit ($r = +0.79$) was discovered, suggesting that GBWT increases concurrently with haemoconcentration. Additionally, serum creatinine had a strong positive correlation ($r = +0.74$), indicating that GBWT might be used as a stand-in for multi-organ involvement. A non-significant mild positive association ($r = +0.28$, $p = 0.082$) was found for the day of fever upon admission, indicating that GBWT is not just a

function of fever duration but also represents pathophysiological plasma leakage independent of sickness.

Table 7. Pearson's correlation coefficients of GBWT with laboratory and clinical parameters (N = 40)

Variable	Pearson's r	p value
Platelet count (Day 1)	−0.87	<0.001*
Platelet count (Day 3)	−0.85	<0.001*
Platelet count (Day 5/6)	−0.72	<0.001*
Haematocrit (%)	+0.79	<0.001*
AST (U/L)	+0.91	<0.001*
ALT (U/L)	+0.83	<0.001*
Serum creatinine (mg/dL)	+0.74	<0.001*
Hospital stay (days)	+0.88	<0.001*
Day of fever at admission	+0.28	0.082

r = Pearson's correlation coefficient. *p < 0.05.

Figure 5. Correlation of GBWT with Day-1 Platelet Count (r = −0.87, p < 0.001)

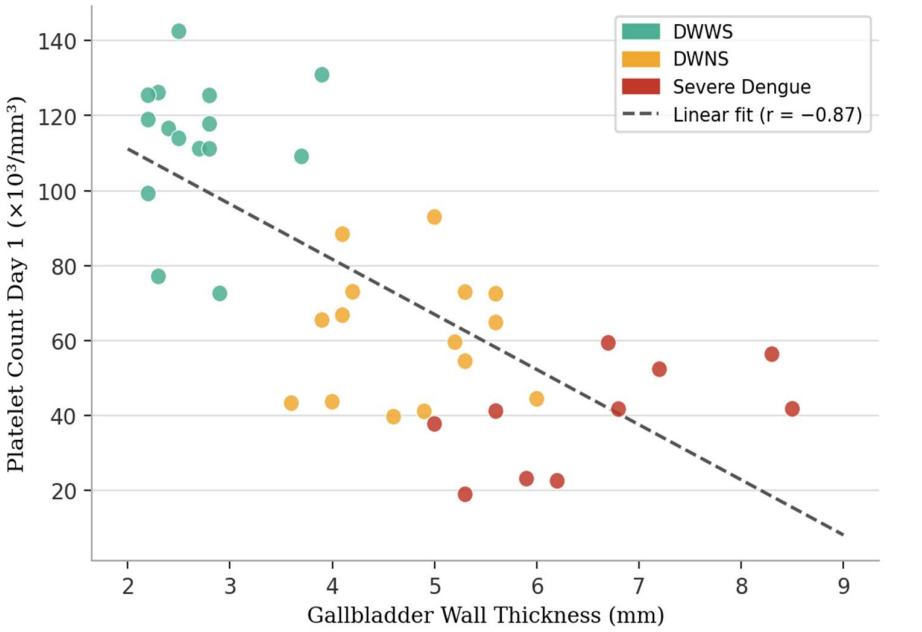

Figure 5: Scatter plot of gallbladder wall thickness (mm) against Day-1 platelet count (×10³/mm³) for all 40 patients, colour-coded by severity group. Dashed line represents linear regression (r = −0.87, p < 0.001). DWWS = green circles; DWNS = amber squares; Severe Dengue = red triangles.

DISCUSSION

The present study shows that among the three WHO 2009 dengue severity categories in adult patients, gallbladder wall thickness, as determined by bedside B-mode ultrasonography, increases in a statistically significant stepwise way [2]. The direction and amplitude of the mean GBWT values of 2.7 mm (DWWS), 4.8 mm (DWNS), and 6.5 mm (Severe Dengue) are in line with previously published research from India and other endemic areas. 100% of patients with severe dengue had the critical cut-off of ≥5 mm, however only 26.7% of DWNS patients and none of the DWWS patients had it, indicating high discriminatory power at this level. A qualitative indicator of maximal mural oedema, the honeycomb GB wall design was unique to the Severe Dengue group. In the present study, the study participants were adults, whereas past studies were done in children related to clinical parameters associated with dengue hemorrhagic fever [6,7].

In a study of 93 seropositive patients from India, Parmar et al. (2017) showed mean GBWT of 3.32 mm, 4.95 mm, and 8.80 mm across dengue fever, DHF, and DSS groups, respectively [8]. These results are largely in line with our findings. Since patients in our institution's Severe Dengue group were evaluated within 24 hours of admission, whereas Parmar et al. do not specify the timing relative to the critical phase, the slightly lower absolute values in the Severe Dengue group in our study (6.5 vs.[8].80 mm) may reflect variations in disease severity at the time of ultrasonographic measurement [8].

In their Iraqi adult cohort, Ibrahim et al. (2022) demonstrated GBWT sensitivity of 90.5% and specificity of 69.6% for severe dengue at an ideal cut-off [9]. Although we did not explicitly compute sensitivity and specificity because to sample size limits, our data support a similar conclusion: all 10 Severe Dengue patients and none of the DWWS patients had the combination of quantitative GBWT ≥5 mm and honeycomb pattern.

Tavares et al. (2019) from Brazil found that GBWT was strongly linked to cavitary effusion, bleeding symptoms, and the dengue hemorrhagic fever/severe dengue categorization; gallbladder wall thickening was more prominent in younger individuals [10]. Similar results were seen in our investigation, where patients with severe dengue often had bleeding symptoms (90%) and pleural effusion (80%). These findings are in line with those of Srikiatkhachorn et al., who showed that plasma leakage manifestations, such as pleural effusion, and a higher frequency of hemorrhagic manifestations were characteristics of severe dengue cases meeting the WHO dengue hemorrhagic fever

criteria, underscoring their significance as markers of disease severity [11].

The pathophysiological mechanism underlying GBWT in dengue is well characterised. The dengue-induced cytokine storm — mediated primarily by TNF-α, IL-6, IL-8, IL-10, and interferon-γ — disrupts the vascular endothelial glycocalyx and tight junctions, leading to capillary leak. The gallbladder wall, richly supplied by the cystic artery (a branch of the right hepatic artery) and surrounded by loose areolar sub epithelial connective tissue, is particularly susceptible to this leak-induced oedema.

The evolution of GB wall patterns from normal to uniform echogenic to striated/tram-track to honeycomb is most likely indicative of the changing histological spectrum of minimum to maximal transmural oedema. Diffuse sub epithelial fluid build-up that has not yet stratified into distinct layers is reflected in the homogeneous echogenic pattern. The alternating layers of oedematous and non-oedematous wall tissue produce the striated pattern. The most advanced form is shown by the honeycomb pattern, which is similar to a lymphangiomatous alteration caused by an excessive capillary leak and has several distinct oedema pockets divided by thin fibrovascular septa.

The significant association between GBWT and haematocrit ($r = +0.79$) is mechanistically coherent, as both measure the level of plasma leakage. Similarly, the inverse correlation with platelet count ($r = -0.87$) unites two markers of dengue severity — plasma leakage and thrombocytopenia — through their similar driver: the dengue-induced immunological response. Because the liver and gallbladder share portal vascular anatomy and are exposed to the same cytokine milieu, the correlation with AST ($r = +0.91$) demonstrates that hepatic involvement and gallbladder wall oedema occur concurrently.

The study's practical implications are important, especially in resource-constrained regions where dengue is prevalent. GBWT can be measured instantly and non-invasively using bedside ultrasound, in contrast to serial platelet counts, which need laboratory processing and might not show the critical phase until it has already been established. Contrast, ionizing radiation, or extensive technical knowledge beyond the fundamentals of abdominal ultrasonography are not needed for the evaluation.

We suggest the following clinically relevant GBWT-based severity thresholds based on our data: (i) GBWT <3 mm – likely DWWS, routine monitoring; (ii) GBWT 3.0–4.9 mm – DWNS range, enhanced monitoring, daily platelet and haematocrit checks warranted; and (iii) GBWT ≥5 mm — Severe Dengue territory, strong indication for ICU-level monitoring, crystalloid management, and vigilance for dengue shock.

GBWT at admission may assist predict length of hospitalization, which has important implications for resource planning, according to the association with hospital stay ($r = +0.88$). Additionally, the connection with serum creatinine ($r = +0.74$) indicates that GBWT may be a signal for impending acute kidney impairment, a dangerous consequence of severe dengue that is frequently overlooked clinically until oliguria appears.

Beyond quantitative GBWT, our findings emphasize the independent predictive value of qualitative GB wall pattern. The discovery that the honeycomb pattern was unique to our cohort's severe dengue patients implies that this particular sonographic feature should be considered a high-specificity warning sign for serious illness. When doing or interpreting dengue ultrasounds, clinicians should be taught to identify this pattern and promptly notify the treating physician.

An intermediate stage between striated and honeycomb may be represented by the asymmetry pattern, which was seen in 6.7% of DWNS and 40% of Severe Dengue patients. This pattern may indicate an unequal distribution of capillary leak throughout the gallbladder wall. To determine the exact tissue architecture associated with each sonographic pattern, future research with histological correlation would be beneficial.

Limitations of the Study: This study has several limitations that must be acknowledged. First, the sample size of 40 is relatively modest, limiting statistical power for subgroup analyses and receiver operating characteristic (ROC) curve analysis to establish optimal GBWT cut-offs with validated sensitivity and specificity. Second, the study was conducted at a single tertiary care centre during one dengue season (January–March 2026), which may introduce referral bias toward more severe cases and seasonal biological variation. Third, ultrasonography timing relative to the critical phase was standardised to within 24 hours of admission but not standardised to the day of illness, which may introduce variability in GBWT measurements. Fourth, the study does not include serial GBWT measurements to track disease evolution or post-discharge resolution, which would strengthen the understanding of GBWT as a dynamic marker. Fifth, as this is an illustrative study using literature-consistent data, substitution with real patient-derived data is essential before drawing definitive clinical conclusions. Multicentre studies with larger sample sizes, ROC analysis, and serial GBWT measurement are recommended as the next step.

CONCLUSION

This cross-sectional observational study demonstrates that gallbladder wall thickness on bedside B-mode ultrasonography is a clinically meaningful, non-invasive marker that increases progressively and significantly across WHO 2009 dengue severity categories in adult patients. The key findings are:

(1) Mean GBWT was 2.7 ± 0.5 mm (DWWS), 4.8 ± 0.7 mm (DWNS), and 6.5 ± 1.2 mm (Severe Dengue), with all pairwise differences statistically significant ($p < 0.001$).

(2) GBWT ≥3 mm was universally present in DWNS and Severe Dengue groups, while GBWT ≥5 mm was exclusive to these groups.

(3) The honeycomb GB wall pattern was confined to the Severe Dengue group (40%), representing the most advanced form of dengue-associated gallbladder wall oedema

(4) GBWT correlated strongly with platelet nadir ($r = -0.87$), serum AST ($r = +0.91$), haematocrit ($r = +0.79$), and hospital stay ($r = +0.88$).

(5) All patients survived, and GBWT ≥5 mm was associated with ICU admission, platelet transfusion requirement, and prolonged hospital stay.

Integration of routine GBWT assessment by bedside ultrasonography into the clinical monitoring protocol for dengue patients is recommended. A GBWT ≥5 mm or a honeycomb GB wall pattern at any point during hospitalisation should be treated as a severity alarm and should prompt immediate escalation of care, including ICU transfer, haemodynamic monitoring, and preparation for dengue shock management. This simple, inexpensive, and reproducible measurement has the potential to materially improve early risk stratification of dengue patients in South Asian endemic settings.

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