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A Study of Prognostic Markers for Dengue Infection

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Abstract

Introduction: Early diagnosis and prognostication of infections such as dengue are crucial for better patient outcomes, as they help predict the likelihood of patients developing severe dengue, allowing more comprehensive patient triage and therapeutic interventions. This study aimed to determine clinical, laboratory, and radiological factors predicting prognosis in dengue infection.

Methods: This prospective observational study included 250 patients seropositive for dengue. They were classified into dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS); and evaluated both on admission and at the end of their hospital course, the latter was performed for factors responsible for the progression of dengue to severe dengue. Data were statistically analyzed using R 3.6.1, with $P<0.05$ considered statistically significant.

Results: Final diagnosis correlated significantly with systolic blood pressure ($P=0.004$), lowest platelet count ($P<0.001$), serum glutamic-oxaloacetic transaminase ($P=0.001$), urine protein ($P<0.001$), urine red blood cells ($P<0.001$), pleural effusion ($P=0.0064$), serositis ($P<0.001$), vomiting ($P<0.001$), rash ($P<0.001$), restlessness ($P<0.001$), and bleeding manifestations ($P<0.001$).

Conclusion: The prognosis of dengue is significantly associated with blood pressure, lowest platelet count, serum transaminases, serum creatinine, proteinuria, hematuria, pleural effusion, abdominal pain, persistent vomiting, rash, restlessness, serositis, and bleeding manifestations. Monitoring these parameters is useful for the effective management of dengue.

Keywords: Dengue, Platelet Count, Serositis, Severe Dengue

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Introduction

Dengue is an acute mosquito-borne viral disease and a global public health issue, extremely affecting the tropical and sub-tropical countries.[1] Over 50–100 million people are infected with dengue annually, while > 3.97 billion people are at risk of contracting the disease.[1,2] In the past five decades, the prevalence of dengue has exhibited a 30-fold increase.[1,2] Dengue is endemic in nearly 100 countries, including India.[3] In India, annually, 390 million people are infected with dengue, and > 5.7 million patients suffer from severe dengue.[1]

In 2009, the World Health Organization (WHO) dengue case classification was revised to classify dengue infection into two forms, namely dengue and severe dengue, which was introduced to simplify 1997 WHO dengue case classification comprising dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS).[4] Dengue is a complex, dynamic, and rapidly progressing disease, mediated by intricate interactions between the vector, virus, and host.[3] Often, DF rapidly progresses to its severe form, i.e., DHF or DSS, which are the foremost causes of morbidity and mortality.[5,6] Nevertheless, appropriate disease management effectively improves patient outcome.[6]

Considering the unavailability of antiviral drugs, disease management is primarily based on early supportive treatment. Thus, early diagnosis of patients at risk of developing a severe prognosis is crucial.[7] Potential predictors of prognosis comprise clinical symptoms and laboratory parameters, including fever, body ache, skin rash, platelet/blood cell count, biomarkers, including liver enzymes, and markers of vascular functions.[7] Various clinical, radiological, laboratory and immunological parameters predict the severity of dengue, permitting early disease management and reduction in morbidity and mortality.[8]

Limited studies have analyzed dengue in different demographic settings in the Indian subcontinent.[1] Moreover, to our knowledge, only a few studies have investigated prognostic markers for dengue among the adult population of India.[1,3] Such research should be conducted to better comprehend the burden of dengue and design appropriate therapeutic interventions for improved quality of life of

patients.[1] The present study aimed to evaluate clinical, laboratory, and radiological factors predicting prognosis in dengue infection.

Methods

Study Design and Sampling

This prospective observational study enrolled 250 patients seropositive for dengue in Ramaiah Medical College, Bengaluru, Karnataka, India from October 2014 to June 2016. The study was approved by the institutional ethics committee, and written informed consent was obtained from all the study participants. Inclusion criteria included patients who were > 18 years old and seropositive [nonstructural protein 1 (NS1) antigen-positive and/or IgM antibody positive] for dengue. Those who presented with mixed infections, such as dengue with malaria and those with any other systemic bleeding and/or coagulation disorders were excluded from the study.

Sample Size

A sample size of 250 was calculated as described by WHO using a random sampling method with absolute precision of 3% and desired confidence level of 95%.[10]

Data Collection

Routine investigations, including complete blood test, platelet count, packed cell volume, liver function test with liver enzyme analysis, renal function test, and serum sodium level, along with routine urine analysis, including urine protein and red blood cell count, were performed in a diagnostic laboratory of the hospital under study. Moreover, clinical spectrum, abdominal ultrasonography, and chest X-ray were evaluated and correlated with the course of illness and with each other.

According to the National Guidelines for Clinical Management of Dengue Fever (2014), study patients were classified into three groups as per their symptoms, *i.e.*, DF, DHF, and DSS.[9] This classification was conducted at two-time points, upon admission and at the end of the hospital course. Considering that DF can progress to DHF or DSS throughout illness, patients were further analyzed by categorizing them into two groups. Those having DF both on admission and final diagnosis were classified under group 1 (N = 172; 89.1%), whereas those having DF on admission who later developed DHF or DSS were classified under group 2 (N = 21; 10.9%). Variables were compared between both groups, labeled as second analysis hereafter. A total of 193 patients were included in the second analysis, while 57 patients, i.e., 54 (21.6%) patients with DHF and 3 (1.2%) with DSS on admission, were excluded from the second analysis.

Statistical Analysis

Data were analyzed using statistical software R 3.6.1. All the parameters were not normally distributed and were accordingly analyzed. Qualitative parameters were assessed and expressed as percentages. Quantitative parameters were analyzed and expressed as mean ± standard deviation. A univariate chi-square test was performed to investigate the association between the study parameters and the course of the disease. $P < 0.05$ was considered statistically significant.

Results

Based on the status of dengue serology, 173 (69.2%), 47 (18.8%), and 30 (12%) patients exhibited the presence of NS1 antigen, dengue-specific IgM antibodies, and both, respectively. Table 1 presents an assessment of dengue on admission and the final diagnosis.

On final diagnosis, the number of patients with DF had decreased by 8.4%, whereas the number of patients with DHF and DSS had increased by 3.6% and 4.8%, respectively.

Of 250 patients, 166 (66.4%) were males and 84 (33.6%) were females. Of 193 patients in the second analysis, in group 1, 121 (70.3%) were males and 51 (29.7%) were females, and in group 2, 10 (47.6%) were males and 11 (52.4%) were females. The sex of patients was not associated with the final diagnosis ($P = 0.088$) and second analysis ($P = 0.06$). Age was also not associated with the final diagnosis ($P = 0.57$) and second analysis ($P = 0.61$) The patients were classified based on their age as depicted in Table 2.

Table 3 depicts the classification of patients based on quantitative parameters.

Final diagnosis correlated significantly with systolic blood pressure ($P < 0.004$), lowest platelet count ($P < 0.001$), and serum glutamic-oxaloacetic transaminase (SGOT) ($P = 0.001$). The second analysis correlated significantly with the lowest platelet count ($P = 0.002$) and SGOT ($P < 0.001$).

Table 4 depicts the classification of patients based on qualitative parameters.

Final diagnosis correlated significantly with urine protein ($P < 0.001$), urine red blood cells or RBCs ($P < 0.001$), pleural effusion ($P = 0.0064$), and serositis ($P < 0.001$). The second analysis also correlated significantly with urine protein ($P < 0.001$), urine RBC ($P < 0.001$), and serositis ($P < 0.001$).

Table 5 presents the classification of patients based on their clinical variables.

The final diagnosis correlated significantly with vomiting ($P < 0.001$), rash ($P < 0.001$), restlessness ($P < 0.001$), and bleeding manifestations ($P < 0.001$). The second analysis correlated significantly with vomiting ($P < 0.001$), abdominal pain ($P = 0.002$), rash ($P = 0.012$), restlessness ($P = 0.003$), and bleeding manifestations ($P < 0.001$).

Table 1. Assessment of Dengue on Admission and Final Diagnosis

Diagnosis	Number of Patients, N = 250; n (%)		% Change
	On Admission	Final Diagnosis	
DF	193 (77.2)	172 (68.8)	−8.4
DHF	54 (21.6)	63 (25.2)	+3.6
DSS	3 (1.2)	15 (6.0)	+4.8

DF: dengue fever, DHF: dengue hemorrhagic fever, DSS: dengue shock syndrome.

Table 2. Classification of Patients Based on Age

Variables	Final Diagnosis					Second Analysis			
	DF, n=172, n (%)	DHF, N=63, n (%)	DSS, n=15, n (%)	Total, N=250, n (%)	*P* Value	Group 1, n=172, n (%)	Group 2, n=21, n (%)	Total, N=193, n (%)	*P* Value
Gender									
Male	121 (70.4)	38 (60.3)	7 (46.7)	166 (66.4)	0.08	121 (70.4)	10 (47.6)	131 (67.9)	0.06
Female	51 (29.6)	25 (39.7)	8 (53.3)	84 (33.6)		51 (29.6)	11 (52.4)	62 (32.1)	
Age group									
18–30	87 (50.6)	35 (55.6)	6 (40.0)	128 (51.2)	0.57	87 (50.6)	11 (52.4)	98 (50.8)	0.61
31–40	42 (24.4)	9 (14.3)	5 (33.3)	56 (22.4)		42 (24.4)	4 (19)	46 (23.8)	
41–50	21 (12.2)	12 (19)	1 (6.7)	34 (13.6)		21 (12.2)	5 (23.8)	26 (13.5)	
51–60	10 (5.8)	3 (4.8)	1 (6.7)	14 (5.6)		10 (5.8)	0	14 (7.3)	
61–70	10 (5.8)	3 (4.8)	1 (6.7)	14 (5.6)		10 (5.8)	1 (4.8)	11 (5.7)	
>70	2 (1.2)	1 (1.6)	1 (6.7)	4 (1.6)		2 (1.2)	0	2 (1)	

DF: dengue fever, DHF: dengue hemorrhagic fever, DSS: dengue shock syndrome; n (%) represents number of patients.

Discussion

The prevalence of dengue is increasing globally, mainly in tropical and sub-tropical countries, due to climatic conditions, unclean environments especially in the rainy season, fast urbanization, and inefficiently planned urban colonization.[1,11] Early diagnosis of patients and predicting prognosis of infection is crucial for better patient outcome.[7] The study evaluated clinical, laboratory, and radiological factors predicting prognosis in dengue infection.

The present study included patients with NS1 antigen and IgM antibodies. NS1 antigen is one of the earliest markers identified in the blood of a patient with dengue within one to nine days of infection.[12] IgM antibodies are the first antibodies to appear and are identifiable in nearly 50% of patients from the third or fifth day onward until the second or third month.[6,12] The presence of NS1 and IgM antibodies indicates a recent/active infection.[12]

Male sex is commonly associated with the incidence of dengue.[13] With respect to age, in the present study, dengue infection and the course of illness were reportedly independent of age. Literature suggests that young age is more commonly associated with the incidence of dengue.[14] Contrastingly, literature also suggests that adults are more likely to contract dengue infection than children.[15] In Southeast Asia, the incidence of DF and DHF is high among children, whereas, in Western countries, the incidence is high among adults.[16] Reportedly, the association between dengue infection and age needs to be studied more extensively.[15] Moreover, in a study conducted by Chau et al., regardless of immunological immaturity, <6-month-old infants infected with dengue presented vigorous neutralizing antibody responses that lasted >1 year after the infection.[17] Thus, in line with the findings of Chau et al., in the present study, IgM antibodies and NS1 antigen could have attributed, to some extent, to the study findings in which the prognosis of dengue is independent of age.[15] Moreover, in the present study, patients could not be equally distributed in the respective age groups, and over 50% of patients were in the age group of 18–30 years, which also could have influenced the study findings.

Of all hematological predictors of dengue, the platelet count is the most common. As observed in the present study, platelet count decreases as the infection progresses. The lowest platelet count of 10–20 thousand/cumm is often observed in case of severe infection, which is an indicator for bleeding.[2,13] However, the lowest platelet count alone cannot strongly predict the incidence of bleeding and is dependent on liver function status and coagulation parameters.[2,13,18]

In the present study, white blood cell or white blood cell (WBC) count was observably low on the final diagnosis, concurrent with the literature.[18,19] Of note, WBC count is often consistently low throughout illness.[19] This could be the reason that in the present study, the final diagnosis was independent of the WBC count. However, a normal WBC count was also observed in 89 (35.6%) patients. Reportedly, WBC count can be within the normal range in severe dengue owing to physiological stress. [18]

Elevated levels of liver enzymes are often present in severe dengue. Concurrent with the literature, in the present study, SGOT and SGPT levels were remarkably high in DHF and DSS cases.[18] Such high levels exhibit the severity of the hepatocellular injury.[20] However, levels of liver enzymes peak typically around the second week of infection and thus should be carefully evaluated for prognosis.[13]

Increased serum creatinine levels and proteinuria observed in dengue commonly indicate kidney dysfunction.[13,21] Degree of proteinuria indicates the severity of the infection and presents a manifestation of the pathogenic mechanisms triggered by the dengue virus on the lymphoreticular system, which subsequently leads to glomerular leakage, suggesting an incidence of DHF.[22] Reportedly, urine protein/creatinine ratio is a potential predictor for DF, where a higher ratio is more common in DHF than DSS.[13] Plasma leakage, suggesting hypoalbuminemia due to dengue, is an indicator of severity.[23] However, the severity of the infection cannot be well differentiated based on serum albumin levels.[13] This may be due to the fact that in the present study, the final diagnosis was independent of serum albumin levels. Hyponatremia was also observed in 124 (49.6%) patients. Although the final

Table 3. Classification of Patients According to Quantitative Study Parameters

Parameter	No. of Patients, N=250, n (%)	Final Diagnosis					Second Analysis			
		DF, n=172, mean ± SD	DHF, n=63, mean ± SD	DSS, n=15, mean ± SD	Total, N=259, mean ± SD	*P* Value	Group 1, n=172, mean ± SD	Group 2, n=21, mean ± SD	Total, N=193, mean ± SD	*P* Value
Pulse rate (bpm)										
<60	67 (26.8)	68.84 ± 11.98	68.21 ± 12.14	63.20 ± 11.90	68.34 ± 12.04	0.156	68.84±11.98	67.14±15.09	68.65±12.32	0.286
60–90	177 (70.8)									
>90	6 (2.4)									
Systolic blood pressure (mm Hg)										
<100	9 (3.6)	114.23 ± 9.00	113.71 ± 9.11	103.60 ± 15.03	113.46 ± 9.76	<0.004*	114.23 ± 9.00	110.10 ± 10.32	113.78±9.22	0.085
100–120	215 (86.0)									
>120	26 (10.4)									
Diastolic blood pressure (mm Hg)										
<60	1 (0.4)	73.76 ± 5.84	72.38 ± 6.52	69.87 ± 10.65	73.18 ± 6.44	0.109	73.76 ± 5.84	71.52 ± 8.07	73.51 ± 6.14	0.121
60–90	154 (61.6)									
>90	95 (38.0)									
HCT levels (%)										
<40	89 (35.6)	41.22 ± 4.09	39.91 ± 5.07	39.27 ± 5.48	39.27 ± 5.48	0.156	41.22 ± 4.09	39.51 ± 5.01	41.03 ± 4.22	0.179
40.1–49.9	156 (62.4)									
>50	5 (2.0)									
WBC count (thousand/cumm)										
<4000	155 (62.0)	4180.41 ± 2083.7	4115.90 ± 2609.12	5035.33 ± 2413.02	4215.45 ± 2246.78	0.087	4180.41 ± 2083.7	4925.24 ± 2802.12	4261.45 ± 2176.9	0.245
4000–10000	89 (35.6)									
>10000	6 (2.4)									
Platelet count (thousand/cumm)										
On admission										
<20	31 (12.4)	57.55 ± 30.12	52.92 ± 30.80	52.00 ± 45.92	56.05 ± 31.35	0.279	57.55±30.12	50.24±32.42	56.76±30.37	0.186
20–50	68 (27.2)									
>50	151 (60.4)									
Lowest platelet										
<10	6 (2.4)	27.74 ± 14.13	16.19 ± 4.98	31.60 ± 25.09	25.06 ± 14.36	<0.001*	27.74 ± 14.13	18.00 ± 8.12	26.68 ± 13.93	<0.001*
10–20	103 (41.2)									
>20	141 (56.4)									
SGOT level (U/L)										
<100	106 (42.4)	130.52 ± 117.06	230.95 ± 604.38	371.07 ± 476.58	170.26 ± 342.90	0.001*	130.52± 117.06	412.52 ± 1035.64	161.2 ± 362.88	0.011*
101–200	101 (40.4)									
>200	43 (17.2)									
SGPT level (U/L)										
<100	108 (43.2)	133.92 ± 106.11	142.40 ± 208.01	220.33 ± 227.36	141.24 ± 147.74	0.621	133.92 ± 106.11	212.38 ± 351.92	142.46 ± 153.39	0.526
101–200	105 (42.0)									
>200	37 (14.8)									
Serum albumin level (g/dL)										
<3.5	202 (80.8)	3.35 ± 0.35	3.33 ± 0.32	3.18 ± 0.68	3.34 ± 0.37	0.671	3.35 ± 0.35	3.42 ± 0.42	3.36 ± 0.36	0.267
>3.5	48 (19.2)									
Serum creatinine level (mg/dL)										
<1.2	234 (93.6)	0.82 ± 0.21	0.77 ± 0.21	0.97 ± 0.46	0.82 ± 0.24	0.154	0.82 ± 0.21	0.73 ± 0.21	0.81 ± 0.21	0.071
>1.2	16 (6.4)									
Serum sodium level (mEq/L)										
<135	124 (49.6)	134.49 ± 2.36	133.87 ± 3.56	134.20 ± 3.82	134.32 ± 2.80	0.679	134.49 ± 2.36	133.71 ± 3.45	134.4 ± 2.50	0.358
>135	126 (50.4)									

DF: dengue fever, DHF: dengue hemorrhagic fever, DSS: dengue shock syndrome; HCT: Hematocrit; WBC: White blood cells; SGOT: Serum glutamic-oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase.

Table 4. Classification of Patients According to Qualitative Study Parameters

Parameter	Final diagnosis					Second analysis			
	DF, N=172, n (%)	DHF, N=63, n (%)	DSS, N=15, n (%)	Total, N=250, n (%)	*P* value	Group 1, N=172, n (%)	Group 2, N=21, n (%)	Total, N=193, n (%)	*P* value
Urine Protein (Per High Power Field)									
Absent	138 (80.2)	15 (23.8)	2 (13.3)	155 (62.0)	<0.001*	138 (80.2)	8 (38.1)	146 (75.6)	<0.001*
Present	34 (19.8)	48 (76.2)	13 (86.7)	95 (38.0)		34 (19.8)	13 (61.9)	47 (24.4)	
Urine RBC (Per High Power Field)									
Absent	150 (87.2)	37 (58.7)	3 (20)	190 (76.0)	<0.001*	150 (87.2)	11 (52.38)	161 (83.42)	<0.001*
Present	22 (12.8)	26 (41.3)	12 (80)	60 (24.0)		22 (12.8)	10 (47.62)	32 (16.58)	
Pleural Effusion on Chest X-Ray									
Absent	126 (73.26)	35 (55.56)	6 (40)	167 (66.8)	0.0064*	126 (73.26)	16 (76.20)	142 (73.58)	0.793
Present	46 (26.74)	28 (44.44)	9 (60)	83 (33.2)		46 (26.74)	5 (23.80)	51 (26.42)	
Serositis									
Absent	87 (50.6)	1 (1.59)	0	88 (35.2)	<0.001*	87 (50.6)	0	87 (45.1)	<0.001*
Ascites only	38 (22.1)	20 (31.7)	4 (26.7)	62 (24.8)		38 (22.1)	6 (28.6)	44 (22.8)	
Pleural effusion only	21 (12.2)	23 (36.5)	3 (20)	47 (18.8)		21 (12.2)	12 (57.1)	33 (17.1)	
Both ascites and pleural effusion	26 (15.1)	19 (30.2)	8 (53.3)	53 (21.2)		26 (15.1)	3 (14.3)	29 (15)	

DF: dengue fever, DHF: dengue hemorrhagic fever, DSS: dengue shock syndrome; RBC: Red blood cells; n (%) represents number of patients, Chi square test.

Table 5. Classification of Patients According to Clinical Variables

Clinical variables		Final diagnosis					Second analysis			
		DF, n=172, n (%)	DHF, n=63, n (%)	DSS, n=15, n (%)	Total, N=250, n (%)	*P* value	Group 1, n=172, n (%)	Group 2, n=21, n (%)	Total, N=193, n (%)	*P* Value
Fever	Yes	163 (94.8)	62 (98.4)	15 (100)	240 (96)	0.323	163 (94.8)	20 (95.2)	183 (94.8)	0.999
	No	9 (5.23)	1 (1.59)	0	10 (4)		9 (5.2)	1 (4.8)	10 (5.2)	
Vomiting	Yes	71 (41.3)	48 (76.2)	15 (100)	134 (53.6)	<0.0001*	71 (41.3)	18 (85.7)	89 (46.1)	<0.0001*
	No	101 (58.72)	15 (23.81)	0	116 (46.4)		101 (58.7)	3 (14.3)	104 (53.9)	
Abdominal pain	Yes	19 (11)	11 (17.5)	3 (20)	33 (13.2)	0.317	19 (11.1)	8 (38.1)	27 (14)	0.002*
	No	153 (88.95)	52 (82.54)	12 (80)	217 (86.8)		153 (88.9)	13 (61.9)	166 (86)	
Headache	Yes	146 (84.9)	54 (85.7)	10 (66.7)	210 (84)	0.166	146 (84.9)	20 (95.2)	166 (86)	0.338
	No	26 (15.12)	9 (14.29)	5 (33.33)	40 (16)		26 (15.1)	1 (4.8)	27 (14)	
Body ache	Yes	152 (88.4)	58 (92.1)	13 (86.7)	223 (89.2)	0.684	152 (88.4)	19 (90.5)	171 (88.9)	0.999
	No	20 (11.63)	5 (7.94)	2 (13.33)	27 (10.8)		20 (11.6)	2 (9.5)	22 (11.4)	
Retro-orbital pain	Yes	6 (3.5)	5 (7.9)	2 (13.3)	13 (5.2)	0.135	6 (3.5)	2 (9.5)	8 (4.1)	0.465
	No	166 (96.51)	58 (92.06)	13 (86.67)	237 (94.8)		166 (96.5)	19 (90.5)	185 (95.9)	
Rash (maculopapular)	Yes	19 (11)	25 (39.7)	5 (33.3)	49 (19.6)	<0.0001*	19 (11)	7 (33.3)	26 (13.5)	0.012*
	No	153 (88.95)	38 (60.32)	10 (66.67)	201 (80.4)		153 (89)	14 (66.7)	167 (86.5)	
Restlessness	Yes	0	3 (4.8)	7 (46.7)	10 (4)	<0.0001*	0	2 (9.5)	2 (1)	0.003*
	No	172 (100)	60 (95.24)	8 (53.33)	240 (96)		172 (100)	19 (90.5)	191 (99)	
Bleeding manifestations	Yes	0	63 (100)	15 (100)	79 (31.5)	<0.0001*	0	10 (47.6)	10 (5.2)	<0.0001*
	No	172 (100)	0	0	172 (68.5)		172 (100)	11 (52.4)	183 (94.8)	

DF: dengue fever, DHF: dengue hemorrhagic fever, DSS: dengue shock syndrome; n (%) represents number of patients, chi square test.

diagnosis was independent of serum sodium, presumably, the reduced levels of serum sodium present a higher incidence of DF-associated complications. [24]

Reportedly, a combination of leucopenia, thrombocytopenia, elevated liver enzymes, and low C-reactive protein strongly predicts prognosis during the early phases of dengue.[17,25] On admission, patients with dengue exhibit fever, vomiting, rash, aches or pain, bleeding manifestations, and clinical fluid accumulation, such as ascites or pleural effusion.[14,26,27] Similar findings were noted in the present study. The presence of bleeding manifestations, pleural effusion, and ascites are strongly predictive of DSS.[13,14]

Skin involvement is prevalent in dengue.[28] Owing to capillary permeability, there is an increase in leakage of plasma, RBCs, and electrolytes in patients with DHF and/or DSS.[14] Skin rashes either dissolve entirely or generalize with progressing infection.[28] In the present study, rashes persisted over the course of infection. In DHF, body temperature surpasses 39°C and persists for two to seven days. [29] For those who develop DSS, health further deteriorates after prolonged fever. The clinical deterioration occurs as the temperature falls.[29] Considering the course of high temperature, and as observed in the present study, fever cannot be considered as a prognostic marker for dengue.[29] In severe cases, dengue damages the heart, lungs, or liver, and the blood pressure decreases remarkably, leading to shock or death.[30]

The study possesses certain limitations. Because only adult patients were enrolled, the findings cannot be extrapolated to pediatric patients, which is important considering the high prevalence of dengue among children. Patients did not receive post-discharge follow-up. Future studies with long-term follow-up would help understand the comprehensive prognosis of the infection. The study lacked data on the onset of the infection and did not evaluate immunological parameters as potential biomarkers. Although these might not have altered the study outcomes, they would have allowed a better comprehension of the prognosis of dengue.

The present study was conducted in a tertiary care hospital in Bengaluru, Karnataka. The findings may not apply to all parts of India, because although dengue is endemic in the Indian subcontinent, its clinical manifestations can be substantially altered based on epidemiological and climatic parameters, including temperature and rainfall.[3] Thus, to validate the prognosis of dengue in India, future studies must span various states across the country and assess the influence of climatic parameters on the prognosis of dengue. The present study also provides a basis for establishing a prognostic prediction paradigm comprising clinical, radiological, and laboratory factors for dengue to understand the severity of the infection. The findings proffer sizeable data for appropriate triage and treatment. The findings also help identify high-risk patients and subsequently decrease the morbidity rates. Future studies with a gender-based classification of patients can be conducted to better understand the prognosis of the infection and implement appropriate effective treatment. Moreover, large-scale multi-centered trials are needed to confirm the present findings.

Research Highlights

What Is Already Known?

Dengue is a complex disease regulated by the complicated host-virus interactions. However, various clinical, radiological, laboratory and immunological parameters predict the severity of dengue, permitting early disease management and reduction in morbidity and mortality. Fascinatingly, the studies that have analyzed dengue in different demographic settings in the Indian subcontinent are rather limited. In addition to this, only a few studies have investigated prognostic markers for dengue in the adult population in India.

What Does This Study Add?

his study adds to the knowledge of predicting prognosis in dengue infection considering the various factors, including clinical, laboratory, and radiological; which would significantly contribute to early diagnosis and adequate management of dengue infection.

Conclusion

Blood pressure, lowest platelet count, SGOT, SGPT, serum creatinine, proteinuria, hematuria, pleural effusion, abdominal pain, persistent vomiting, bleeding manifestations, rash, restlessness, and serositis are predictive of severe dengue. These parameters should be implemented as prognostic markers in clinical practice for vigilant monitoring of the progress of dengue. Early anticipation of severe dengue allows the implementation of appropriate therapeutic interventions and can substantially decrease morbidity and mortality. These parameters can be implemented to design a scoring system that would predict the severity of dengue early in the course of the infection, and manage the same effectively.

Authors' Contributions

RPK developed the study concept and also contributed to the study design. Data collection and analysis were performed by both authors. Data were interpreted by SVK. Both authors approved the final version of the manuscript for submission.

Conflict of Interest Disclosures

The authors report no known conflict of interest.

Ethical Approval

This study was approved by the MS Ramaiah Medical College, Mathikere, Bangalore, Karnataka, and informed consent was taken from all participants.

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