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Clinical and laboratory correlation in dengue with emphasis on expanded dengue in a tertiary care center

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Abstract

Background: Dengue fever has rapidly emerged as the most prevalent mosquito-borne viral disease, with a 30-fold increase in global incidence over the past fifty years. This study aims to investigate the clinical, laboratory, and radiological features of dengue with a special focus on expanded dengue cases in a tertiary care center.

Methods: The study was conducted in the inpatient Department of General medicine, Saveetha medical college, Chennai, Tamil Nadu, including 150 patients aged 15 years and above with confirmed dengue infection. Data collection involved detailed history, clinical examination, and routine and special investigations. Dengue was screened using the Dengue NS1 Ag or IgM Ab tests. Statistical analysis was performed using SPSS version 16 and R version 3.6.1, with a p-value < 0.05 considered statistically significant.

Results: The study included 150 participants, predominantly males (64.7%), with the largest age group being 21-35 years (48%). Dengue Fever (DF) was the most common type (54%), followed by Expanded Dengue (ED) at 30%, Dengue Hemorrhagic Fever (DHF) at 12.7%, and Dengue Shock Syndrome (DSS) at 3.3%. Serological markers showed 37.33% positive for IgM antibodies, 36.66% for NS1 antigen, 24% for both NS1 and IgM, and 2% for both IgM and IgG. Fever was universal (100%), with other symptoms like retro-orbital pain (20%), muscle pain (17.3%), vomiting (23.3%), and bleeding manifestations (45.3%). Significant differences were noted in vomiting ($p = 0.025$) and bleeding manifestations ($p = 0.005$) among dengue classes.

Conclusion: The study highlights the varied clinical, laboratory, and radiological profiles of dengue, especially expanded dengue cases. It underscores the importance of early diagnosis, comprehensive assessment, and a broader classification system for effective dengue management, contributing valuable insights to global dengue research.

Keywords: Dengue fever, NS1 Ag, dengue hemorrhagic fever, dengue shock syndrome

Introduction

Dengue fever has rapidly emerged as the most prevalent mosquito-borne viral disease, with a staggering 30-fold increase in global incidence over the past fifty years. The World Health Organization (WHO) estimates that approximately 50-100 million new dengue cases occur annually across more than 100 endemic countries, indicating a significant and growing public health challenge [1]. Dengue fever has been a prominent health issue since the 1950s, with notable expansions in the 1980s and subsequent outbreaks in various regions of India since 1996. Particularly since 2013, dengue has escalated into an epidemic across India, highlighting the urgent need for comprehensive research and intervention [2].

Globally, the WHO's South-East Asia Region (SEAR) and Western Pacific Region bear nearly 75% of the current global dengue disease burden. In these regions, dengue has transitioned from an endemic to an epidemic pattern, driven by multiple dengue virus serotypes [3]. India, being one of the ten SEAR countries endemic for dengue, has witnessed recurrent and severe outbreaks, making it imperative to understand the disease's clinical, laboratory, and radiological profiles, especially in cases of expanded dengue [4].

Previous studies have extensively documented the clinical and epidemiological aspects of dengue fever. For instance, research conducted in Brazil and Thailand has highlighted the significance of early clinical diagnosis and the role of laboratory markers in predicting disease severity [5]. However, there is a noticeable gap in research regarding the comprehensive correlation of clinical, laboratory, and radiological profiles in expanded dengue, particularly in the Indian context. Most studies have focused on standard dengue fever and dengue hemorrhagic fever, with limited exploration of the broader spectrum of expanded dengue and its varied manifestations.

The present study aims to fill this gap by investigating the clinical, laboratory, and radiological features of dengue in patients from a tertiary care center, with a special focus on expanded dengue. This research seeks to identify new or previously unreported clinical, laboratory, or radiological features associated with dengue, to enhance understanding and improve patient management. The study also aims to determine the incidence and outcomes of expanded dengue cases, thereby contributing valuable insights to the global discourse on dengue fever and its management.

Materials and Methods

- Source of data:** The present study was carried out in the inpatient Department of General Medicine, Saveetha Medical College, Chennai, Tamil Nadu. The study group comprises patients with confirmed dengue virus infection.
- Methods of collection of data:** A proforma was drafted to collect comprehensive data from all patients diagnosed with dengue virus infection. The data collected included:
 - Detailed history
 - Clinical examination findings
 - Routine and special investigations

Sample size: Based on the current dengue incidence in the area, 150 cases were included in this study.

Inclusion criteria

Indoor patients, aged 15 years and above, with confirmed dengue positivity (NS1 Ag/IgM) in IMS and SUM Hospital.

Exclusion criteria

- Pediatric patients (below 15 years).
- Outpatient cases of dengue.
- Patients with known chronic liver disease (CLD).
- Patients with known chronic renal failure.
- Patients with a history of cerebrovascular accident.

Study tools and techniques

Laboratory parameters: Dengue was screened using a positive result in the Dengue kit test for Dengue NS1 Ag or Dengue IgM Ab. Other laboratory parameters measured included total leucocyte count, total platelet count, hematocrit, liver function tests and renal function tests.

Statistical Analysis: The collected information was tabulated in Microsoft Excel and analyzed using SPSS version 16 and R version 3.6.1. Qualitative variables were expressed as proportions and percentages, while quantitative

variables were expressed as mean and standard deviation (SD). T-tests and Chi-square tests were used to compare quantitative and qualitative parameters among the four different classes of dengue. A p-value < 0.05 was considered statistically significant.

Results

Table 1: Age and sex distribution of the Study Participants

Age Groups	Count (n)	Percentage (%)
15-20 Yrs	12	8.00%
21-35 Yrs	72	48.00%
36-45 Yrs	21	14.00%
46-60 Yrs	34	22.70%
>60 Yrs	11	7.30%
Sex		
Female	53	35.3%
Male	97	64.7%

Table1 provides a detailed breakdown of the age distribution among the study participants. The largest age group represented in the study is the 21-35 years age group, comprising 72 individuals, which accounts for 48.00% of the total participants. This is followed by the 46-60 years age group, which includes 34 participants, making up 22.70% of the study population. The 36-45 years age group has 21 participants, representing 14.00% of the total. The youngest age group, 15-20 years, consists of 12 participants, accounting for 8.00% of the study population. The oldest age group, those aged over 60 years, includes 11 participants, constituting 7.30% of the total. Overall, the study includes 150 participants, covering a wide range of age groups to provide a comprehensive understanding of the age distribution in relation to the clinical, laboratory, and radiological profiles of dengue, with a special focus on expanded dengue in a tertiary care center.

Table 2: Types of Dengue Cases among participants

Types of Dengue	Count (n)	Percentage (%)
Dengue Fever (DF)	81	54.0%
Dengue Hemorrhagic Fever (DHF)	19	12.7%
Dengue Shock Syndrome (DSS)	5	3.3%
Expanded Dengue (ED)	45	30.0%
Total	150	100%

The table illustrates the distribution of different types of dengue among the study participants. Out of the total 150 participants, the majority were diagnosed with Dengue Fever (DF), accounting for 81 individuals or 54.0% of the total. Dengue Hemorrhagic Fever (DHF) was observed in 19 participants, representing 12.7%. Dengue Shock Syndrome (DSS), a more severe form, was identified in 5 participants, making up 3.3% of the cases. Expanded Dengue (ED), which includes cases with atypical manifestations not classified under DHF or DSS, was found in 45 participants, accounting for 30.0% of the total. This distribution highlights the varying severity and presentation of dengue infections among the participants in the study.

Table 3: Age and Sex Distribution among various Dengue class among study participants

Age Groups	DF (N=81)	DHF (N=19)	DSS (N=5)	ED (N=45)	Total (N=150)	p-value
15-20 Yrs.	6 (7.4%)	3 (15.8%)	0 (0.0%)	3 (6.7%)	12 (8.0%)	0.466
21-35 Yrs.	39 (48.1%)	10 (52.6%)	4 (80.0%)	19 (42.2%)	72 (48.0%)	
36-45 Yrs.	15 (18.5%)	2 (10.5%)	0 (0.0%)	4 (8.9%)	21 (14.0%)	
46-60 Yrs.	14 (17.3%)	4 (21.1%)	1 (20.0%)	15 (33.3%)	34 (22.7%)	
>60 Yrs.	7 (8.6%)	0 (0.0%)	0 (0.0%)	4 (8.9%)	11 (7.3%)	
Sex						0.821
Female	28 (34.6%)	8 (42.1%)	1 (20.0%)	16 (35.6%)	53 (35.3%)	
Male	53 (65.4%)	11 (57.9%)	4 (80.0%)	29 (64.4%)	97 (64.7%)	

*Chi-square test was used and the p value <0.05 was considered as statistically significant.

Table 3 presents the age and sex distribution among various dengue classifications among the study participants. The distribution is categorized into Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS), and Expanded Dengue (ED), with a total of 150 participants. In the 15-20 years age group, 7.4% had DF, 15.8% had DHF, none had DSS, and 6.7% had ED, totaling 8.0% of the participants. The 21-35 years age group had the highest representation, with 48.1% having DF, 52.6% having DHF, 80.0% having DSS, and 42.2% having ED, accounting for 48.0% of the total participants. The 36-45 years age group included 18.5% with DF, 10.5% with DHF, none with DSS, and 8.9% with ED, making up 14.0% of the total. Participants aged 46-60 years included 17.3% with DF, 21.1% with DHF, 20.0% with DSS, and 33.3% with ED, totaling 22.7%. In the >60 years age group, 8.6% had DF, none had DHF or DSS, and 8.9% had ED, making up 7.3% of the participants. Regarding sex distribution, females accounted for 34.6% of DF cases, 42.1% of DHF cases, 20.0% of DSS cases, and 35.6% of ED cases, totaling 35.3% of the participants. Males represented 65.4% of DF cases, 57.9% of DHF cases, 80.0% of DSS cases, and 64.4% of ED cases, making up 64.7% of the total participants. The p-value indicates the statistical significance of the distribution differences, with 0.466 for age groups and 0.821 for sex distribution.

Table 4: Dengue Serology among the study participants

Dengue Serology	Count (n)	Percentage (%)
IgM & IgG Positive	3	2.00%
IgM Positive	56	37.33%
NS1 & IgM Positive	36	24.00%
NS1 Positive	55	36.66%
Total	150	100%

Table 4 presents the distribution of dengue serology results among the study participants, categorized based on the presence of different antibodies and antigens indicative of dengue infection. Only 3 participants (2.00%) tested positive for both IgM and IgG antibodies, suggesting either a recent secondary infection or a late primary infection. A larger proportion, 56 participants (37.33%), tested positive for IgM antibodies, which typically appear early in the course of dengue infection. Additionally, 36 participants (24.00%) tested positive for both NS1 antigen and IgM antibodies, indicating a recent infection. Furthermore, 55 participants (36.66%) tested positive for the NS1 antigen, an early marker of dengue virus infection.

Table 5 presents the distribution of serological markers among the study participants, indicating different stages of dengue infection. Three participants (2.00%) tested positive for both IgM and IgG antibodies, suggesting a recent secondary infection or late primary infection.

Table 5: Dengue Serology among the Study Participants

Dengue Serology	Count (n)	Percentage (%)
IgM & IgG Positive	3	2.00%
IgM Positive	56	37.33%
NS1 & IgM Positive	36	24.00%
NS1 Positive	55	36.66%
Total	150	100%

Fifty-six participants (37.33%) tested positive for IgM antibodies, which typically indicate an early stage of dengue infection. Additionally, thirty-six participants (24.00%) tested positive for both the NS1 antigen and IgM antibodies, reflecting a recent dengue infection. Fifty-five participants (36.66%) tested positive for the NS1 antigen, an early marker of dengue infection.

Table 6: Serological investigation of various dengue classes

Dengue serology	DF (N=81)	DHF (N=19)	DSS (N=5)	ED (N=45)	Total (N=150)	p-value
IgM & IgG Positive	2 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	3 (2.0%)	0.24
IgM Positive	25 (30.9%)	5 (26.3%)	2 (40.0%)	24 (53.3%)	56 (37.3%)	
NS1 & IgM Positive	18 (22.2%)	8 (42.1%)	1 (20.0%)	9 (20.0%)	36 (24.0%)	
NS1 Positive	36 (44.4%)	6 (31.6%)	2 (40.0%)	11 (24.4%)	55 (36.7%)	

*Chi-square test was used and the p-value < 0.05 was considered as statistically significant.

Table 6 shows the serological investigation results for various dengue classifications among the study participants, including Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS), and Expanded Dengue (ED). The p-value indicates the statistical significance of the differences among the groups.

Two participants (2.5%) with DF, none with DHF or DSS, and one participant (2.2%) with ED tested positive for both

IgM and IgG antibodies, making up 2.0% of the total, with a p-value of 0.24, indicating no significant difference. IgM antibodies were positive in 25 participants (30.9%) with DF, five participants (26.3%) with DHF, two participants (40.0%) with DSS, and 24 participants (53.3%) with ED, totaling 37.3% of the study population. Additionally, 18 participants (22.2%) with DF, eight participants (42.1%) with DHF, one participant (20.0%) with DSS, and nine participants (20.0%)

with ED tested positive for both NS1 antigen and IgM antibodies, accounting for 24.0% of the total. Finally, NS1 antigen was positive in 36 participants (44.4%) with DF, six participants (31.6%) with DHF, two participants (40.0%) with DSS, and 11 participants (24.4%) with ED, making up 36.7% of the study population.

Table 8 compares the frequency of various clinical symptoms among different classes of dengue: Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS), and Expanded Dengue (ED). Fever was universal across all classes (100%, $p < 0.001$). Retro-orbital pain was present in 20% of participants overall, with no significant difference ($p = 0.341$). Muscle pain was most common in DF (23.5%) and least in ED (8.9%), with no significant difference ($p = 0.142$). Joint pain showed similar rates across groups ($p = 0.724$). Rash was notably higher in DSS (40%, $p = 0.054$). Vomiting was significantly higher in DHF (47.4%, $p = 0.025$). Loose stools, abdominal pain, and chest pain showed no significant differences across groups (p -values 0.607, 0.814, and 0.649, respectively). Constipation was significantly different, being absent in DHF and ED ($p = 0.046$). Bleeding manifestations varied significantly, being most common in DHF ($p = 0.005$). Breathlessness was rare and not significantly different across groups ($p = 0.631$).

Table 7 provides an overview of the frequency of various clinical symptoms observed among the study participants, all of whom experienced fever, making it a universal symptom of dengue with a 100% occurrence rate. Retro-orbital pain was reported by 20% of the participants, while muscle pain and joint pain were observed in 17.3% and 12% of the participants, respectively. Rash was seen in 8.7% of the participants, and vomiting was reported by 23.3%, indicating a significant occurrence of gastrointestinal symptoms. Loose stools and abdominal pain were present in 5.3% and 16% of the participants, respectively, and constipation affected 6%. Bleeding manifestations were notably prevalent, with 45.3%

of the participants exhibiting symptoms. Among these, gingival bleeding was observed in 4%, hematuria in 2.7%, ophthalmic bleeding in 6.7%, and epistaxis in 5.3% of the participants. Malena was reported by 10%, while petechiae were seen in 13.3% of the participants. Despite these bleeding manifestations, 54.7% of the participants reported no bleeding symptoms.

Table 7: Frequency of Various Clinical Symptoms among the study participants

Symptoms	Count (n)	Percentage (%)
Fever	150	100.00%
Retro-orbital pain	30	20.00%
Muscle pain	26	17.30%
Joint pain	18	12.00%
Rash	13	8.70%
Vomiting	35	23.30%
Loose stools	8	5.30%
Abdominal pain	24	16.00%
Constipation	9	6.00%
Bleeding manifestation	68	45.30%
Gingival bleeding	6	4.00%
Hematuria	4	2.70%
Ophthalmic bleeding	10	6.70%
Epistaxis	8	5.30%
Malena	15	10.00%
No bleeding	82	54.70%
Petechiae	20	13.30%
Chest pain	5	3.30%
Breathlessness	2	1.30%

Other symptoms included chest pain in 3.3% of the participants and breathlessness in 1.3%, indicating less common but significant respiratory symptoms. This distribution highlights the diverse clinical presentation of dengue among the participants, emphasizing the need for comprehensive clinical assessment in dengue cases.

Table 8: Comparison of Clinical Symptoms of various Dengue Classes

Symptoms	DF (N=81)	DHF (N=19)	DSS (N=5)	ED (N=45)	Total (N=150)	p-value
Fever						<0.001
Yes	81 (100.0%)	19 (100.0%)	5 (100%)	45 (100%)	150 (100.0%)	
Retroorbital pain						0.341
No	61 (75.3%)	15 (78.9%)	4 (80.0%)	40 (88.9%)	120 (80.0%)	
Yes	20 (24.7%)	4 (21.1%)	1 (20.0%)	5 (11.1%)	30 (20.0%)	
Muscle pain						0.142
No	62 (76.5%)	16 (84.2%)	5 (100.0%)	41 (91.1%)	124 (82.7%)	
Yes	19 (23.5%)	3 (15.8%)	0 (0.0%)	4 (8.9%)	26 (17.3%)	
Joint pain						0.724
No	72 (88.9%)	17 (89.5%)	5 (100.0%)	38 (84.4%)	132 (88.0%)	
Yes	9 (11.1%)	2 (10.5%)	0 (0.0%)	7 (15.6%)	18 (12.0%)	
Rash						0.054
No	73 (90.1%)	18 (94.7%)	3 (60.0%)	43 (95.6%)	137 (91.3%)	
Yes	8 (9.9%)	1 (5.3%)	2 (40.0%)	2 (4.4%)	13 (8.7%)	
Vomiting						0.025
No	68 (84.0%)	10 (52.6%)	3 (60.0%)	34 (75.6%)	115 (76.7%)	
Yes	13 (16.0%)	9 (47.4%)	2 (40.0%)	11 (24.4%)	35 (23.3%)	
Loose stools						0.607
No	78 (96.3%)	18 (94.7%)	5 (100.0%)	41 (91.1%)	142 (94.7%)	
Yes	3 (3.7%)	1 (5.3%)	0 (0.0%)	4 (8.9%)	8 (5.3%)	
Abdominal pain						0.814
No	70 (86.4%)	16 (84.2%)	4 (80.0%)	36 (80.0%)	126 (84.0%)	
Yes	11 (13.6%)	3 (15.8%)	1 (20.0%)	9 (20.0%)	24 (16.0%)	
Constipation						0.046
No	73 (90.1%)	19 (100.0%)	4 (80.0%)	45 (100.0%)	141 (94.0%)	

Yes	8 (9.9%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	9 (6.0%)	
Bleeding manifestation						0.005
Gingival bleeding	1 (1.2%)	2 (10.5%)	0 (0.0%)	3 (6.7%)	6 (4.0%)	
Hematuria	2 (2.5%)	1 (5.3%)	0 (0.0%)	1 (2.2%)	4 (2.7%)	
Ophthalmic bleeding	4 (4.9%)	4 (21.1%)	0 (0.0%)	2 (4.4%)	10 (6.7%)	
Epistaxis	2 (2.5%)	2 (10.5%)	0 (0.0%)	4 (8.9%)	8 (5.3%)	
Gingival bleeding	2 (2.5%)	2 (10.5%)	0 (0.0%)	1 (2.2%)	5 (3.3%)	
Melena	8 (9.9%)	4 (21.1%)	1 (20.0%)	2 (4.4%)	15 (10.0%)	
No bleeding	56 (69.1%)	0 (0.0%)	3 (60.0%)	23 (51.1%)	82 (54.7%)	
Petechiae	6 (7.4%)	4 (21.1%)	1 (20.0%)	9 (20.0%)	20 (13.3%)	
Chest pain						0.649
No	77 (95.1%)	19 (100.0%)	5 (100.0%)	44 (97.8%)	145 (96.7%)	
Yes	4 (4.9%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	5 (3.3%)	
Breathlessness						0.631
No	79 (100%)					

Discussion

The present study provides a comprehensive analysis of the clinical, laboratory, and radiological profiles of dengue fever, with a particular focus on expanded dengue cases in a tertiary care center. The findings of this study contribute valuable insights into the understanding of dengue fever, its varied manifestations, and its management, especially in the context of expanded dengue.

The age distribution observed in this study is consistent with previous research, which indicates that dengue fever predominantly affects younger age groups. The largest age group in our study was 21-35 years, comprising 48% of the total participants, followed by the 46-60 years age group (22.7%). This aligns with studies conducted earlier, where a similar age distribution was reported. The higher prevalence among males (64.7%) compared to females (35.3%) is also consistent with findings from earlier studies, suggesting that gender-related exposure factors may play a role in dengue transmission [6].

The distribution of different types of dengue among the study participants reveals that Dengue Fever (DF) was the most common type, accounting for 54% of the cases. This is in line with the general trend observed in endemic regions, where DF is the predominant form. The study also highlights the significant proportion of Expanded Dengue (ED) cases (30%), which include atypical manifestations not classified under Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS). This finding underscores the need for a broader classification system that captures the diverse clinical presentations of dengue, as noted in recent literature [7].

The serological investigation results indicate that IgM antibodies were the most commonly detected marker (37.33%), followed by NS1 antigen (36.66%). The presence of both NS1 antigen and IgM antibodies in 24% of participants reflects a recent infection. The low proportion of participants testing positive for both IgM and IgG antibodies (2%) suggests that secondary infections were relatively uncommon in this cohort. These findings are comparable to those reported in studies from Southeast Asia, where NS1 antigen and IgM antibodies are frequently used for early diagnosis of dengue [8].

The frequency of various clinical symptoms observed in this study, such as fever (100%), retro-orbital pain (20%), muscle pain (17.3%), and vomiting (23.3%), aligns with the classic presentation of dengue fever [9]. However, the high prevalence of bleeding manifestations (45.3%), including gingival bleeding, hematuria, and petechiae, highlights the severe nature of dengue cases in this cohort [10]. The significant

difference in the occurrence of vomiting and bleeding manifestations among the different dengue classes ($p = 0.025$ and $p = 0.005$, respectively) underscores the variability in clinical presentation and the importance of careful clinical assessment.

The findings of this study corroborate the results of earlier research conducted in dengue-endemic regions. For instance, earlier study reported similar age and sex distribution patterns, as well as a high prevalence of DF and significant proportions of DHF and DSS cases [11]. The serological profiles observed in our study are also consistent with those reported in earlier studies, where NS1 antigen and IgM antibodies are key diagnostic markers [12]. Additionally, the clinical symptoms documented in this study, particularly the high incidence of bleeding manifestations, align with findings from studies in Sri Lanka and the Philippines [13].

To conclude, present study highlights the diverse clinical, laboratory, and radiological profiles of dengue fever, with a special emphasis on expanded dengue cases. The findings underscore the importance of early diagnosis, comprehensive clinical assessment, and a broader classification system to capture the varied manifestations of dengue. By filling the gap in research on expanded dengue, this study contributes valuable insights to the global discourse on dengue fever and its management, particularly in the Indian context. Future research should focus on longitudinal studies and the development of targeted interventions to reduce the burden of dengue fever in endemic regions.

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