## Juliet Anitha Sean Martin,<sup>1</sup> Karthikeyan Annadurai<sup>2</sup>

<sup>1</sup>Consultant Paediatrician, SJ Clinic, Mettupalayam, Tamil Nadu, India <sup>2</sup>Consultant Pediatrician, Nalam Child Centre, Chennai, Tamil Nadu, India

#### Article History

Abstract

Received: September 6, 2024 Accepted: September 27, 2024 Published: October 4, 2024

DOI: 10.15850/ijihs.v12.n2.4100 IJIHS. 2024;12(2):109–116

#### Correspondence:

Karthikeyan Annadurai, Consultant Pediatrician, Nalam Child Centre, Chennai, Tamil Nadu, India Email: Kannadurai19@gmail. com **Objective**: To study ultrasound findings of children with dengue and analyze the possible correlation between ultrasound findings and severity of dengue in children.

**Methods**: This retrospective study, which was conducted over one year, analyzed 50 pediatric dengue patients. Ultrasound findings such as gallbladder wall edema, pleural effusion and ascites were assessed. Cases were categorized into dengue without warning signs, dengue with warning signs, and severe dengue according to the World Health Organization's classification of dengue. Correlation between ultrasound abnormalities, severity of dengue, and thrombocytopenia were analyses. A p-value of less than 0.05 was taken as statistically significant.

**Results**: Of 50 pediatric patients diagnosed with dengue participated in this study, 72% were boys, and 28% were girls with a male-to-female ratio of 1:0.38. Fever was the most frequent symptom (100%), followed by nausea/vomiting (84%) and body ache/myalgia (78%). Ultrasound findings revealed that gallbladder wall edema (48%), pleural effusion (44%), and ascites (50%) were significantly associated with severe dengue and dengue with warning signs (p<0.001). Thrombocytopenia was documented in 58% of cases and correlated significantly with ultrasound abnormalities such as gallbladder wall edema, ascites, and pleural effusion (p=0.0017).

**Conclusion**: Ultrasound findings, such as gallbladder wall edema, pleural effusion and ascites, are significantly associated with severe dengue and dengue with warning signs. These features aid in early identification of high-risk patients.

**Keywords**: Ascites, dengue, gall bladder wall edema, pleural effusion, ultrasound

## Introduction

Dengue fever is a mosquito-borne viral infection that poses a significant public health challenge in tropical and subtropical countries worldwide. The disease is caused by the dengue virus, which belongs to the Flaviviridae family and has four distinct serotypes DENV-1, DENV-2, DENV-3, and DENV-4. Transmission of dengue occurs primarily through the bites of Aedes mosquitoes, particularly Aedes aegypti and Aedes albopictus. Over the past few decades, the incidence of dengue has increased dramatically, with the World Health Organization estimating approximately 390 million infections annually.<sup>1</sup>

The burden of dengue is especially high in tropical and subtropical regions such as Southeast Asia, the Pacific Islands, the Americas, and Africa. In India, dengue has become endemic, with frequent outbreaks causing significant morbidity and mortality. The country contributes a substantial proportion of the global dengue burden with

This is an Open Access article licensed under the Creative Commons Attribution-NonCommercial 4.0 International License (http:// creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original author and source are properly cited

millions of cases reported each year. Factors such as rapid urbanization, increased travel and climate change have further exacerbated the spread of dengue, underscoring the need for ongoing surveillance and effective public health interventions. In pediatric populations, dengue fever presents unique challenges due to differences in immune response and clinical manifestations compared to adults. Children are often at a higher risk of severe symptoms and complications.<sup>2</sup>

The World Health Organization's 2009 classification divides dengue into three categories: dengue without warning signs, dengue with warning signs and severe dengue. This categorization is crucial for clinical management as early identification of warning signs (severe abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, restlessness, hepatomegaly, and rise in hematocrit and rapid decline in platelet count) is crucial in preventing progression to more severe forms of the disease. Severe dengue, previously known as dengue Hemorrhagic fever and dengue shock syndrome is characterized by plasma leakage, severe bleeding and organ dysfunction requiring prompt and intensive medical care.<sup>3</sup>

The clinical presentation of dengue in children can vary widely, ranging from mild febrile illness to severe, life-threatening conditions. In mild cases, symptoms such as high-grade fever, headache, retro-orbital pain, myalgia, arthralgia and a maculopapular rash are common. As the disease progresses to a more severe form, children may exhibit warning signs that signal a higher risk for outcomes including hemorrhagic severe manifestations, thrombocytopenia and plasma leakage leading to shock. Severe dengue characterized by significant plasma leakage, bleeding and organ dysfunction is a major cause of pediatric hospital admissions and can cause significant morbidity and even mortality if not promptly managed.<sup>4</sup>

The diagnostics for children suspected of having dengue fever includes a thorough clinical evaluation and laboratory investigations. The assessment of hematological profiles is vital for determining disease severity and guiding treatment decisions. Typical findings in dengue include leukopenia, thrombocytopenia, and elevated hematocrit levels, which reflect the degree of plasma leakage. Additionally, biochemical tests may show elevated liver enzymes, indicating hepatic involvement, a common finding in severe cases. Ultrasonography (USG) plays an important role in the evaluation of children with dengue. USG can identify signs such as gallbladder wall thickening, pleural effusion, and ascites which are critical in assessing the severity of the disease and guiding clinical management. Early and accurate diagnosis is essential for timely intervention and can significantly reduce morbidity and mortality in pediatric patients with dengue.<sup>5</sup>

It has been suggested that the degree of thrombocytopenia, hematocritlevels, as well as the evidence of plasma leakage on ultrasound can help predict the risk of progression to severe dengue and guide clinical decisionmaking.<sup>6</sup> A rapidly falling platelet count and rising hematocrit are strong indicators of severe disease , warranting closer monitoring and more aggressive management.<sup>7</sup> Imaging findings such as pleural effusion, ascites and gall bladder wall edema indicate vascular leakage and impending shock. Utilizing a combination of clinical, laboratory, and imaging criteria allows for a more comprehensive assessment of disease severity.<sup>8</sup>

Despite the growing body of literature on dengue fever, a significant knowledge gap remains regarding the correlation between laboratory and imaging findings and the clinical severity of dengue in pediatric patients. This study was undertaken to analyze the ultrasound findings of children with dengue and to determine whether there is a correlation between various ultrasound findings and the severity of dengue in children.

# Methods

This was a retrospective study conducted in the Department of Pediatrics at a tertiary care medical institute located in an urban area, specifically SJ Clinic, Mettupalayam, Tamil Nadu, India. The study duration was one year, extending from January 2023 to December 2023. The sample size was calculated using the formula  $n=(Z \alpha 2) X$  $\sigma^2/d^2$ , based on pilot studies examining ultrasound findings in dengue hemorrhagic fever (Thulkar *et al.*<sup>11</sup>). Assuming 90% power and a 95% confidence interval, the required sample size was 40 patients; therefore, 50 patients were included in this study. The study included pediatric patients under 18 years of age who were diagnosed with dengue based on a positive NS1 antigen, IgM antibody, or RT-PCR test, and whose complete electronic medical records were available. Patients were excluded if they were over 18 years of age, had

#### Juliet Anitha Sean Martin and Karthikeyan Annadurai

incomplete electronic medical records, or if an ultrasound had not been performed. Since this was a purely retrospective observational study and the confidentiality of participants was strictly maintained, no ethical committee clearance was required. It was ensured that all data used in this study was anonymized and that no identifiable information was included in the analysis.

Pediatric patients diagnosed with dengue fever (positive NS1 antigen, IgM antibody, or RT-PCR) during the study period were included based on predefined inclusion and exclusion criteria. Data was extracted from electronic medical records. All pediatric patients with either NS1 antigen or IgM positive for dengue serological markers were included. Cases were categorized into dengue without warning signs, dengue with warning signs, and severe dengue according to the World Health Organization's classification of dengue (Table 1).<sup>9</sup>

Detailed information was obtained from the medical records regarding the duration of illness and the presence of warning symptoms, such as severe abdominal pain or restlessness. Clinical data, including pulse rate, respiratory rate, and blood pressure, were recorded from the patients' charts. Laboratory results, such as serological markers (IgG, IgM, and NS1 or RT PCR), serum electrolytes, complete blood count, hepatic and renal function tests, and coagulation profiles, were also extracted from the electronic medical records. Records of abdominal ultrasounds performed during the patients' hospital stay were reviewed, focusing on findings such as gallbladder wall thickening, fluid collection in the gallbladder fossa, and the presence of pleural effusion and ascites, as reported by the radiologist.

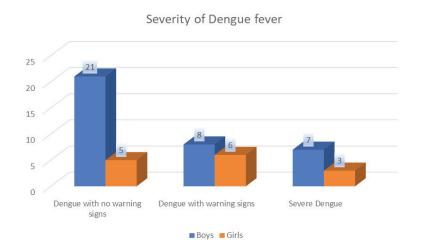
A correlation between ultrasound findings and the type of dengue (dengue without warning signs, dengue with warning signs, and severe dengue) was established. Statistical analysis was conducted using SPSS 22.0 software, and for statistical purposes, a p-value of less than 0.05 was considered statistically significant.

#### Results

In this study, out of 50 pediatric patients diagnosed with dengue, 36 (72%) were boys and the remaining 14 (28%) were girls. There

Category	Criteria		
Dengue without Warning Signs	<ul> <li>Fever and two of the following:</li> <li>Nausea, vomiting</li> <li>Rash</li> <li>Aches and pains</li> <li>Positive tourniquet test</li> <li>Leukopenia</li> <li>Laboratory-confirmed dengue (important when no sign of plasma leakage)</li> </ul>		
Dengue with Warning Signs	<ul> <li>Dengue as defined above with any of the following warning signs:</li> <li>Abdominal pain or tenderness</li> <li>Persistent vomiting</li> <li>Clinical fluid accumulation (ascites, pleural effusion)</li> <li>Mucosal bleed</li> <li>Lethargy or restlessness</li> <li>Liver enlargement &gt;2 cm</li> <li>Laboratory findings : increase in hematocrit concurrent with rapid decrease in platelet count</li> </ul>		
Severe Dengue	<ul> <li>Dengue with at least one of the following:</li> <li>Severe plasma leakage leading to shock (dengue shock syndrome, DSS) and/or fluid accumulation with respiratory distress</li> <li>Severe bleeding as evaluated by the clinician</li> <li>Severe organ involvement (e.g., liver AST or ALT &gt;= 1000, CNS impairment, heart and other organ involvement)</li> </ul>		

International Journal of Integrated Health Sciences (IIJHS), Vol 12, Number 2, September 2024



#### Fig. 1 Classification of Dengue on the Basis of Severity

was a male preponderance with a M:F ratio of 1:0.38. The most commonly affected age group in boys was 11–15 years (20%), whereas among girls, the most commonly affected age group was 5–10 years (14%). The mean age of boys was 10.4 $\pm$ 3.4 years, while the mean age of girls was 9.2 $\pm$ 2.8 years. The mean ages of boys and girls were found to be comparable in the studied cases (p=0.2467).

Cases were divided into dengue without warning signs, dengue with warning signs, and severe dengue according to the World Health Organization's classification of dengue. There were 21 (42%) boys and 5 (10%) girls who were found to have dengue without warning signs whereas dengue with warning signs was present in 14 (28%) cases and severe dengue was seen in 10 (20%) patients (Fig. 1).

The most common presenting complaint was fever, which was present in all patients (100%). Other complaints included nausea and vomiting (84%), body ache/myalgia (78%), skin rash (62%), conjunctival injection (46%), restlessness (48%), periorbital edema (44%), headache (42%), tachypnea (34%) and hypotension (24%). Less common features included bleeding manifestations (20%), and icterus (6%) (Table 2).

A detailed review of imaging findings showed that 24 (48%) patients had gallbladder wall edema on ultrasound imaging. Other imaging findings indicated that unilateral

Sign and Symptom	Number of Cases	Percentage (%)	
Fever	50	100	
Body ache/myalgia	39	78	
Headache	21	42	
Nausea/vomiting	42	84	
Skin rash	31	62	
Conjunctival injection	23	46	
Restlessness	24	48	
Periorbital edema	22	44	
Tachypnoea	17	34	
Hypotension	12	24	
Icterus	3	6	
Bleeding manifestation	10	20	

#### Table 2 Signs and Symptoms of Dengue

Juliet Anitha Sean Martin and Karthikeyan Annadurai



Fig. 2 Common Ultrasound Abnormalities In Patients with Dengue Include Thickened Gall Bladder Wall (Gall Bladder wall edema) (Left), Ascites in the form of Free Fluid in Peritoneal Cavity (Middle) and Right Pleural Effusion (Right)

USG feature	Total n out of 50 (%)	Non-Severe Dengue (n=26) (%)	Non-Severe Dengue with Warning Signs or Severe Dengue (n=24) (%)	p-value
Pleural effusion	22 (44)	4 (8)	18 (36)	< 0.001*
GB Wall edema	24 (48)	5 (10)	19 (38)	< 0.001*
Ascites	25 (50)	7 (6)	18 (36)	=0.001*
Hepatomegaly	16 (32)	9 (18)	7 (14)	0.54
Splenomegaly	24 (48)	13 (26)	11 (22)	0.40

# Table 3 Ultrasound Findings and Their Correlation with Severity of Dengue

\*Chi Square test

## Table 4 Imaging Abnormalities and Their Correlation with Thrombocytopenia

	Thrombocytopenia Present (platelet count < 1, 50,000/microliter)		Thrombocytopenia Absent platelet count > 1, 50,000/microliter	
	Number of cases	Percentage	Number of cases	Percentage
Gall bladder wall edema, Ascites, pleural Effusion or organomegaly present (1 or more)	21	42	6	12
Gall bladder wall edema, Ascites, pleural Effusion or organomegaly Absent	7	14	16	32

p=0.0017 (Significant)\*

\*Chi Square test

or bilateral pleural effusion was present in 22 (44%) patients. Additional ultrasound abdominal findings included ascites (50%), splenomegaly (48%), and hepatomegaly (32%). Ultrasound abnormalities such as gallbladder wall edema, unilateral or bilateral pleural effusion, and ascites were found to be more prevalent in patients with non-severe dengue with warning signs and severe dengue, and the difference was statistically significant. In cases of non-severe dengue, organomegaly was more common compared to non-severe dengue; however, the difference was not statistically significant (p=0.068) (Table 4) (Fig. 2).

Out of 28 (56%) patients who had documented thrombocytopenia during the course of their illness, 21 (42%) patients had some imaging abnormality, whereas out of 22 (44%) patients with normal platelet counts, 6 (12%) patients had imaging abnormalities. There was a significant correlation between ultrasound abnormalities such as gallbladder wall edema, ascites, pleural effusion, or organomegaly and thrombocytopenia in cases of dengue in pediatric patients (Table 5).

## Discussion

Dengue fever is one of the endemic viral diseases prevalent in developing countries, including India. Poor sanitation, rapid urbanization, increasing construction activities, and water clogging contribute to the breeding of Aedes mosquitoes, which act as vectors for the transmission of dengue fever.<sup>10</sup> Though in many cases, dengue fever remains mildly symptomatic and does not require any treatment other than symptomatic management, in some instances, the disease may advance. In these cases, patients may develop complications, including shock, hemorrhagic manifestations, and multiorgan dysfunction.<sup>11</sup>

Dengue is commonly associated with derangements in hematological parameters, such as rising hematocrit, decreasing platelet count, and elevated hepatic enzyme levels.<sup>12</sup> laboratory parameters, In addition to imaging findings such as gallbladder wall edema, ascites, and pleural effusion are also common, particularly in patients with severe dengue. These imaging findings suggest a strong possibility of plasma leakage, which is a hallmark of severe dengue.<sup>13</sup> Although gallbladder wall edema, pleural effusion, and ascites are not specific findings attributable to dengue fever and can be seen in many other

conditions where plasma oncotic pressure is low—such as in cases of hypoalbuminemia secondary to liver diseases or malnutrition and in cases of nephrotic syndrome—their presence in pediatric patients suspected of or diagnosed with dengue may indicate the possibility of progression to severe dengue.<sup>14</sup>

Several studies have reported various ultrasound imaging findings in cases of dengue. V R Santhosh et al. conducted a retrospective study to determine the role of ultrasound in diagnosing dengue fever and predicting disease severity by correlating imaging findings with platelet count. For this purpose, the authors studied 96 serologically confirmed dengue patients who underwent ultrasound scanning. The study found that 66.7% had edematous gallbladder wall thickening, 64.5% had ascites, and 50% had pleural effusion. The findings were correlated with lower platelet counts. Based on these findings, the authors concluded that sonographic features like gallbladder wall thickening and pleural effusion are important indicators of dengue fever severity. Similar correlations between abdomen USG findings and the severity of dengue were reported by authors such as Dewan N et al<sup>16</sup> and Colbert J et al.<sup>17</sup>

In this study, there was a significant correlation between thrombocytopenia and dengue severity. Ultrasound abnormalities such as gallbladder wall edema, ascites, or pleural effusion were found to be significantly associated with non-severe dengue with warning signs and severe dengue, as well as the possibility of thrombocytopenia during the course of illness. Donaldson CD et al. conducted a prospective study to assess the utility of ultrasonography in predicting thrombocytopenia and disease severity in dengue patients. For this purpose, the authors undertook a study comprising 176 patients (86 males and 90 females). All patients underwent ultrasound scans upon admission, and disease severity was classified using WHO guidelines. The study found that abnormal ultrasound findings, particularly gallbladder wall thickening, were associated with severe dengue and more pronounced thrombocytopenia from day two of admission. Based on these findings, the authors concluded that admission ultrasonography can predict severe dengue and thrombocytopenia. Similar correlations between thrombocytopenia and ultrasound abnormalities were also reported by authors such as Pothapregada S *et al*<sup>19</sup>. and Sharma et al.<sup>20</sup>

One important limitation of this study

#### Juliet Anitha Sean Martin and Karthikeyan Annadurai

was its retrospective nature; a randomized controlled trial would have been a better study design. Moreover, this study did not analyze ultrasound abnormalities and their correlation with outcomes in terms of mortality, which would have been an important factor to consider in cases of dengue in the pediatric age group.

Ultrasound findings such as gallbladder wall edema, pleural effusion, or ascites were

References

- Zeng Z, Zhan J, Chen L, Chen H, Cheng S. Global, regional, and national dengue burden from 1990 to 2017: A systematic analysis based on the global burden of disease study 2017. EClinicalMedicine. 2021;32:100712. doi: 10.1016/j.eclinm.2020.100712. PMID: 33681736; PMCID: PMC7910667.
- Alejandria MM. Dengue haemorrhagic fever or dengue shock syndrome in children. BMJ Clin Evid. 2015;2015:0917.
- Islam S, Hasan MN, Kalam SB, Islam MS, Hasan MJ, Sami CA, Chowdhury FR. Clinical Profile, Severity Spectrum, and Hospital Outcome of Dengue Patients in a Tertiary Care Hospital in Dhaka City. Cureus. 2022;14(9):e28843. doi: 10.7759/cureus.28843.
- 4. Wakimoto MD, Camacho LA, Guaraldo L, Damasceno LS, Brasil P. Dengue in children: a systematic review of clinical and laboratory factors associated with severity. Expert Rev Anti Infect Ther. 2015;13(12):1441–56. doi:10. 1586/14787210.2015.1100534
- Sachdev A, Pathak D, Gupta N, Simalti A, Gupta D, Gupta S, Chugh P. Early Predictors of Mortality in Children with Severe Dengue Fever: A Prospective Study. Pediatr Infect Dis J. 2021 Sep 1;40(9):797–801. doi: 10.1097/ INF.00000000003179.
- Uthraraj NS, Sriraam LM, Hiriyur Prakash M, Kumar M, Palanisamy U, Chettiakkapalayam Venkatachalam KU. Predictive factors for the complications of dengue fever in children: a retrospective analysis. Cureus. 2022;14(12):e33027. doi: 10.7759/ cureus.33027.
- Faridah IN, Dania H, Chen YH, Supadmi W, Purwanto BD, Heriyanto MJ, Aufa MA, Chang WC, Perwitasari DA. Dynamic changes of platelet and factors related dengue haemorrhagic fever: a retrospective study in Indonesian.

associated with severe dengue in pediatric patients. These imaging features were significantly linked to severe dengue and dengue with warning signs, highlighting their value in the early identification of patients at higher risk for complications. Therefore, it can be concluded that routine ultrasound evaluation can be a valuable tool in guiding management and improving outcomes in severe dengue cases.

Diagnostics (Basel). 2022;12(4):950. doi: 10.3390/diagnostics12040950.

- Ren ZZ, Zheng Y, Sun T, Wang GY, Chen XM, Zhou YM. A survey of clinical and laboratory characteristics of the dengue fever epidemic from 2017 to 2019 in Zhejiang, China. Medicine (Baltimore). 2022;101(42):e31143. doi:10.1097/MD.00000000031143
- Hadinegoro SR. The revised WHO dengue case classification: does the system need to be modified?. Paediatr Int Child Health. 2012;32 Suppl 1(s1):33–38. doi:10.1179/204690471 2Z.0000000052
- McGregor BL, Connelly CR. A Review of the Control of Aedes aegypti (Diptera: Culicidae) in the Continental United States. J Med Entomol. 2021;58(1):10–25. doi:10.1093/jme/tjaa157
- 11. Uzair H, Waseem R, Kumar N, Hussain MS, Shah HH. Fatal outcome of dengue fever with multi-organ failure and hemorrhage: A case report. SAGE Open Med Case Rep. 2023;11:2050313X231220808. doi:10.1177/2050313X231220808
- 12. Rao SM. Correlation of clinical and laboratory parameters in dengue fever patients and its usefulness as bedside markers. Indian J Crit Care Med. 2014;18(3):183–4. doi:10.4103/0972-5229.128713
- 13. Kaagaard MD, Matos LO, Evangelista MVP, Wegener A, Holm AE, Vestergaard LS, *et al.* Frequency of pleural effusion in dengue patients by severity, age and imaging modality: a systematic review and meta-analysis. BMC Infect Dis. 2023;23(1):327. doi:10.1186/ s12879-023-08311-y
- 14. Sami CA, Tasnim R, Hassan SS, Khan AH, Yasmin R, Monir-Uz-Zaman M, *et al.* Clinical profile and early severity predictors of dengue fever: Current trends for the deadliest dengue infection in Bangladesh in 2022. IJID Reg.

2023;9:42-8. doi:10.1016/j.ijregi.2023.09.001

- Santhosh VR, Patil PG, Srinath MG, Kumar A, Jain A, Archana M. Sonography in the diagnosis and assessment of dengue Fever. J Clin Imaging Sci. 2014;4:14. doi:10.4103/2156-7514.129260
- 16. Dewan N, Zuluaga D, Osorio L, Krienke ME, Bakker C, Kirsch J. Ultrasound in dengue: a scoping review. Am J Trop Med Hyg. 2021;104(3):826–35. doi: 10.4269/ ajtmh.20-0103.
- 17. Colbert J, Gordon A, Roxelin R, Silva S, Silva J, Rocha C *et al.* Ultrasound measurement of gallbladder wall thickening as a diagnostic test and prognostic indicator for severe dengue in pediatric patients. Pediatr Infect Dis J. 2007;26:850–2.
- 18. Donaldson CD, de Mel S, Clarice CSH, et al. Admission ultrasonography as a predictive tool for thrombocytopenia and disease severity in dengue infection. Trans R Soc Trop Med Hyg. 2021;115(12):1396–402. doi:10.1093/ trstmh/trab064
- Pothapregada S, Kullu P, Kamalakannan B, Thulasingam M. Is Ultrasound a Useful Tool to Predict Severe Dengue Infection?. Indian J Pediatr. 2016;83(6):500-4. doi:10.1007/ s12098-015-2013-y
- 20. Sharma G.K, Ajmera M, Gurjar R.S, Bairwa A.L. Role of ultra sonography (chest and abdomen) in diagnosis and early prediction of severity of dengue fever. Int J Pediatr Res. 2019;6(05):201– 6. doi:10.17511/ijpr.2019.i05.02