

Association of NS1 Antigen, IgM/IgG Antibodies with Haematological Indices and Inflammatory Markers in Suspected Dengue Cases: A Cross-sectional Study

MOHD TABISH ANSARI¹, SUCHETA JITENDRA LAKHANI², DINESH KANHAIYALAL KHANDHADIA³

ABSTRACT

Introduction: Dengue Virus (DENV) has been re-emerging as a major public health challenge in tropical and subtropical regions, including India, with increasing incidence, changing epidemiology, and seasonal outbreaks. Early diagnosis supported by laboratory markers is essential for effective clinical management and disease control.

Aim: To evaluate the association of serological markers with haematological, biochemical and inflammatory parameters in clinically suspected cases of dengue.

Materials and Methods: This cross-sectional study was conducted from March 2025 to December 2025 at Adarsh Multispecialty Hospital, Gandhinagar, Gujarat, India. The study included 154 patients presenting with Acute Febrile Illness (AFI). DENV diagnosis was performed using an immunochromatographic kit for NS1 antigen and IgM and IgG antibodies from the serum sample. Haematological indices, Inflammation markers and liver function tests Serum Glutamic Pyruvic Transaminase (SGPT) and Serum Glutamic Oxaloacetic Transaminase (SGOT) were examined. Chi-square test was used for statistical analysis, and a p-value of <0.05 was considered statistically significant.

Results: A total of 154 suspected Dengue Fever (DF) samples were collected, out of which 38 cases of dengue infection were

confirmed. The highest positivity was seen in the age group of 21 to 30 years, 14 (36.8%), with males being more affected, making up 24 (63.2%) of the cases. The seasonal peaks happened during August and September, with 11/34 (32.4%) and 11/42 (26.2%) of cases, respectively. Testing for the NS1 antigen alone found 17/74 (23%) of infections, but combining NS1 and antibody testing raised the rate to about 20/73 (27.3%). Dengue patients showed significantly decreased platelet counts 35/38 (92.1%), White Blood Cell (WBC) counts 21/38 (55.26%), and also lymphocyte counts 20/38 (52.63%). Liver enzymes were also elevated (SGOT 161.58±372.44 U/L and SGPT 187.46±456.09 U/L). They also showed raised C-Reactive Protein (CRP) in 33/38 (86.8%) of cases and higher Erythrocyte Sedimentation Rate (ESR) in 23/38 (60.5%) of cases.

Conclusion: Detection of the NS1 antigen with antibody testing gives more specific results. Significant increase in CRP levels and a drop in platelet levels in dengue-positive patients are early indicators of presumptive diagnosis. Integrated haematological, and inflammatory markers facilitate efficient risk stratification and enhance early dengue identification, enabling prompt clinical therapy during periods of peak transmission.

Keywords: C-reactive protein, Dengue virus, Erythrocyte sedimentation rate, Platelet count

INTRODUCTION

The DENV is a single-stranded positive-sense RNA belongs to the family of flaviviruses [1]. It is transmitted by the *Aedes aegypti* mosquito, represents a major AFI case, and is found in tropical and sub-tropical climates worldwide [2]. In India and around the world, the severity of DENV infections varies from DF to Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) [3]. There are four different varieties of DENV: DENV-1, DENV-2, DENV-3 and DENV-4. By 1996-2003, almost all four serotypes had been reported, and the frequency of outbreaks in Indian populations had also increased [4]. In India, it remains such a serious public health problem that it is the most significant cause of hospitalisation across the nation [5].

The global prevalence of dengue has climbed considerably, ranging from 505,430 recorded cases in 2000 to 14.6 million in 2024. Between January and July 2025, approximately four million illnesses and more than 3,000 deaths were reported across 97 countries [2]. The earliest virologically confirmed outbreak of dengue in India was reported during 1963-1964 along the eastern coast, including Kolkata (then Calcutta) [6]. According to the National Centre for Vector-Borne Disease Control, a total of 1,21,824 dengue cases with 131 deaths were reported in India in 2025. The highest number of cases was seen in Tamil Nadu and Maharashtra, 23407 and

14168, respectively, whereas in Gujarat, a decreased number of cases (4233) with a minimum mortality rate was observed [7].

The differential diagnosis of DENV infection is among the most difficult ones because it shows similar combinations of clinical manifestations as other febrile illnesses [8]. In addition, over half of the people infected with DENV may be asymptomatic, making early detection problematic [9]. To facilitate the early detection of dengue infection, the non-dengue parameter thrombocytopenia is used as a predictive marker [10]. Dengue-specific IgM and IgG antibodies are commonly used diagnostic markers, but they usually appear only after the first few days of illness, reducing their sensitivity during the early viremic phase [11]. More recently, the detection of NS1 antigen during the early phase has been well documented as a dependable diagnostic marker to provide an early diagnosis of primary and secondary dengue infections [10].

Given the urgent need to limit the burden of viral infection, early detection and vector control measures are critical methods. Given this need, the current study sought to determine the incidence and occurrence rates of DENV infection among patients in a tertiary care hospital setting. Proactively identifying and making a specific diagnosis is critical for minimising the severity and death rates of dengue infections [12].

Against this background, this study represents the conventional diagnostic component of a broader AFI research project, to evaluate the association of serological markers with haematological, biochemical and inflammatory parameters in clinically suspected cases of dengue and to evaluate seasonal trends in DENV infection among patients hospitalised with AFI.

MATERIALS AND METHODS

A cross-sectional study was conducted from March to December 2025 in the Microbiology Department of Adarsh Multispecialty Hospital, affiliated to Ananya College of Medicine and Research, Kalol, Gandhinagar, Gujarat, India. This study was approved by the Ananya Institutional Ethics Committee (Letter no. AIEC/2024/010), and informed consent was secured from all participants or their guardians.

Sample size calculation: The sample size was calculated using the single population proportion formula:

$$n = \frac{Z^2 \times P \times (1-P)}{d^2}$$

where, $Z=1.96$ (95% confidence level), $P=0.10$ (expected dengue prevalence based on previous regional study) (Chandra M et al.) [13], and $d=0.05$ (absolute precision). The calculation yielded a minimum sample size of 138.3, which was rounded to 138 participants.

$$(1.96^2 \times 0.10 \times 0.90) / 0.05^2 = 138.3.$$

After allowing for approximately 10% non-response or incomplete samples, the required sample size was approximately 152. A total of 154 participants were ultimately enrolled. The sample size calculation was based on the primary objective of estimating dengue prevalence.

Inclusion criteria: Patients of all age groups and any sex presenting with fever ($\geq 38^\circ\text{C}$) of up to 14 days duration and cases clinically suspected of dengue by the treating physician were included in the study.

Exclusion criteria: Patients with confirmed alternative diagnoses for AFI (e.g., malaria, typhoid fever, or bacterial sepsis) were excluded from the study.

Sample collection and processing: A 2-3 mL of blood was collected during the febrile phase of infection, aseptically in a plain vacutainer for serological and biochemical testing and 1-2 mL of blood was collected in an Ethylenediaminetetraacetic acid vacutainer for Complete Blood Count (CBC). Serum was separated by centrifugation and stored at $2-8^\circ\text{C}$.

1. NS1 Antigen, IgM and IgG antibodies detection: The NS1 antigen, IgM and IgG antibodies were detected by Med Source Ozone Biomedicals Dengue combo (NS1 Antigen+IgG/IgM Antibody) immunochromatographic method using a rapid kit. A 5-10 μL serum was added to the buffer well. The results were then obtained after 20 minutes. The kit demonstrated sensitivity and specificity against NS1 (96.6%/99.7%), IgG (97.14%/96.8%), and IgM (97.5%/97.6%). NS1 and IgM were interpreted as signs of a recent infection. Isolated IgG was thought to be a sign of prior exposure. Diagnostic testing was guided by the duration of fever at presentation. NS1 antigen testing was performed in patients presenting within five days of illness, while IgM/IgG antibody testing, alone or in combination with NS1, was used in patients presenting after five days, according to the temporal kinetics of dengue biomarkers.

2. Haematological and inflammatory parameters: A sysmex XP 100 haematology analyser was used for testing of CBC using 5 μL whole blood. ESR was calculated using the Westergren technique with a normal range 0-20 mm/hr [14], and CRP was detected using the Beacon CRP Turbilatex kit, which uses a latex-enhanced immunoturbidimetry method (semi-quantitative) with an analytical sensitivity of (5-10) mg/L and a diagnostic sensitivity of (95.6%) and specificity of (96.2%). Serum samples taken during a febrile episode

are analysed by the EM 200 instrument for Serum Glutamate Pyruvate Transaminase (SGPT/ALT) and Serum Glutamate Oxaloacetate Transaminase (SGOT/AST), which were expressed as U/l, using kinetic, colorimetric, and immunoassay techniques.

Confirmed dengue cases were categorised according to the World Health Organisation (WHO) 2009 dengue classification system as dengue without warning signs, dengue with warning signs, or severe dengue based on the clinical and laboratory information available in patient records [15].

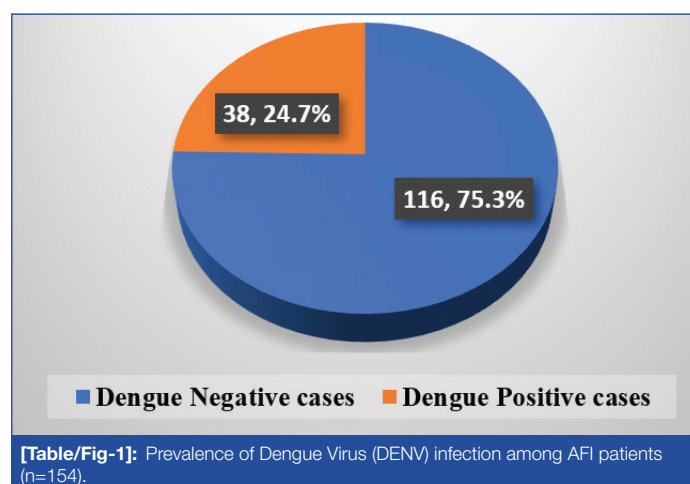
STATISTICAL ANALYSIS

Statistical analysis was performed using the online statistical calculator available through the Social Science Statistics online platform (<https://www.socscistatistics.com>). Continuous variables were expressed as mean $\pm$ Standard Deviation (SD), whereas categorical variables were presented as frequencies and percentages. Associations between categorical variables were analysed using the Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

During the study period, 154 patients presenting with sudden illness with fever and suspected clinically of this infection were enrolled of which 38 cases of dengue infection were confirmed. Laboratory-confirmed cases were classified according to the WHO 2009 dengue classification system. The majority of cases, 35/38 (92.1%) were classified as dengue with warning symptoms, mainly because of the presence of thrombocytopenia and related haematological abnormalities. Only 3/38 (7.9%) had dengue without any warning symptoms.

In the current investigation, no cases met the criteria for severe dengue. Evaluation in the laboratory confirmed infection with the virus in 38 patients, which resulted in a rate of 24.7% among the suspected cases [Table/Fig-1].



The group between 21-30 years showed the main positivity pattern with 14 cases, representing 36.8% of the total positive cases. The age group between 31-40 years had six positive cases. Individuals between 11-20 years contributed nine cases at which shows significant patterns in these groups. Cases in individuals from 0-10 years showed two cases. Individuals over fifty years provided four cases, indicating patterns that differ from other groups. Out of 154 clinically suspected patients, 24 cases (63.2%) were males and 14 cases (36.8%) were females. The findings show that males across age categories have a greater dengue-positive rate [Table/Fig-2].

Among 154 individuals with possible infection, 74 (48.1%) individuals received examination using the NS1 antigen only, and this pattern indicates 17 (23%) individuals showed positive results in the initial stage of disease. Testing using three measures that include the NS1, IgM, and IgG occurred in 73 individuals, representing 47.4% of the

Age group (years)	Male		Female		Total patients	
	Suspected case	Positive case n (%)	Suspected case	Positive case n (%)	Suspected case	Positive case n (%)
0-10	16	1 (6.3)	6	1 (16.7)	22	2 (9.1)
11-20	20	4 (20.0)	19	5 (26.3)	39	9 (23.1)
21-30	24	10 (41.7)	22	4 (18.2)	46	14 (30.4)
31-40	8	5 (62.5)	15	1 (6.7)	23	6 (26.1)
41-50	3	1 (33.3)	7	2 (28.6)	10	3 (30.0)
51-60	3	1 (33.3)	4	1 (25.0)	7	2 (28.6)
61-70	4	2 (50.0)	3	0 (0.0)	7	2 (28.6)
Total	78	24 (30.8)	76	14 (18.4)	154	38 (24.7)

[Table/Fig-2]: Distribution by age and gender of dengue cases.

total suspected cases. Among these, 20 (27.4%) patients showed positive results, and this group includes predominantly those individuals presenting in the later stage of the disease. Individuals who received the three-measure testing approach showed positive results in patterns that include NS1 (5 positive patients, both NS1 and IgM positive (2 patients), all three- the NS1, IgM and the IgG- and patterns that include only one patient positive and five patients showed IgM and IgG positive. Testing using measures to examine IgM and IgG occurred in seven patients. Among these patients, 1 (14.3%) patient showed positive results [Table/Fig-3].

Testing approach	NS1	IgM	IgG	No. of samples tested	No. of negative cases n (%)	No. of positive cases n (%)
Single-marker testing	+	Not tested	Not tested	74	57 (77)	17 (23)
Triple-marker testing	+	-	-	73	53 (72.6)	5 (6.84)
	+	+	-			2 (2.73)
	+	+	+			1 (1.36)
	-	+	-			7 (9.58)
	-	+	+			5 (6.84)
Antibody -only testing	Not tested	+	+	7	6 (85.7)	1 (14.3)
Total				154	116 (75.3)	38 (24.7)

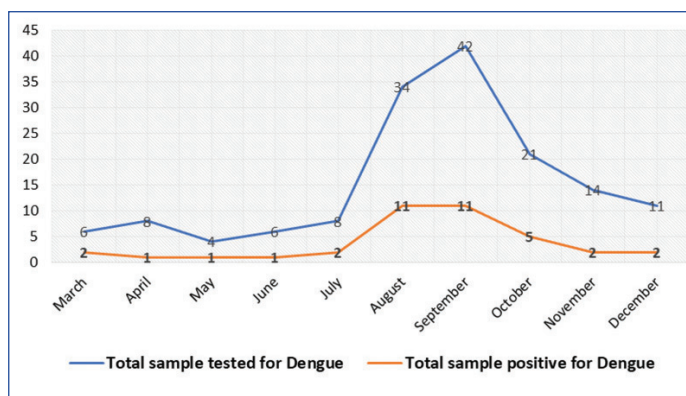
[Table/Fig-3]: Serological testing strategy and positivity pattern in dengue-suspected patients.

*Diagnostic testing was based on the duration of illness and routine clinical protocols. NS1 antigen was used in early cases (≤ 5 days of fever), while IgM/IgG testing, alone or in combination with NS1, was performed in later stages, reflecting the known kinetics of dengue biomarkers rather than random selection

A relatively low number of samples and cases were observed from March to July, and rates of positive results across months in this period ranged from 12.5% to 33.3%, respectively. Data show a steep incline in cases during months following the monsoon, with cases beginning in August and reaching highest levels in September. August shows 34 cases; among these, 11 (32.4%) show positive results, while September presents 42 samples with 11 (26.2%) cases showing positive results. The data obtained after the peak indicate a decline from October to December, meaning that the rates fall significantly in October (23.8%), November (14.3%), and December (18.2%), respectively; moreover, the transmission stays at low levels [Table/Fig-4].

The average SGPT level among dengue patients (187.46 ± 456.09 U/L) was notably different from the average level in suspected cases (74.05 ± 415.71 U/L) and surpassed the reference range of 0-40 U/L. The average SGOT level among dengue patients was 161.58 ± 372.44 U/L, while that for suspected cases was 76.35 ± 428.91 U/L. The reference range is 0-45 U/L. The patterns observed indicate that the confirmed cases experience more marked changes in liver function [Table/Fig-5].

The dengue-positive cases showed higher prevalence of anaemia and lower RBC counts; however, the difference was not significant (haemoglobin: $\chi^2=0.7012$, p-value=0.4023; RBC count: $\chi^2=2.0593$,



[Table/Fig-4]: Month-wise distribution and positivity rate of laboratory-confirmed dengue cases.

Parameter	Normal range (U/L)	Dengue positive cases (Mean $\pm$ SD)	Suspected cases (Mean $\pm$ SD)
SGPT	0-40	187.46 $\pm$ 456.09	74.05 $\pm$ 415.71
SGOT	0-45	161.58 $\pm$ 372.44	76.35 $\pm$ 428.91

[Table/Fig-5]: Serum transaminase profiles in dengue-positive and dengue-suspected patients.

Note: Formal normality testing was not performed; however, the large dispersion (SD larger than mean) indicates a skewed distribution of liver enzyme values. This is a known pattern in dengue-related hepatic involvement

p-value=0.1512). On the other hand, the remarkable leucocyte disturbances were very clear in dengue-positive patients. Additionally, leucopenia seemed to be strongly associated with dengue infection ($\chi^2=26.9677$, p-value <0.00001), as was lymphopenia ($\chi^2=12.4769$, p-value <0.00041). This suggests that the patients' immunity is very seriously weakened. Thrombocytopenia was the most prominent finding of dengue, appearing in an overwhelming majority of all cases with a positive dengue test and showing a high statistical association with infection status ($\chi^2=69.873$, p-value <0.00001) [Table/Fig-6].

Blood cell type	Normal range		Dengue positive =38 n (%)	Dengue negative =116 n (%)	Chi-square test	p-value
Haemoglobin	12.0-16.0 g%	<12.0	20 (52.6)	70 (60.3)	0.7012	0.4023
		>12.0	18 (47.4)	46 (39.7)		
RBC count	4.0-5.5 million / μ L	<4.0	9 (23.7)	16 (13.8)	2.0593	0.1512
		>4.0	29 (76.3)	100 (86.2)		
WBC count	4,000-10,000 / μ L	<4,000	21 (55.3)	16 (13.8)	26.9677	<0.001
		>4,000	17 (44.7)	100 (86.2)		
Lymphocyte count	20-40%	<20	20 (52.6)	26 (22.4)	12.4769	0.00041
		>20	18 (47.4)	90 (77.6)		
Platelet count	1.5-4.5 L / μ L	<1,50,000	35 (92.1)	20 (17.2)	69.873	<0.001
		>1,50,000	3 (7.9)	96 (82.8)		

[Table/Fig-6]: Haematological signatures of dengue infection in Acute Febrile Illness (AFI) patients.

Footnote: Data are presented as n (%). Comparisons between groups were performed using the Chi-square (χ^2) test. A p-value < 0.05 was considered statistically significant.

The majority of the cases of dengue positivity were marked by the presence of elevated CRP (CRP >6 mg/L), and a very strong association with dengue infection was revealed ($\chi^2=39.8538$, p-value <0.00001). A higher ESR (>20 mm/hr) was likewise found to be significantly more common in the dengue-positive group so that it was possible to state that systemic inflammation was intensified ($\chi^2=12.7281$, p-value <0.00036) [Table/Fig-7].

Inflammatory marker	Range	Dengue positive=38 n (%)	Dengue negative=116 n (%)	Chi-square test	p-value
CRP (mg/L)	>6	33 (86.8)	33 (28.4)	39.8538	0.00001
	<6	5 (13.2)	83 (71.6)		
ESR (mm/hr)	> 20	23 (60.5)	33 (28.4)	12.7281	0.00036
	< 20	15 (39.5)	83 (71.6)		

[Table/Fig-7]: Inflammatory marker profiles in dengue-positive and dengue-negative patients.

DISCUSSION

Dengue is one of the most prevalent mosquito-borne viral diseases worldwide. It is a serious public health problem because the number of cases has been rising significantly over time. Several factors contribute to the increasing burden of dengue. In regions where dengue was previously rare, the primary mosquito vectors, *Aedes aegypti* and *Aedes albopictus*, are spreading. Additionally, mosquito hatching and survival are made easier by shifting climate conditions, such as increasing humidity, rainfall, and temperatures [2,3]. In the current study of 154 samples, 38 (24.7%) turned out to be positive for dengue. Similar seroprevalence rates have been reported by Gupta N and Bareja R (25.6%), Mohan K et al., (25.0%), and Pooja PS et al., (25.41%). These findings are consistent with the present study and suggest a comparable burden of dengue infection across geographically diverse regions of India, highlighting its continued public health importance [10,12,16]. This indicates that dengue infection is currently escalating and spreading across India.

Adolescents and young adults had the highest prevalence of dengue infection in this study, with the age group of 11 to 30 years having the largest number of cases (23 cases, 60.5%). These individuals have higher levels of outdoor activities, occupational exposure and mobility, which increases contact with vectors of *Aedes* mosquitoes. A similar age distribution was reported by Patel SD et al., who observed that 24.63% of cases occurred in the 11-20- years age group and 36.30% in the 21-30 years age group, accounting for a cumulative 60.93% of cases [17]. There was a clear male predominance as males formed 63.2% of all dengue-positive cases. This was in concordance with multiple Indian studies by Patel P et al., Chhotala YH and Suva C and Chakravarti A and Bhatnaga R [18-20].

Serological profiling demonstrated distinct diagnostic patterns reflective of disease stage and immune response. NS1 antigen alone was detected in 17 out of 74 patients (23%), which supports its usage as a sensitive marker in the early febrile phase of infection. This is concurring with Patel SD and Bhatnaga R and Chakravarti A et al., [17,20]. However, it has been reported earlier that the NS1 positivity may vary significantly depending on the timing of sample collection with respect to the onset of fever and stage of disease, as reported by Mohan K et al., who observed an NS1 positivity rate of 55.3% [12]. The presence of serological profiles with positivity for IgM and IgG (heterogeneous profile) has also been supported by Mohan K et al., and it is well known that with the passage of time, the immune response also changes, and secondary dengue infection also occurs in endemic areas [12].

A seasonal variation in dengue incidence was observed, with the highest positivity during the monsoon and post-monsoon months. Dengue positivity was 32.4% in August (11/34), 26.2% during September (11/42) and 23.8% during October (5/21). These coincided with the season when the environment was suitable for breeding of the dengue vector *Aedes aegypti*. There was an increase in the number of cases from July (8 cases), reaching a peak during September (42 cases) and then decreasing by November (14 cases). This pattern of seasonality was in line with those reported from Maharashtra, Gujarat and Kerala by Pooja PS et al., [16] and Raji TK and Sudhakaran M [21], which supports the previous

reports that dengue transmission varies with rainfall, humidity and water stagnation [18,19].

Biochemical analyses showed that hepatic function was significantly impaired in dengue-positive patients exhibiting warning signs. An increase in the levels of serum transaminases was observed. In most cases, the SGPT level was higher than the SGOT level, similar to the findings of Naik NS et al., whereas Swamy AM et al., reported higher SGOT levels than SGPT levels [3,22]. Infection associated with the liver is due to direct effects of the virus on the cell, immune-mediated hepatocyte injury, hypoxic damage, and extensive inflammation throughout the body [3,22].

Haematological abnormalities were predominant in dengue-positive patients. Haemoglobin values were nearly normal reduced in the majority of non-severe dengue cases, as reported by Naik NS et al., [3]. Following infection, the virus targets monocytes and macrophages, triggering a cytokine-mediated inflammatory response. Leucopenia was more frequent among dengue-positive patients ($\chi^2=26.9677$, p-value <0.00001), and relative lymphopenia was noted in 20 out of 38 cases ($\chi^2=12.4769$, p-value <0.00041), which was in agreement with the findings of Ferede G et al., who reported that the depletion of leucocytes is due to transient bone marrow suppression in the midst of viremic phase. A distinctive haematological hallmark of dengue is the combination of leucopenia and lymphopenia, which improves its ability to distinguish from bacterial infection [23]. Thrombocytopenia, seen in 35 out of 38 dengue patients, was the most prevalent blood disorder and it was demonstrated to be highly related to the disease ($\chi^2=69.873$, p-value <0.00001), resulting from decreased platelet production, peripheral destruction, and increased consumption secondary to endothelial activation, which goes along with the findings of Naik NS et al., Sharma P et al., Gupta N and Bareja R and Swamy AM et al., [3,10,22]. Therefore, platelet count monitoring is an indispensable forecaster for prognosis. Collectively, these findings highlight immune dysregulation and vascular involvement as central mechanisms underlying the haematological and biochemical alterations in dengue infection.

Subsequently, the increased levels of CRP in 33 out of 38 (86.85%) patients ($\chi^2=39.8538$, p-value <0.00001) and ESR in 23 out of 38 (60.52%) patients ($\chi^2=12.7281$, p-value <0.00036) identified the inflammatory markers that were suggestive of the systemic inflammation brought on by DENV infection. These results support earlier findings from Vuong NL et al., who reported an increase in CRP levels during early dengue infection [24]. CRP and ESR lacks disease specificity, but their increase reflects the inflammatory milieu of dengue.

The results have important clinical implications. When definitive testing is scarce, leucopenia, lymphopenia, and thrombocytopenia may serve as early markers of dengue. The necessity of regular hepatic monitoring is supported by elevated liver enzymes. The significance of clinical attentiveness during peak times is shown by seasonal clustering. Larger, multicentric populations and molecular diagnostics like Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) should be included in future research. Predictive models for early identification of severe dengue may be developed by combining clinical and laboratory characteristics.

Limitation(s)

This study used a hospital-based convenience not a population-representative sample, a single-centre, and a short-period study of 10 months. Haematological and biochemical parameters may have been impacted by potential confounders such as underlying comorbidities (e.g., diabetes, hepatic diseases) and differences in treatment received prior to presentation, which could have affected the observed relationships. The day of illness at the time of liver function testing was not recorded; therefore, phase-wise variations in transaminase levels could not be assessed. Future studies may include median and interquartile ranges to improve representation. Further work-up on serotype consideration is in progress.

CONCLUSION(S)

DENV infection, particularly in endemic areas, still presents a serious clinical and public health concern. The current study emphasises how crucial it is to combine standard haematological and biochemical measures with serological testing in order to identify dengue illness early. Particularly in environments with low resources where advanced diagnostics might not be easily accessible, basic laboratory indicators can offer important diagnostic support. Appropriate clinical surveillance and better patient care can be facilitated by prompt identification using a combined diagnostic strategy. Effective management and prevention still depend on early suspicion and seasonal awareness. All things considered, optimising dengue diagnosis and treatment requires a systematic laboratory-based approach.

Authors' contribution: All authors have given approval for the publication of this study. Each author has made substantial, direct, and meaningful contributions to the work, including its conception, design, data collection, analysis, and/or interpretation. MTA: Methodology, Data collection, Investigation, Data analysis, writing-original draft and writing review- editing; SJL: Conceptualisation, supervision and critical revision; DKK: Data curation, project administration and final approval.

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PARTICULARS OF CONTRIBUTORS:

1. Ph.D. Scholar, Department of Microbiology, Smt. B. K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth (Deemed to be University), Vadodara, Gujarat, India.
2. Professor, Department of Microbiology, Smt. B. K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth (Deemed to be University), Vadodara, Gujarat, India.
3. Clinical Microbiologist, Department of Microbiology, U.N. Mehta Institute of Cardiology and Research Centre Affiliated to B.J. Medical College and Gujarat University, Ahmedabad, Gujarat, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Mohd Tabish Ansari,
Ph.D. Scholar, Department of Microbiology, Smt. B. K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth (Deemed to be University), Vadodara, Gujarat, India.
E-mail: tabishansari793@gmail.com

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