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EVALUATION OF CLINICO-RADIOLOGICAL AND LABORATORY PARAMETERS IN DENGUE AND ITS CORRELATION WITH HOSPITAL STAY AND OUTCOME

Dr. Shubham Telang[1], Dr. Sudipta Saha[2], Dr.Suranjan Pal[3*], Dr Vicky Subhash Telang.[4]

[1]Senior Resident, Department of General Medicine, Government Medical College and Hospital Chandrapur.
[2]Associate Professor & HOD, Department of General Medicine Raiganj Government Medical College and Hospital
[3*]Associate Professor, Department of Microbiology, Raiganj Government Medical College and Hospital
[4]Project Research Scientist , Jawahar Lal Nehru Medical College, Dutta Meghe Institute of Higher Education and Research (DU), Wardha.

***Corresponding author:** Dr.Suranjan Pal
[*]Associate Professor, Department of Microbiology, Raiganj Government Medical College and Hospital

Abstract:
Dengue fever remains a significant public health concern, particularly in tropical regions. This study aims to evaluate the clinico-radiological and laboratory parameters in patients diagnosed with dengue and to analyze their correlations with hospital stay duration and clinical outcomes. **Methods:** A cohort of 108 patients was retrospectively reviewed, assessing key clinical features, laboratory findings (e.g., hematocrit, platelet count), and imaging results. Statistical analyses, including correlation coefficients, were employed to determine associations between these parameters and hospital length-of-stay, as well as patient outcomes (recovery, complications, mortality). **Results:** Preliminary findings indicate that specific laboratory markers, particularly thrombocytopenia and elevated hematocrit, AST, ALT, ALP are significantly associated with prolonged hospitalization and severe dengue. Furthermore, radiological evaluations often provided additional early insights into the severity of the disease and potential complications. **Conclusion:** The results underscore the importance of comprehensive clinical assessment and the integration of radiological and laboratory data in the management of dengue patients. These insights aim to enhance predictive models for disease progression, enabling more effective and prompt interventions and resource allocation in clinical settings. Further multicentric studies are recommended to validate these findings and explore the implications for patient management strategies.

Keywords: Dengue, Lab parameters, Radiological markers.

Introduction: Dengue, a fast-growing vector-borne febrile illness, is responsible for nearly 400 million infections worldwide annually. The incidence of dengue around the world has grown perilously, placing over half of the world's population at risk. Global estimates suggest that annually about 50 million population are dengue affected[1]. In 1780, India reported the first outbreak of dengue like illness in Chennai. Dengue is prevalent in India affecting both urban and

rural areas nationwide [2]. It is seen more in peri-urban areas due to change in demographic settings, unplanned urbanisation, poor access to safe water supply and storage, and unhealthy sanitation. In 2022, India reported 233,251 cases and 303 deaths [3]. The disease presentations vary from simple fever to having bleeding manifestations and going into shock. In the past, dengue was classified as Dengue Fever, Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). In 2009, World Health Organization (WHO) revised dengue fever classification as dengue not with warning signs (DNWS), dengue with warning signs (DWWS) and severe dengue (SD) [4]. Severe dengue encompasses syndromes related to dengue infection, such as DHF and DSS, which can be fatal. Although the overall case fatality rate is about 5%, timely interventions can reduce the mortality to less than 1% [5]. Additionally, the expanded dengue syndrome refers to uncommon manifestations involving various organs. Diagnosing dengue accurately is challenging due to overlapping symptoms with other diseases, and severe cases left untreated can have high mortality rates. Understanding the clinical features and utilizing laboratory findings are crucial for effective management and prognosis of dengue. To overcome these challenges the study was aimed to evaluate and correlate the clinical and laboratory parameters in dengue patients with a stay in Raiganj Government Medical Collage and Hospital and overall patient outcomes.

Material and Methods: We conducted a cross-sectional observational type study in Department of Medicine at Raiganj Government Medical College & Hospital, Uttar Dinajpur, West Bengal. The study period was from January 2024 to December 2024. The sample size was calculated using the Cochran Formula considering 95% confidence level 5% margin of error, and taking reported proportion of DENV to /be 19.5%, and absolute precision of 7.5% minimum sample size was calculated 107.2. Thus, 108 Patients were selected consecutively based on predetermined inclusion and exclusion criteria as follows: Inclusion Criteria: 1) Patient with positive Dengue serology (either NS1 Antigen or Dengue IgM antibody positive or the both) above 18 years.
Exclusion Criteria: 1) Patient positive for infections - Malaria, Influenza, Zika, Chikungunya, Measles COVID -19 and 2) Subjects with chronic renal, hepatic, cardiac, gastro-intestinal, skeletal, or endocrine diseases (except diabetes), acute critical illness, and pregnancy.
The tests conducted were the Dengue NS1 antigen ELISA by ELISA Test [make Bhat Bio-Tech] and ELISA for dengue IgM antibodies Ultra Dengue IgM Capture ELISA [make SD Biosensor Health Care Pvt. Ltd.] the samples were tested on Erba Lisa wash™ and Lisa Scan™ [make Erba Manheim]. Details of the demographic variables, symptoms, clinical examination, and laboratory investigations on admission were noted. Details about the presence of warning signs, if any, were noted. The patients were followed up until the outcome. Among laboratory investigations, a complete hemogram was done for every child. Other investigations like liver function test [serum total proteins, serum albumin, serum direct bilirubin, serum alanine aminotransferase (ALT), serum Aspartate Aminotransferase (AST) and serum alkaline phosphatase (ALP)] were done as per the patient's condition at baseline. The hematological and biochemical parameters were tested using Cobas Auto analyser and Sysmex 5 part machines. Investigations were repeated as deemed necessary by the treating doctor. For the study, the haemoglobin, lowest platelet count, lowest total leukocyte count (TLC), highest values for haematocrit and liver function tests was noted.
Clinical risk factors such as high-grade fever, and any of the warning signs are usually present in the initial febrile phase, while laboratory values derangement, especially a significant fall in platelet counts or severe rises in liver enzymes or coagulation profile are observed late in the disease phase. So, a separate analysis was done for clinical and laboratory parameters.
The study was initiated after approval from the Institutional Ethics Committee (Ref: RGMC/IEC/2023/05 dated 26/04/2023). Informed written consent was sought from all the study participants. Confidentiality of all study participants was maintained throughout the study. Treating physician managed the patients as per hospital protocol. Data was entered into Microsoft Excel and checked for error and inconsistencies. The categorical data was analyzed in the form of frequency and proportion. The quantitative data was analyzed in the form of mean, median, frequency and

percentages. The complete data analyzed in SPSS version 17. A P-value <0.05 will be considered as significant. Data were collected through an investigator administered pre-designed pre-validated structured questionnaire. Relevant medical history and laboratory parameters were obtained.

Result & Analysis: In this study, 108 admitted cases were included. World Health Organization (WHO) guidelines 2009 were followed and cases were divided into three categories dengue not with warning signs (DNWS) consisting of 52 cases(48.15%), dengue with warning signs (DWWS) consisting of 44 cases(40.74%) and severe dengue (SD) consisting of 12 cases (11.11%) at presentation. In this study, we have highlighted the clinical, laboratory and radiological parameters that suggest which patient is more prone to progression to dengue with warning signs and severe dengue. Among a total of 56 cases of DWWS and SD, all 56 cases were dengue IgM positive. The DNWS group was either Dengue IgM ELISA or Dengue NS1 antigen ELISA positive depending upon the fever duration at presentation the serological test chosen as per protocol. Patients included in this study lived in the locality of Raiganj, Uttar Dinajpur, and West Bengal. The present study demonstrates the peak incidence of cases in between August-October.

Majority of the cases were Male in the age group of 25-50 years, all of the admitted 108 cases recovered and discharged subsequently with varying length of stay according to the severity of dengue ranging from 5-10 days of median hospital stay.(Table1)

Table1. Distribution of demographic and hospitalization-related characteristics of dengue patients according to the severity

Demographic & hospitalization related characteristics		DNWS n=52(%)	DWWS	SD	Total
Gender	Male	30	24	8	62
	Female	22	20	4	46
Age Group	18-24 yrs	15	13	4	32
	25-50 yrs	29	19	5	53
	>50 yrs	08	12	3	23
Outcome	Discharge	52	44	12	108
	Death	0	0	0	0
Median length of stay (in days)		5.0(3-8)	7.0(6-10)	10.0(10-13)	

Fever was the most common symptom reported by all the patients, and 48.85% had ≥39°C temperature, followed by vomiting (62%), exanthema (57%), and decreased oral intake (57%). The clinical parameters showing significant association of severity of the dengue were Tachycardia defined as resting pulse rate > 100bpm, Hepatomegaly defined as Liver palpable below Right Costal Margin and Tourniquet test positivity.(Table 2)

Table2. Clinical risk factors for severe dengue

Risk factors		DNWS	DWWS	SD	Total
Tachycardia	Yes	0	4	5	9
	No	52	40	7	99
Heapatomegaly	Yes	0	17	12	29
	No	52	27	0	79
Tourniquet test	Positive	0	4	7	11
	Negative	52	40	5	97

The mean pulse rate in SD is 118.6 and the standard deviation is 7.101 with p-value of < 0.0001 suggesting a significant association with SD. Dengue virus directly infects liver cells, causing damage and inflammation, while an altered immune response further injures the liver, leading to

enlargement. Among a total of 56 cases of DWWS and SD, 29 cases were associated with hepatomegaly with p-value of < 0.0001 suggesting significant association of hepatomegaly with DWWS.

Dengue infection increases capillary permeability, making blood vessels fragile and prone to rupture under pressure, causing visible petechiae on the skin. Among a total of 56 cases of DWWS and SD, 11 cases are associated with positive tourniquet test with p-value of < 0.0001 suggesting significant association of positive tourniquet with DWWS and SD.

Table 3. Laboratory risk factors for severe dengue

Parameters	Type of Dengue	Number	Mean	Median	Std Dev.	p-value
PCV	DNWS	52	34.4531	34.20	3.3867	<0.0001
	DWWS	44	36.9698	37.20	4.4953	
	SD	12	29.1717	27.21	6.2590	
Hb%	DNWS	52	11.2846	11.30	1.1161	<0.0001
	DWWS	44	10.8932	11.10	1.5686	
	SD	12	8.7917	8.50	1.9412	
Platelet (in thousands)	DNWS	52	100.269	78.50	54.3298	<0.0001
	DWWS	44	65.8432	67.50	21.8923	
	SD	12	62.5833	63.00	22.7774	
ALP	DNWS	52	58.9808	60.00	18.9576	<0.0001
	DWWS	44	81.6795	76.50	36.3149	
	SD	12	157.9167	159.50	12.1615	
Bilirubin	DNWS	52	0.5962	0.6	0.2169	<0.0001
	DWWS	44	0.7777	0.7	0.4368	
	SD	12	2.1917	2.2	0.1881	
AST	DNWS	52	85.4423	90.5	26.74	<0.0001
	DWWS	44	162.5227	144.0	52.9016	
	SD	12	197.1667	198.50	10.2144	
ALT	DNWS	52	62.8250	55	27.1546	<0.0001
	DWWS	44	157.9545	145.5	42.3331	
	SD	12	177.0	178	8.7594	
Albumin	DNWS	52	3.6558	3.7	0.2754	<0.0001
	DWWS	44	3.4023	3.4	0.1677	
	SD	12	2.6417	2.65	0.2466	

The mean PCV in SD is 29.17 with a standard deviation of 6.25 and a p-value < 0.0001, suggesting a significant association with SD. In severe dengue with bleeding and plasma leakage, PCV may drop due to red blood cell loss. The mean Hb in SD is 8.79 with a standard deviation of 1.94 and a p-value < 0.0001, suggesting a significant association with SD. Hb levels may decrease due to internal bleeding or increases due to plasma leakage and hemoconcentration. Platelet count usually declines as dengue progresses in severity due to impaired platelet production and immune-mediated platelet destruction. The mean platelet count in SD is 62,583.33 with a standard deviation of 22,777.41 and a p-value < 0.0001, suggesting a significant association with SD. ALP is elevated in dengue, indicating liver dysfunction as the virus directly affects the liver. The mean ALP in SD is 157.91 with a standard deviation of 12.16 and a p-value of 0.0001, suggesting a significant association with SD. Bilirubin levels rise due to liver damage in dengue infection. The mean serum bilirubin in SD is 2.19 with a standard deviation of 0.18 and a p-value < 0.0001, suggesting a significant association with SD. AST levels rise due to liver damage in dengue infection. The mean AST in SD is 197.16 with a standard deviation of 10.21 and a p-value < 0.0001, suggesting a significant association with SD. ALT levels rise due to liver damage in dengue. The mean ALT in SD is 177.00 with a standard deviation of 8.75 and a p-value < 0.0001, suggesting a significant association with SD. Albumin levels decline as dengue severity increases due to plasma leakage.

The mean serum albumin in SD is 2.6 with a standard deviation of 0.24 and a p-value < 0.0001, suggesting a significant association with SD. Another striking hematology finding is mean neutrophil count in SD is 67.51 with a standard deviation of 4.28 and a p-value of < 0.043, suggesting a significant association with SD.

Table 4. Radiological risk factors for severe dengue

Radiological parameter	Findings	DNWS n=52(%)	DWWS n=44	SD n= 12	Total	P- value
Chest X-Ray	Pleural effusion Rt side	0	1	0	1	Chi-square value: 21.8208; df: 6; p-value: 0.0013
	Pleural effusion Lt side	0	0	2	2	
	Pleural effusion B/L	0	1	1	2	
	Within Normal Limits	52	42	9	103	
USG of Gall Bladder	GB wall Oedematous	0	17	12	29	Chi-square value: 54.8893; df: 2; p-value: <0.0001
	Within Normal Limits	52	27	0	89	

Among a total of 56 cases of DWWS and SD, 5 cases were associated with different patterns of pleural effusion (bilateral pleural effusion / right side pleural effusion / left side pleural effusion) with p-value < 0.0013 suggesting significant association of pleural effusion with DWWS and SD. Among total of 56 cases of DWWS and SD 29 cases had gall bladder wall oedema with p-value < 0.0001 suggesting significant association of gall bladder wall oedema with DWWS and SD.

Discussion: Dengue fever is endemic in India. It shows a seasonal pattern, with an upsurge in cases after the monsoon from July to November. Our study aimed to classify all the cases as per the WHO classification of dengue, find their outcomes, and determine the risk factors for severe disease. In our study, as per the WHO classification, 48.15 % reported absence of warning signs, 40.74% reported warning signs and 11.1% severe dengue. A similar distribution was reported by another Indian study carried conducted over two years in Odisha, India, reported 13% of severe cases. [6]. The distribution of severe and non-severe cases depends on many factors, including basic endemicity of the disease, climate, mosquito breeding, and circulating virus serotypes. The patient catchment area does not have any proper drainage system, no decontamination of stagnant water from larvae and poor sanitary practices, thus high endemicity of dengue fever. The male predominance (male-to-female ratio of 3:2) could be attributed to greater outdoor exposure among men, increasing their likelihood of mosquito bites. The median length of stay in this study was significantly longer in severe dengue patients, which was not observed in the study in North India. [7,8]

As per WHO, the neutrophil percentage of total WBCs typically ranges from 50% to 70%. In sever dengue (SD), the virus activates neutrophils, triggering the release of myeloperoxidase and the formation of neutrophil extracellular traps (NETs). In our study we found significant association of Neutrophil count with SD. Among a total of 108 cases of DWWS, DNWS, and SD, all had raised CRP levels, indicating a significant association of raised CRP with DWWS, DNWS, and SD. Rising PCV, low Hb% and platelet count suggests plasma leakage and hemoconcentration, these parameters are found to be strongly associated with SD. Similar findings are also seen in other studies from eastern and south India. [9-15]

Most participants had normal serum bilirubin with mild to significant elevations in SD indicating liver involvement. ALT and AST were high manifold reflecting significant liver damage in severe cases. ALP levels were normal in 88.89% of participants, with mild elevations in SD indicating potential hepatobiliary involvement. Most participants had low to normal albumin (55.26%), though

some SD cases showed deviations indicating potential liver stress or chronic inflammation. This findings were similar to other Indian studies. [16-18]

The virus causes "plasma leakage," leading to fluid leakage from blood vessels into the pleural cavity. Gallbladder wall edema in dengue occurs due to increased vascular permeability, causing fluid leakage into surrounding tissues, including the gallbladder, leading to thickening on imaging. Fluid leakage could be detected radiologically earlier than PCV rise. [19-21]

Limitation: This study was conducted in a tertiary care center, where referral bias could not be avoided. Additionally, antibody titers were not quantitatively measured.

Conclusion: This study suggests that certain clinical and laboratory parameters that can be used to assess the severity of dengue fever are neutrophil count, PCV, platelet count, hemoglobin, serum alkaline phosphatase, AST, ALT, albumin, bilirubin, CRP, tourniquet test, chest X-ray – pleural effusion, ultrasonography – gallbladder wall edema and hepatomegaly. These will help us to identify the proneness for progression to dengue with warning sign and severe dengue in case of acute fever caused by dengue, thus help clinicians to reduce dengue-related morbidity and mortality. Additionally, the creation and implementation of dengue control and management recommendations will benefit from our research.

Conflict of interest: None

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