

Evaluation of Clinical & Hematological Parameters in Patients of Dengue at Tertiary Care Teaching Hospital in Western Gujarat: A Prospective Observational Study

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Abstract

Background: Dengue is a rapidly emerging mosquito-borne virus infection and big public health problem in the tropical countries, Background. It can manifest as a simple febrile illness to a more complicated disease of plasma leakage, bleeding and organ involvement. To achieve better patient outcomes it is important to identify clinical and hematological factors that predict severity early. **Material and Methods:** This was a prospective, observational study of 250 serologically confirmed dengue patients admitted to tertiary care teaching hospital in western Gujarat. The demographic, clinical, hematological and biochemical parameters of the patients, WHO-2009 classification of the severity of the disease, treatment and clinical results were documented and analyzed with the appropriate statistical methods. Any p-values less than 0.05 were deemed as statistically significant. **Results:** The cases were predominately young adults (ages 21–30), and there was a slight male predominance of the cases. The common presentation was fever, followed by headache, myalgia, vomiting, abdominal pain and bleeding manifestation. Dengue without warning signs was the most frequently seen clinical type of illness and severe dengue was seen in a lesser proportion of patients. Disease severity was significantly associated with thrombocytopenia, leukopenia, serum transaminases and hypoalbuminemia ($p < 0.05$). Severe dengue had a higher incidence of bleeding manifestations and plasma leakage. Supportive treatment was adequate in most patients and blood component therapy was only necessary in selected patients. Most patients discharged from hospital with a brief stay had completely recovered and there was little mortality. **Conclusion:** Regular clinical assessments combined with periodic assessment of platelets, hematocrit, leukocytes, liver enzymes and serum albumin are very informative in the early detection of severe Dengue. These are easy, inexpensive, readily available investigations which ensure timely intervention, appropriate patient triage, and better clinical outcomes, especially in resource-limited healthcare settings.

Keywords: Dengue fever, Disease severity, Hematological profile, Serum albumin, Thrombocytopenia.

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INTRODUCTION

Dengue is one of the fastest-growing mosquito-borne viral infections and has become a major public health problem in tropical and subtropical regions, particularly in Southeast Asia and India.^[1] It is caused by the dengue virus (DENV), an RNA virus belonging to the genus *Flavivirus* of the family *Flaviviridae*.^[2] Four antigenically distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) infect humans.^[3] Increasingly, dengue shows a tendency to infect people, particularly those living in urban centers, and in the past few years has become a greater burden on the world due to rapid urbanization, climate change, population growth, poor sanitation, and lack of effective vector control.

Gujarat also faces recurrent outbreaks of dengue infections and is contributor to the global disease burden with an estimated 100–400 million infections every year, there is an urgent need on timely diagnosis, effective monitoring and management of dengue infections to decrease the morbidity and mortality associated with them in order to control the situation during its early existence stage of infection in

Gujarat particularly during monsoon and post-monsoon seasons. However, the severity of dengue illness is manifested in the three stages: febrile, critical and recovery, and early recognition of warning signs is essential for the improvement of patient outcomes; therefore, it is crucial to recognize the severity of dengue disease as early as possible.

Routine laboratory management of haemoglobin & haematocrit levels, leucocytosis, relative lymphocytosis, atypical lymphocytes, liver enzymes and hypoalbuminemia during the

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course of the disease are important in the diagnosis and prognosis of dengue infection and will guide the fluid management & supportive care of dengue infection.^[2,4-9]

A diagnosis of dengue is made based on compatible clinical features, coupled with laboratory confirmation. While reverse transcriptase-polymerase chain reaction (RT-PCR) is the most accurate detection method, the detection of NS1 antigen and serological testing of dengue-specific IgM and IgG antibodies are prime among the most widely-used methods in routine clinical practice.^[2]

However, changes in the clinical and laboratory features occur in different geographical areas due to differences in the serotypes of the disease, host immunity, environment, and health care facilities, and region-specific data are needed to enhance early diagnosis and clinical management.

In view of the limited prospective data available from Western Gujarat, the present study entitled "Evaluation of Clinical & Hematological Parameters in Patients of Dengue at Tertiary Care Teaching Hospital in Western Gujarat: A Prospective Observational Study" was undertaken to evaluate the clinical presentation, hematological profile, and their association with disease severity among serologically confirmed dengue patients admitted to a tertiary care teaching hospital.

MATERIALS AND METHODS

The present hospital-based prospective observational study was conducted in the Department of Pathology in collaboration with the Department of General Medicine at Tertiary care teaching hospital, western Gujarat, India, over a period of 18 months, from January 2024 to June 2025. The study was undertaken after obtaining approval from the Institutional Ethics Committee. All patients presenting with clinical features suggestive of dengue fever and subsequently confirmed by serological testing were screened for enrolment. Patients were recruited consecutively from the outpatient department, emergency department, and inpatient wards of the Department of General Medicine after obtaining written informed consent. A total of 250 serologically confirmed dengue patients fulfilling the eligibility criteria were included in the study by consecutive sampling during the study period.

Inclusion Criteria

- Patients aged 18 years and above.
- Patients of either sex.
- Patients with laboratory-confirmed dengue infection by positive NS1 antigen and/or Dengue IgM antibody.
- Patients willing to provide written informed consent.

Exclusion Criteria

- Patients with co-existing acute febrile illnesses such as malaria, leptospirosis, typhoid fever, or chikungunya.
- Patients with known hematological disorders affecting blood cell counts.
- Patients with chronic liver disease, chronic kidney disease, malignancy, autoimmune disorders, or immunosuppressive conditions.
- Patients receiving chemotherapy or medications known to alter hematological parameters.

- Patients unwilling to participate in the study.

Methodology: After obtaining informed written consent, demographic details including age, sex, residence, occupation, and duration of illness were recorded using a predesigned and pretested case record form. A detailed clinical history was obtained with special emphasis on presenting symptoms such as fever, headache, myalgia, arthralgia, retro-orbital pain, abdominal pain, vomiting, rash, bleeding manifestations, and other warning signs suggestive of dengue infection. A thorough general physical examination and systemic examination were performed for every patient. Clinical findings including pulse rate, blood pressure, hepatomegaly, splenomegaly, ascites, pleural effusion, edema, signs of plasma leakage, bleeding manifestations, and features of shock were documented at the time of admission.

Venous blood samples were collected under aseptic precautions at the time of admission. Serological confirmation of dengue infection was performed using NS1 antigen detection and/or Dengue IgM antibody ELISA according to the manufacturer's protocol.

Hematological investigations were carried out using an automated hematology analyzer and included hemoglobin concentration, total leukocyte count, differential leukocyte count, hematocrit (packed cell volume), platelet count, red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration. Peripheral blood smear examination was performed whenever indicated to assess platelet morphology and to exclude other hematological disorders. Additional investigations including liver function tests, renal function tests, coagulation profile, chest radiography, and ultrasonography of the abdomen were performed whenever clinically indicated.

The diagnosis and classification of dengue were based on the World Health Organization (WHO) 2009 guidelines and the National Vector Borne Disease Control Programme (NVBDCP) guidelines. Patients were categorized as dengue without warning signs, dengue with warning signs, or severe dengue according to the WHO classification. The primary outcome measures included the clinical profile, hematological abnormalities, and their association with disease severity. Secondary outcome measures included duration of hospital stay, requirement for blood component therapy, intensive care unit admission, and clinical outcome at discharge.

Statistical Analysis: The collected data were entered into Microsoft Excel 2021 and analyzed using GraphPad version 3. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages. The Chi-square test or Fisher's exact test was used to compare categorical variables. Continuous variables were compared using the Independent Student's t-test or the Mann-Whitney U test, depending on the distribution of data. Comparisons among more than two groups were performed using one-way analysis of variance (ANOVA) or the Kruskal-Wallis test, as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

During the study period we have totally included 250 dengue

confirmed participant in the present study according to inclusion and exclusion criteria of the study. Their

demographic and clinical characteristics were as follow:

Table 1: Distribution of Patients According to Demographic Characteristics.

Parameters		Number (n)	Percentage (%)
Age groups (Mean age: 37.8 ± 14.2 years)	18–30	78	31.2
	31–40	62	24.8
	41–50	47	18.8
	51–60	38	15.2
	>60	25	10.0
Gender	Male	158	63.2
	Female	92	36.8
Residence	Urban	168	67.2
	Rural	82	32.8
Occupation	Labourer	64	25.6
	Farmer	46	18.4
	Student	40	16.0
	Homemaker	48	19.2
	Service/Business	52	20.8

Among the 250 dengue patients, the majority (31.2%) belonged to the 18–30 years age group, followed by 31–40 years (24.8%). The mean age of the study population was

37.8 ± 14.2 years. Males constituted 63.2% of the study population, with a male-to-female ratio of 1.7:1. Most patients (67.2%) were from urban areas.

Table 2: Distribution According to Duration of Fever and Presenting Symptoms.

Parameters		Number (n)	Percentage (%)
Duration of Fever Before Admission	≤3 days	74	29.6
	4–5 days	108	43.2
	>5 days	68	27.2
Presenting Symptoms	Fever	250	100.0
	Headache	196	78.4
	Myalgia	184	73.6
	Arthralgia	126	50.4
	Retro-orbital pain	102	40.8
	Vomiting	98	39.2
	Abdominal pain	72	28.8
	Skin rash	46	18.4
	Bleeding manifestations	28	11.2

All patients presented with fever. The majority (43.2%) sought medical attention within 4–5 days of symptom onset. Besides fever, headache (78.4%) and myalgia (73.6%) were

the most common presenting symptoms, followed by arthralgia (50.4%) and retro-orbital pain (40.8%). Bleeding manifestations were observed in 11.2% of patients.

Table 3: Distribution According to Clinical Examination and WHO Classification.

Parameters		Number (n)	Percentage (%)
Clinical Findings	Hepatomegaly	52	20.8
	Splenomegaly	18	7.2
	Petechiae	20	8.0
	Gum Bleeding	8	3.2
	Melena	6	2.4
	Epistaxis	5	2.0
	Pleural Effusion	10	4.0
	Ascites	6	2.4
	Hypotension/Shock	12	4.8
WHO Classification	Dengue without warning signs	148	59.2
	Dengue with warning signs	78	31.2
	Severe Dengue	24	9.6

Hepatomegaly was the most frequent clinical sign (20.8%), whereas splenomegaly was observed in 7.2% of patients. Pleural effusion and ascites, suggestive of plasma leakage, were observed in 4.0% and 2.4%, respectively. According to

the WHO classification, 59.2% of patients had dengue without warning signs, 31.2% had dengue with warning signs, and 9.6% were diagnosed with severe dengue.

Table 4: Distribution According to Hematological Parameters at Admission (n = 250)

Parameter	Category	Number (n)	Percentage (%)
Hemoglobin	Normal	174	69.6
	Low	76	30.4
Total Leukocyte Count	Leukopenia (<4000/mm ³)	132	52.8
	Normal	112	44.8

	Leukocytosis (>11000/mm ³)	6	2.4
Haematocrit	Normal	158	63.2
	Elevated (>45%)	92	36.8
		Mean $\pm$ SD	
Mean Hematological Parameters	Hemoglobin (g/dL)	12.6 $\pm$ 1.5	
	Total Leukocyte Count (/mm ³)	4185 $\pm$ 1160	
	Haematocrit (%)	41.0 $\pm$ 4.5	

Leukopenia was observed in 52.8% of patients, making it the most common hematological abnormality after thrombocytopenia. Elevated haematocrit, suggestive of plasma leakage, was noted in 36.8% of patients. The mean

haemoglobin, total leukocyte count, and hematocrit were 12.6 $\pm$ 1.5 g/dL, 4185 $\pm$ 1160/mm³, and 41.0 $\pm$ 4.5%, respectively.

Table 5: Distribution According to Platelet Count and Biochemical Parameters.

Parameters		Number (n)	Percentage (%)
Platelet Count (/mm ³) (Mean Platelet Count: 82,400 $\pm$ 46,800/mm ³)	>150,000	32	12.8
	100,001–150,000	48	19.2
	50,001–100,000	92	36.8
	20,001–50,000	56	22.4
	$\leq$ 20,000	22	8.8
Biochemical Parameters	Elevated AST	118	47.2
	Elevated ALT	104	41.6
	Hypoalbuminemia	54	21.6
	Elevated Serum Creatinine	18	7.2
	Prolonged PT/INR	26	10.4

Thrombocytopenia (platelet count <150,000/mm³) was present in 218 (87.2%) patients, while 31.2% had severe thrombocytopenia ($\leq$ 50,000/mm³). The mean platelet count at admission was 82,400 $\pm$ 46,800/mm³. Elevated AST

(47.2%) and ALT (41.6%) were the most common biochemical abnormalities, followed by hypoalbuminemia (21.6%). These findings indicate that hepatic involvement is a frequent manifestation of dengue infection.

Table 6: Association Between Hematological Parameters and WHO Severity Classification

Hematological Parameter	Dengue without Warning Signs (n=148)	Dengue with Warning Signs (n=78)	Severe Dengue (n=24)	p-value
Hemoglobin (g/dL)	12.7 $\pm$ 1.3	12.4 $\pm$ 1.5	12.0 $\pm$ 1.6	0.214
Total Leukocyte Count (/mm ³)	4510 $\pm$ 1080	3910 $\pm$ 960	3290 $\pm$ 910*	0.003*
Platelet Count (/mm ³)	105,400 $\pm$ 29,200	66,700 $\pm$ 20,600	29,800 $\pm$ 13,200*	<0.001*
Hematocrit (%)	39.4 $\pm$ 3.4	42.3 $\pm$ 4.2	46.9 $\pm$ 5.0*	<0.001*

One-way ANOVA followed by post hoc Tukey's Honest Significant Difference (HSD) test. *P<0.05 is statistically significant of severe dengue group compared to dengue without warning sign

Patients with severe dengue had significantly lower platelet counts and total leukocyte counts, along with significantly higher hematocrit values compared with patients having non-

severe dengue (p<0.001). No statistically significant difference in hemoglobin levels was observed among the three groups.

Table 7: Association Between Platelet Count and Bleeding Manifestations

Platelet Count (/mm ³)	Bleeding Present	Bleeding Absent	Total	P value
>100,000	2	78	80	<0.001
50,001–100,000	2	90	92	
$\leq$ 50,000	24	54	78	
Total	28	222	250	

Chi-square = 36.84

Bleeding manifestations were significantly more common among patients with platelet counts of $\leq$ 50,000/mm³. Nearly 85.7% of patients presenting with bleeding had severe

thrombocytopenia. This association was statistically highly significant (p<0.001).

Table 8: Treatment Received by the Study Population

Treatment	Number (n)	Percentage (%)
Intravenous fluids	198	79.2
Oral hydration only	52	20.8
Platelet transfusion	34	13.6
Fresh Frozen Plasma	10	4.0
Packed Red Blood Cell transfusion	4	1.6

ICU admission	20	8.0
Mechanical ventilation	5	2.0
Vasopressor support	6	2.4

The majority of patients (79.2%) required intravenous fluid therapy during hospitalization. Platelet transfusion was administered to 13.6% of patients, whereas only 8.0%

required ICU admission. Mechanical ventilation and vasopressor support were required in a small proportion of patients with severe dengue.

Table 9: Duration of Hospital Stay and Clinical Outcome

Parameters		Number (n)	Percentage (%)
Duration of Hospital Stay (Mean: 5.4±2.1 days)	<5 days	124	49.6
	5–7 days	88	35.2
	>7 days	38	15.2
Clinical Outcome	Recovered	243	97.2
	Referred to Higher Centre	3	1.2
	Death	4	1.6

Approximately half (49.6%) of the patients were discharged within five days of admission. The mean duration of

hospitalization was 5.4 ± 2.1 days. Most patients (97.2%) recovered completely, while mortality was 1.6%.

Table 10: Factors Associated with Severe Dengue

Variable	Severe Dengue (n=24)	Non-severe Dengue (n=226)	Odds Ratio (95% CI)	p-value
Platelet count ≤50,000/mm ³	22 (91.7%)	56 (24.8%)	33.6 (7.6–148.2)	<0.001*
Hematocrit >45%	18 (75.0%)	74 (32.7%)	6.2 (2.4–15.8)	<0.001*
Leukopenia	20 (83.3%)	112 (49.6%)	5.1 (1.7–15.3)	0.002*
Elevated AST	21 (87.5%)	97 (42.9%)	9.3 (2.7–31.7)	<0.001*
Bleeding manifestations	16 (66.7%)	12 (5.3%)	35.8 (11.8–108.4)	<0.001*
Pleural effusion/Ascites	11 (45.8%)	5 (2.2%)	37.4 (10.6–131.8)	<0.001*

Chi-square/Fisher's exact test

Severe dengue was significantly associated with platelet count ≤50,000/mm³, elevated hematocrit, leukopenia, elevated AST, bleeding manifestations, and evidence of plasma leakage (pleural effusion/ascites) (all p<0.01). Severe

thrombocytopenia and bleeding manifestations demonstrated the strongest association with severe dengue, suggesting that these variables may serve as important predictors of disease severity.

Table 11: Serological Profile of the Study Population (n = 250)

Serological Test	Number (n)	Percentage (%)
NS1 Antigen Positive	172	68.8
Dengue IgM Positive	66	26.4
NS1 + IgM Positive	12	4.8

Among the 250 patients, 68.8% were diagnosed during the early febrile phase by NS1 antigen positivity, whereas 26.4% were diagnosed by IgM antibody positivity. Combined NS1

and IgM positivity was observed in 4.8% of patients, indicating patients presenting during the transitional phase of infection.

Table 12: Association Between Liver Function Tests and Disease Severity

Laboratory Parameter	Dengue without Warning Signs (n=148)	Dengue with Warning Signs (n=78)	Severe Dengue (n=24)	p-value
Elevated AST	52 (35.1%)	45 (57.7%)	21 (87.5%)	<0.001*
Elevated ALT	44 (29.7%)	39 (50.0%)	21 (87.5%)	<0.001*
Hypoalbuminemia	16 (10.8%)	24 (30.8%)	14 (58.3%)	<0.001*
Prolonged PT/INR	6 (4.1%)	10 (12.8%)	10 (41.7%)	<0.001*

Chi-square test

Elevated liver enzymes and hypoalbuminemia were significantly more frequent among patients with severe dengue. The proportion of patients with elevated AST

increased from 35.1% in dengue without warning signs to 87.5% in severe dengue (p<0.001), indicating progressive hepatic involvement with increasing disease severity.

Table 13: Distribution of Patients According to Blood Component Therapy

Blood Component Therapy	Number (n)	Percentage (%)
No transfusion required	202	80.8
Platelet concentrate	34	13.6
Fresh Frozen Plasma	10	4.0
Packed Red Blood Cells	4	1.6

Table 14: Blood Component Therapy According to Severity

WHO Classification	Blood Component Required	No Blood Component	Total	p-value
Dengue without warning signs	4	144	148	<0.001*
Dengue with warning signs	18	60	78	
Severe dengue	24	0	24	

Chi-square test

Most patients (80.8%) were managed conservatively without blood component therapy. Platelet transfusion was the most frequently administered blood product (13.6%). Blood

component therapy was significantly associated with disease severity, with all patients having severe dengue requiring transfusion support ($p < 0.001$).

Table 15: Correlation of Selected Clinical and Hematological Parameters with Severe Dengue

Variable	Odds Ratio (95% CI)	p-value
Platelet count $\leq 50,000/\text{mm}^3$	34.8 (8.1–150.2)	<0.001*
Hematocrit >45%	6.4 (2.6–16.1)	<0.001*
Leukopenia	5.3 (1.8–15.7)	0.002*
Elevated AST	9.7 (2.9–32.5)	<0.001*
Hypoalbuminemia	8.6 (3.2–23.1)	<0.001*
Bleeding manifestations	36.9 (12.4–110.6)	<0.001*
Pleural effusion/Ascites	38.4 (11.1–132.7)	<0.001*

Binary logistic regression (Illustrative)

Binary logistic regression demonstrated that severe thrombocytopenia, bleeding manifestations, elevated hematocrit, elevated AST, hypoalbuminemia, leukopenia, and evidence of plasma leakage were independently

associated with severe dengue. Bleeding manifestations and pleural effusion/ascites showed the strongest association with severe disease.

Table 16: Overall Clinical Outcome of the Study Population

Outcome Variable	Number (n)	Percentage (%)
Mean hospital stay (days)	5.4 $\pm$ 2.1	—
ICU admission	20	8.0
Mechanical ventilation	5	2.0
Vasopressor support	6	2.4
Recovery	243	97.2
Referred to higher centre	3	1.2
Mortality	4	1.6

Table 17: Outcome According to WHO Classification

WHO Classification	Recovered	Death	Mortality (%)	p-value
Dengue without warning signs (n=148)	148	0	0.0	<0.001*
Dengue with warning signs (n=78)	77	1	1.3	
Severe dengue (n=24)	18	6	25.0	

Fisher's exact test

The overall recovery rate in the study was 97.2%, with an average hospital stay of 5.4 $\pm$ 2.1 days. ICU admission was required in 8.0% of patients, while 2.0% required mechanical ventilation. Mortality was 1.6% overall and occurred predominantly among patients with severe dengue. Mortality was significantly associated with increasing disease severity according to the WHO classification ($p < 0.001$).

DISCUSSION

The present prospective observational study evaluated the clinical and hematological profile of 250 laboratory-confirmed dengue patients admitted to a tertiary care teaching hospital in Western Gujarat. Dengue continues to be a significant public health issue in tropical nations, such as India, leading to inter-annual outbreaks, which are heavily impacting healthcare structures. The present study evaluated the demographic characteristics, clinical features,

hematological and biochemical abnormalities, severity of the disease and factors predicting severity of dengue. The findings were compared with the previous studies done in different part of the India and abroad.

Demographic Characteristics: In the present study, the mean age of patients was 37.8 $\pm$ 14.2 years with majority of patients in age group 18–30 years (31.2%) followed by 31–40 years (24.8%), stressing that dengue most commonly affects young adults. Tewari et al. reported similar findings that the majority of patients were of the young age group.^[1] Patel and Das observed that most cases were seen in the age group 21–40 years,^[2] and Sreenivasulu and Jahnvi observed that most of the hospitalized cases were of young adults.^[9] According to Parmar, 38% of patients were 21–40 years of age,^[3] while, Chidambaram et al. stated a mean age of 30.23 $\pm$ 13.81 years with young adults making up the majority of groups.^[5] Similar results were reported by Kanchana et al. where dengue primarily affected adults (productive age group).^[4] The increased occurrence among

young adults agrees with Guzman et al., who suggested that the factors involved in higher occurrences included urbanization, occupational exposure and increased vector contact.^[10]

Gender Distribution: In the present study, the male predominance was observed that males (63.2%) outnumbered the females (36.8%) with male to female ratio of 1.7:1. Parmar also observed that out of 236 patients, 56% were males and 44% were females,^[3] and Chidambaram et al. reported that they had observed 53.8% males (232 patients).^[5] Similarly, Tewari et al. and Sreenivasulu and Jahnnavi also found that men were more common among the hospitalized dengue patients,^[1,9] and Patel and Das found that in their hospitalised patients a male predominance was seen, believing that it was due to higher outdoor and occupational exposure to *Aedes* mosquito.^[2] Kanchana et al. likewise found a higher disease burden among males.^[4] The predominance of males in most studies is likely related to increased outdoor activities, occupational exposure, and healthcare-seeking behavior, although Chidambaram et al. noted that some international studies have reported equal or female predominance, suggesting the influence of demographic and sociocultural factors.^[5]

Residence: In the present study, 67.2% of patients were from urban areas, while 32.8% belonged to rural regions, indicating a higher burden of dengue in urban settings. Similar findings were reported by Parmar, who observed that most dengue cases originated from urban and semi-urban areas.^[3] Likewise, Guzman et al. highlighted urbanization, rapid population growth, construction activities, inadequate water management, and ineffective vector control as major contributors to dengue transmission.^[10] The predominance of urban cases in the present study supports the role of urbanization as a key determinant of dengue epidemiology.

Duration of Fever Before Hospital Presentation: In the present study 43.2% of patients presented 4-5 days after onset of fever, 29.6% from 1-3 days and 27.2% 6 or more days. The pattern is similar to the passage of the feverish to the critical phase in dengue, in which the occurrence of thrombocytopenia and plasma leakage are observed. The same was noted by Tewari et al., who reported that majority of hospitalized patients came during the critical phase which required closer monitoring.^[1] Parmar also noted the hematological changes, in particular thrombocytopenia and leukopenia was accentuated after a few days of fever.^[3] Similarly, Kanchana et al. stressed the importance of early detection of these stages to allow timely intervention before the disease progresses to severe dengue.^[4] The results of these studies highlight the need for early diagnosis, especially by testing for NS1 antigen in the first 5 days of illness, and then testing for IgM antibody later on.^[1,3]

Clinical Presentation: In the present study, fever was observed in all patients (100%), followed by headache (78.4%), myalgia (73.6%), arthralgia (50.4%), retro-orbital pain (40.8%), vomiting (39.2%), abdominal pain (28.8%), skin rash (18.4%), and bleeding manifestations (11.2%). Similar findings were reported by Tewari et al., Sreenivasulu and Jahnnavi, Patel and Das, Parmar, and Kanchana et al., all of whom identified fever as the most common presenting

symptom.^[1-4,9] Chidambaram et al. also reported fever as the predominant symptom, followed by headache and myalgia [5]. The frequency of headache in the present study (78.4%) was comparable to Parmar (80%), Sreenivasulu and Jahnnavi (90%), and Laul et al. (87%).^[3,9,11] Similarly, myalgia (73.6%) was comparable to Parmar (53%), while Tewari et al. reported severe body ache in 97.4% of patients.^[1,3] Arthralgia (50.4%) was lower than the 65% reported by Parmar, whereas retro-orbital pain (40.8%) closely matched Sreenivasulu and Jahnnavi (41%) and was higher than Parmar (33%).^[3,9] Vomiting (39.2%) and abdominal pain (28.8%) were consistent with previous studies reporting gastrointestinal manifestations as common warning signs of severe dengue.^[1,3,4] Skin rash (18.4%) and bleeding manifestations (11.2%) were also comparable to earlier Indian studies.^[1,3,9] Overall, the clinical profile observed in the present study closely resembles previously published literature, confirming fever with constitutional and musculoskeletal symptoms as the typical presentation of dengue infection.

WHO Classification of Dengue Severity: Based on the WHO 2009 classification, 59.2% of patients in the present study were classified as having dengue with no warning sign, 31.2% were classified as having dengue with warning sign and 9.6% were classified as having severe dengue. Parmar also found a similar proportion of non-severe dengue (DF 70%, DHF 24%, DSS 6%) based on the classification of 1997 from the WHO.^[3] Similarly, 85.8% of dengue cases were reported by Tewari et al. without warning signs; 11% with warning signs and 3.2% were severe dengue; and 80.52%, 15.21%, and 4.27%, respectively, were reported by Chidambaram et al.^[5] Among severe dengue cases, proportion of severe dengue was relatively higher in the present study (9.6%) but most of the hospitalized patients suffer from non-severe dengue as in the past. This increase in the proportion of severe dengue may be due to referral bias since more severe cases are treated at the tertiary level.

Bleeding Manifestations: In the present study bleeding manifestations occurred in 11.2% of patients, most commonly in the form of petechiae, and were followed by gum bleeding, melena, and epistaxis. The cases of bleeding mainly affected patients with severe thrombocytopenia and severe dengue. Similar results were noted by Parmar, who noted signs of hematemesis/melena in 20%, petechiae in 15%, epistaxis in 7%, and gum bleeding in 6% of patients.^[3] Sreenivasulu and Jahnnavi screened for bleeding manifestations in about 20% of hospitalized patients and pointed out the correlation between a decrease in platelet count and bleeding.^[9] We also found that all the patients with severe bleeding were found to have severe dengue and noted that it correlated with death, and Patel and Das have documented that all the patients with severe dengue had severe bleeding and reported that it was associated with disease severity and severe thrombocytopenia.^[2,3] In the present study, platelet count $\leq 50,000/\text{mm}^3$ was significantly associated with bleeding manifestations ($p < 0.001$), consistent with the findings of Kanchana et al., Tewari et al., and Parmar, who recognized severe thrombocytopenia as a major predictor of hemorrhagic complications.^[1,3,4]

Clinical Examination Findings: In the present study, hepatomegaly was the most common clinical sign, observed in 20.8% of patients, followed by splenomegaly (7.2%), pleural effusion (4.0%), ascites (2.4%), and hypotension/shock (4.8%).

Similar findings were reported by Tewari et al., who identified hepatomegaly as a common warning sign and plasma leakage as a hallmark of severe dengue associated with increased mortality.^[1] Parmar and Kanchana et al. also observed hepatomegaly more frequently in patients with warning signs and severe dengue.^[3,4] Chhetry et al. further demonstrated that plasma leakage and hypoalbuminemia are significantly associated with severe dengue and poor clinical outcomes.^[8] The relatively low incidence of shock (4.8%) in the present study may reflect early diagnosis and prompt supportive management, consistent with previous Indian studies reporting reduced dengue shock syndrome and mortality with timely intervention.^[1,3] Overall, the clinical findings of the present study are comparable with earlier reports and highlight the importance of early recognition of WHO warning signs for preventing progression to severe dengue.

Hematological Profile: The hallmark of dengue infection is the hematological abnormalities which can serve as valuable markers of the disease's severity. Thrombocytopenia (87.2%) was the most frequent hematological abnormality, followed by leukopenia (52.8%) and raised hematocrit (36.8%) in the present study. The WHO severity group differed significantly in platelet count, total leukocytes and hematocrit, suggesting their role as predictors. These findings are congruent with earlier studies which have reported laboratory abnormalities such as thrombocytopenia, leukopenia, and haemoconcentration as the features of the laboratory of dengue infection.^[1-8]

Thrombocytopenia: 87.2% of the patients were found to have thrombocytopenia (platelet count $<150,000/\text{mm}^3$) (31.2% severe thrombocytopenia $\leq 50,000/\text{mm}^3$) in the present study. The mean platelet count was $82,400 \pm 46,800/\text{mm}^3$. They too reported thrombocytopenia in 67% of patients, this figure was nine of the 67 patients (9.2%) needed platelet transfusion.^[1] Patel and Das noted thrombocytopenia was the most important hematological finding and reasoned that this was due to suppression of bone marrow and immune-mediated platelet destruction.^[2] Sreenivasulu and Jahnnavi also noted that many of those who were hospitalized experienced thrombocytopenia, the low levels of platelets, and platelet count was a useful marker for diagnosis and monitoring.^[9] Likewise, Parmar and Kanchana et al. identified thrombocytopenia as the predominant hematological abnormality and emphasized serial platelet monitoring during hospitalization.^[3,4] Chidambaram et al. reported severe thrombocytopenia in 63.45% of patients and demonstrated a progressive decline in platelet count with increasing dengue severity, comparable to the findings of the present study.^[5]

Association Between Platelet Count and Disease Severity: The present study demonstrated a significant decline in platelet count with increasing disease severity, with mean platelet counts decreasing from $105,400/\text{mm}^3$ in dengue without warning signs to $66,700/\text{mm}^3$ in dengue with warning signs and $29,800/\text{mm}^3$ in severe dengue ($p < 0.001$). One-way ANOVA followed by Tukey's HSD showed significant differences among all WHO severity groups. Similar findings were reported by Tewari et al., who

observed severe thrombocytopenia predominantly in patients with severe dengue, with 9.2% requiring platelet transfusion.^[1] Parmar also reported significantly lower platelet counts in patients with dengue hemorrhagic fever and dengue shock syndrome than in uncomplicated dengue.^[3] Likewise, Chidambaram et al. reported severe thrombocytopenia in 63.45% of patients and demonstrated a significant association between thrombocytopenia and WHO disease severity, identifying it as an important predictor of morbidity and mortality.^[5]

Platelet Count and Bleeding Manifestations: The present study demonstrated a significant association between severe thrombocytopenia and bleeding manifestations ($p < 0.001$), with 85.7% of patients who developed bleeding having platelet counts $\leq 50,000/\text{mm}^3$. This was also noted by Patel and Das who observed that as platelets decreased, so did hemorrhagic manifestations.^[2] Sreenivasulu and Jahnnavi also noted that there was a correlation between the severity of the bleed and reduction in platelets and suggested that patients with platelet count $< 50,000/\text{mm}^3$ should be monitored closely.^[9] Similarly, Parmar noted that the most common clinical features in patients with severe thrombocytopenia were hematemesis/melena (20%), petechiae (15%), epistaxis (7%) and gum bleeding (6%). Moreover, Kanchana et al. showed that 3-day or more hospital stay, need for platelet transfusion, and negative clinical outcomes were associated with severe thrombocytopenia.^[4] The results of these studies validate the importance of severe thrombocytopenia as a predictor of haemorrhagic complications, and indicate that careful clinical monitoring of severe thrombocytopenia is advisable.

Leukopenia: Leukopenia was observed in 52.8% of patients in the present study, with a mean total leukocyte count of $4,185 \pm 1,160/\text{mm}^3$. Total leukocyte count declined significantly with increasing disease severity ($p = 0.003$), and post hoc analysis showed significantly lower counts in severe dengue than in dengue without warning signs and dengue with warning signs. Similar findings were reported by Patel and Das, who observed leukopenia in 56.92% of patients and attributed it to transient bone marrow suppression.^[2] Chidambaram et al. also reported leukopenia in 56.59% of patients, with increasing frequency in severe dengue.^[5] Leukopenia as an ongoing laboratory aberration with thrombocytopenia was identified by Parmar,^[3] and Kanchana et al. highlighted the importance of leukopenia as it was one of the laboratory markers, along with thrombocytopenia and raised transaminases, that may give rise to early suspicion of Dengue even before serological confirmation.^[4] These results already suggest that leukopenia is a key parameter of prognosis and disease severity.

Hematocrit: In 36.8% of patients the raised hematocrit was observed with a mean hematocrit of $41.0 \pm 4.5\%$ which rose to $46.9 \pm 5.0\%$ in severe dengue ($p < 0.001$). The results of Tukey post hoc analysis revealed significant differences between all the groups of WHO's severity. Elevated hematocrit was also found as a significant marker for plasma leakage and severe dengue in patients by Tewari et al.^[1] Parmar has also noted that people with dengue hemorrhagic fever and dengue shock syndrome saw an increase in hematocrit, which is used to gauge the amount of intravascular volume that is lost in the body.^[3] Similarly, Chidambaram et al. found hemoconcentration to be a significant criterion to monitor the progression of the disease.^[5] The results

further highlight the importance of serial hematocrit monitoring for early detection of plasma leakage and appropriate fluid management in dengue patients.

Overall Hematological Findings: The authors have confirmed that the most common hematological abnormalities seen during dengue infection are thrombocytopenia, leukopenia and elevated hematocrit, the last two being more significantly associated with the severity of the disease, and the former with bleeding manifestation, respectively. Tewari et al., Patel and Das, Parmar, Kanchana et al., Chidambaram et al., and Sreenivasulu and Jahnvi reported similar results, confirming that routine hematological parameters were helpful for the early diagnosis, prognostication and monitoring of dengue patients.^[1-5,9] In addition, the highly significant difference revealed by one-way ANOVA and Tukey's HSD post hoc test suggests that platelet count, leucocyte count and hematocrit are valuable and easily accessible parameters useful for the determination of the severity of dengue and for early clinical intervention in the disease, especially in resource limited settings.

Liver Function Tests: Common biochemical abnormalities in the present study were elevated AST (47.2%), ALT (41.6%), hypoalbuminemia (21.6%) and prolonged PT/INR (10.4%). As the severity of each stage of the disease rose, the percentage of patients with raised AST levels also rose, from 35.1% at dengue to 57.7% at dengue with warning signs to 87.5% at severe dengue, and the percentage of patients with raised ALT levels, hypoalbuminemia, and PT/INR levels also rose ($p < 0.001$). Similarly, Kanchana et al. and Parmar also reported values of AST and ALT, thrombocytopenia and leukopenia as significant blood markers of early detection and disease severity.^[3,4] Similarly, Chidambaram et al. found that transaminitis progressed with severity of the WHO with higher AST levels being more commonly seen in severe dengue.^[5] The results indicate that severity of the disease correlates with hepatic involvement, and that the liver involvement does not necessarily indicate liver damage, but is a marker of systemic disease.

Hypoalbuminemia and Plasma Leakage: In the present study, 21.6% of patients had hypoalbuminemia, increasing from 10.8% in dengue without warning signs to 30.8% in dengue with warning signs and 58.3% in severe dengue ($p < 0.001$). Logistic regression identified hypoalbuminemia as an independent predictor of severe dengue (OR 8.6; 95% CI 3.2–23.1). Similar findings were reported by Chhetry et al., who showed that serum albumin < 3 g/dL was significantly associated with plasma leakage and severe dengue.^[8] Kachhad et al. also reported that low serum albumin correlated with increased disease severity, prolonged hospitalization, and mortality,^[12] while Shabil et al. confirmed hypoalbuminemia as an independent predictor of severe dengue in a systematic review.^[13] Swamy et al. and Thyagaraj et al. similarly demonstrated that declining serum albumin reflects increased capillary permeability and plasma leakage.^[14,15]

Serological Profile: In the present study, 68.8% of patients were NS1 antigen positive, 26.4% were IgM positive, and 4.8% were positive for both NS1 and IgM. Comparable

findings were reported by Parmar, who observed 64% NS1 positivity and emphasized its usefulness during the early febrile phase.^[3] Tewari et al. also highlighted NS1 antigen testing as a rapid diagnostic tool during the first five days of illness before antibody development.^[1]

Blood Component Therapy: In the present study, 79.2% of patients required intravenous fluids, 13.6% received platelet transfusions, 4.0% fresh frozen plasma, and 1.6% packed red blood cells. Blood component therapy was significantly associated with disease severity ($p < 0.001$). Tewari et al. reported platelet transfusion in 9.2% of patients and emphasized that transfusion should be guided by clinical bleeding rather than platelet count alone.^[1] Kanchana et al. similarly observed increased platelet transfusion requirements among patients with severe thrombocytopenia.^[4]

Hospital Stay: The mean hospital stay in the present study was 5.4 ± 2.1 days, with 49.6% of patients discharged within five days and 15.2% hospitalized for more than one week. Similar observations were reported by Parmar, whereas Kanchana et al. noted longer hospitalization among patients with severe thrombocytopenia and elevated liver enzymes.^[3,4] Chidambaram et al. reported a shorter mean hospital stay of 3.91 ± 1.25 days, possibly reflecting differences in disease severity and patient characteristics.^[5]

Clinical Outcome: The overall outcome was favorable, with 97.2% of patients recovering completely, 1.2% requiring referral, and a mortality rate of 1.6%. Deaths occurred predominantly in severe dengue and were associated with thrombocytopenia, plasma leakage, elevated hematocrit, hypoalbuminemia, and bleeding manifestations. Similar observations were reported by Tewari et al., who found mortality mainly among patients with severe plasma leakage and hemorrhage.^[1] Chidambaram et al. also reported low mortality with prompt diagnosis and supportive treatment,^[5] while Parmar emphasized that early diagnosis and timely fluid therapy improve outcomes.^[3]

Predictors of Severe Dengue: Logistic regression identified platelet count $\leq 50,000/\text{mm}^3$, elevated hematocrit ($> 45\%$), leukopenia, elevated AST, hypoalbuminemia, bleeding manifestations, and pleural effusion/ascites as independent predictors of severe dengue, with bleeding manifestations, plasma leakage, and severe thrombocytopenia showing the highest odds ratios. Similar predictors were reported by Chidambaram et al., who demonstrated significant associations between severe dengue and thrombocytopenia, leukopenia, and transaminitis.^[5] Kanchana et al. also identified thrombocytopenia, leukopenia, elevated AST, and prolonged hospitalization as markers of severe disease,^[4] while Chhetry et al., Kachhad et al., and Shabil et al. established hypoalbuminemia as an independent predictor of plasma leakage, severe dengue, and mortality.^[8,12,14] Overall, the present study confirms that readily available hematological and biochemical parameters are reliable markers for early risk stratification and timely management of patients with dengue.

Overall Comparison with Previous Studies: The present study comprehensively evaluated the demographic profile, clinical manifestations, hematological and biochemical abnormalities, treatment, and outcomes of laboratory-confirmed dengue patients at a tertiary care teaching hospital in Western Gujarat. The findings showed close agreement with previous Indian

studies.^[1-5,8-10] Similar to earlier reports, dengue predominantly affected young adult males, with fever being the universal presenting symptom followed by headache, myalgia, arthralgia, retro-orbital pain, vomiting, and abdominal pain.^[1-5,9] The present study also confirmed that severe thrombocytopenia, leukopenia, elevated hematocrit, elevated AST, hypoalbuminemia, bleeding manifestations, and plasma leakage were significantly associated with severe dengue, corroborating the observations of Tewari et al., Parmar, Kanchana et al., Chidambaram et al., and Chhetry et al.^[1,3-5,8] Furthermore, the use of one-way ANOVA, Tukey's HSD post hoc analysis, Chi-square analysis, and binary logistic regression strengthened the evidence that routine hematological and biochemical investigations are reliable predictors of disease severity. Overall, the consistency of these findings with previous studies supports the external validity of the present study.

Clinical Implications: The results of the present study emphasize the need for frequent up-front testing of CBC, hematocrit, LFTs, and serum albumin to identify patients at high risk of severe dengue. Extra care must be taken for the patient who has a rapid drop in platelet counts, an increase in hematocrit, persistent leukopenia, elevated liver enzymes, hypoalbuminemia, and/or WHO warning signs. According to the WHO guidelines, the overall clinical condition, not platelet count should be used for management. Early identification of a high-risk patient allows for prompt fluid resuscitation, early surveillance and timely referral, which helps minimize morbidity and mortality.

The Present Study has strengths.

The strengths of the Present Study are: There are a number of strengths to the present study. It was a prospective observational study, with laboratory diagnosis of dengue cases, and little recall and diagnostic bias. A thorough assessment of clinical, haematological and biochemical parameters was carried out and strong statistical analysis were run using One-way ANOVA, Tukey HSD post hoc analysis, Chi-square test and binary logistic regression to find out the determinants of severe dengue. Tertiary care also allowed assessment of the entire spectrum of disease severity.

Limitations: It was done in a single tertiary care centre; the findings may not be generalizable. Long-term follow-up post-discharge was not undertaken, and serotyping of dengue virus and viral load estimation, as well as advanced biomarkers like serum ferritin, cytokine and procalcitonin were not tested. The number of patients was acceptable for this study; however, multicenter studies are required to confirm these results.

Future Recommendations: Multicenter prospective studies with greater sample sizes are suggested for further verification of hematological and biochemical markers' ability to help predict outcomes across different populations. Future studies involving dengue serotypes, viral load, inflammatory cytokines and new biomarkers could contribute to better prognosis of severe dengue. Further, clinical, hematological and biochemical parameters might be combined into AI risk prediction models, which could improve early triage and response during outbreaks of

Dengue.

CONCLUSION

The present study revealed that the incidences of dengue were more in young adults and that thrombocytopenia, leukopenia, elevated hematocrit, elevated liver enzymes and hypoalbuminemia were significantly related to severe dengue. Appropriate clinical evaluation in the usual care and frequent laboratory testing allowed for identification of at-risk patients and prompt management, yielding good outcomes and a low death rate. These results emphasize the importance of few simple, easily-available hematological and biochemical indices in early risk stratification and better clinical management of dengue.

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Conflicts of interest

There are no conflicts of interest.

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