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A Study of Hematological Profile in NS1 Antigen Positive Dengue Fever Patients at Tertiary Care Center

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ABSTRACT

Dengue fever continues to be a significant public health problem in India. It is a common viral disease, especially in tropical regions. The incidence increases immediately after the monsoon period, coinciding with mosquito breeding in stagnant water. The disease has a varied clinical presentation characterized by sudden onset fever lasting 3-5 days, intense headache, myalgia, retro-orbital pain, anorexia, gastrointestinal disturbances and rash. Complete Blood Count (CBC) values typically show thrombocytopenia as the predominant finding. Most thrombocytopenic patients also exhibit leucopenia with lymphocytosis, which affects the disease prognosis in the initial days of NS1 antigen-positive Dengue fever patients. To evaluate hematological parameters in NS1 antigen positive patients with clinical manifestations of dengue fever at a tertiary care hospital. This study was conducted at the Mediciti Institute Of Medical Sciences in Ghanpur, Telangana state, from January 2023 to March 2024. A total of 250 patients were admitted with fever during this period, with 100 cases testing positive for the NS1 Antigen. The majority of dengue infection cases were observed in the 18-30 years age group (56%). Thrombocytopenia was present in 84% of patients, while 38% exhibited leucopenia and 16% had hematocrit values exceeding 45%. Platelet parameters among those with thrombocytopenia indicated elevated mean platelet volume (MPV) and platelet distribution width (PDW). In our study, we observed that as thrombocytopenia worsens in dengue infection, there is a concurrent increase in mean platelet volume (MPV) and platelet distribution width (PDW). A decrease in plateletcrit (PCT) also signifies the severity of the infection. Although we did not evaluate immature platelet fraction (IPF) levels, assessing these could potentially assist clinicians in refining treatment strategies. Further daily evaluations and larger studies are necessary to validate these findings.

OPEN ACCESS

Key Words

Dengue fever, thrombocytopenia, hematological profile, mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR)

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INTRODUCTION

Dengue is a significant viral disease, particularly prevalent in tropical regions. The World Health Organization (WHO) reports that nearly 50 million people contract dengue annually, with roughly half of the global population residing in countries where dengue is endemic[1]. Dengue fever and dengue hemorrhagic fever has emerged as a global public health problem in recent decades and it continues to be one of the important public health problems in India and is usually an infectious condition caused by an arthropod borne virus[2].

The clinical presentation of Dengue fever (DF) typically manifests as an acute febrile viral illness characterized by symptoms such as headaches, bone and joint pains, muscular aches, rash and a decrease in white blood cell count (leucopenia). Diagnosis relies on a combination of clinical observations and laboratory findings. Non-specific tests including blood counts, platelet counts, prothrombin time (PT) and liver function tests are complemented by specific tests such as viral isolation and serology for antibody detection.

Dengue infection spans a spectrum from mild undifferentiated fever and Dengue Fever (DF) to more severe manifestations such as Dengue Hemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS) and expanded Dengue Syndrome. The most notable hematological changes include thrombocytopenia and leukopenia, often accompanied by lymphocytosis with reactive lymphocytes As the disease progresses, there is a significant rise in hematocrit levels, sometimes increasing by up to 20% from the patient's baseline[5,6]. Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) are significant causes of mortality due to abnormalities in hemostasis, thrombopathy and coagulation disturbances.

Advancements in hematology automation have enabled researchers to measure additional platelet parameters alongside platelet count. These parameters, such as mean platelet volume (MPV) and platelet distribution width (PDW), offer valuable insights into platelet morphology and maturity. Researchers are increasingly investigating these platelet indices across various clinical conditions.

Establishing well-defined and precise laboratory reference ranges for these parameters is crucial for accurate result interpretation and can potentially prevent unnecessary and costly follow-up tests. However, there remains a lack of sufficient data on platelet parameters specifically in dengue patients with thrombocytopenia[7].

In this study, we aimed to assess the hematological profile of seropositive (NS1 antigen) patients with dengue fever and investigate the role of specific hematological parameters-Hematocrit, total leukocyte count, Neutrophil lymphocyte ratio and platelet indices-in cases of laboratory-confirmed dengue associated with thrombocytopenia.

These platelet indices serve as surrogate markers for predicting the risk of bleeding and provide insights into whether ongoing platelet destruction necessitates imminent platelet transfusion. They also offer indications of bone marrow responsiveness, thereby helping to avoid unnecessary platelet transfusions and their associated side effects.

MATERIALS AND METHODS

Study Design: Hospital based Retrospective study.

Study Duration: 1 year 3 months from January 2023 to March 2024.

Sample Size: All the cases during the study period which meet the inclusion criteria.

Inclusion Criteria:

- All the patients, having serologically confirmed dengue (NS1 antigen positive) fever.
- Patients above the age of 18 years admitted in our hospital.
- Informed consent was taken from these cases.

Exclusion Criteria:

- Patients with history of known, other haematological disorder.
- Patients with concomitant infection.
- Patients below the age of 18 years.
- NS1 antigen negative cases were excluded from the study.

Methodology: A total of 250 cases presented to the hospital with suspected dengue fever during the study period (Jan 2023-March 2024), amongst them 100 cases which were positive for NS1 were included in the study irrespective of prior senitisation with dengue. Fever cases with NS1 negative were not considered. NS1 antigen positive dengue cases were correlated with clinical features, hematological parameters.

Patient blood sample collected in EDTA vacutainer and sample was processed within 2 hours by MINDRAY BC 5150 automated 5 part cell counter, peripheral blood smears were made and stained with Leishman stain.

RESULTS AND DISCUSSIONS

All the patients who were above the age of 18 years irrespective of gender, having fever and serologically (NS1 antigen) positive dengue fever were included in this study.

Table 1: Age Distribution of all Cases.

Age	No. of cases	Percentage(%)
18-30	56	56
31-40	24	24
41-50	8	8
51-60	12	12

Majority of the patients were in the age group of 18-30 years (56%).

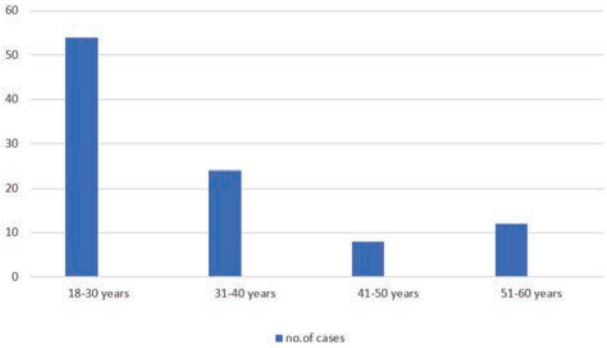

Fig 1: Age Distribution

There were 57 males (57 %) and 43 females (43%); with slight male preponderance with M:F ratio of 1.3:1.

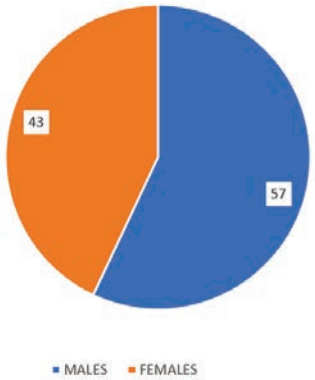

Fig 2: Gender Distribution

Table 2: Distribution of Clinical Features

Clinical features	No of cases	Percentage
Fever	100	100%
Body pains	69	69%
Lethargy	46	46%
Retroorbital pain	22	22%
GI symptoms	8	8%
Rash	6	6%

Fever was the presenting complaint in every case (100%), often accompanied by body aches (69 cases). The least frequent presentation was fever accompanied by a rash, noted in 6 cases.

Clinical Categorization: Out of 250 cases presenting with fever, 100 tested positive for NS1 dengue. Among these, 97 cases (97%) were diagnosed with dengue fever, while only 3 cases were identified as dengue hemorrhagic fever.

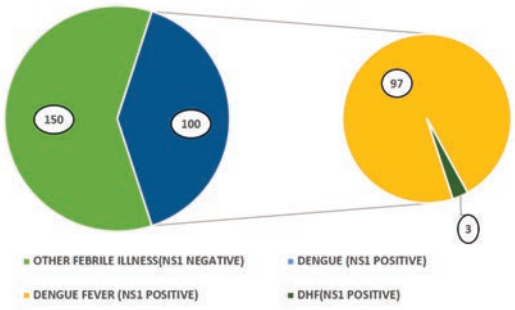

Fig 3: Clinical Categorisation(Number of Cases)

Table 3: Distribution of Cases on the Basis of Hemoglobin and Hematocrit Level.

Hemoglobin level			Hematocrit level		
Hb(gm/dl)	No of cases	Percentage (%)	HCT(%)	No of cases	Percentage (%)
7-9	4	4	20-29.9	8	8
9.1-12	30	30	30-39.9	56	56
12.1-15	48	48	40-49.9	34	34
>15	18	18	>50	2	2
Total	100	100%	Total	100	100%

In our study, the majority of patients, 66 cases (66%), had hemoglobin levels above 12 gm/dl, followed by 30 cases (30%) with Hb levels ranging from 9.1-12 gm/dl. Only 4 cases (4%) had Hb levels below 9 gm/dl. The mean hemoglobin level in our study group was 12.9 gm/dl.

Regarding hematocrit levels, most patients, 56 cases (56%), had levels ranging from 30%-39.9%, followed by 34 cases (34%) with Hct levels between 40% and 49.9%. A smaller number of cases, 8 (8%), had hematocrit levels ranging from 20%-29.9%. The mean hematocrit level in our study was 38.8%.

Table 4 :Distribution of Cases on the Basis of Total Leucocyte Count

TLC	No of cases	Percentage(%)
<4000	38	38
4000-11000	58	58
>11000	4	4

Maximum number of patients i.e 58%(58 cases) had TLC within normal limits, followed by 38% having leucopenia and 4 cases showed mild leucocytosis

Table 5:Distribution of Differential WBC Parameters

Differential count	Leucopenia	Normal WBC count	Leucocytosis
Lymphocytosis	20/38(60.52%)	32/58(55%)	1/4 (25%)
Neutrophilia	8/38(21.05%)	8/58(14.28%)	1/4 (25%)
Within normal limits	10/38(26.3%)	18/58(31.04%)	2/4(50%)

Maximum number of patients i.e. 58 cases (58 %) had TLC within normal limit, followed by 38cases (38%) having leucopenia and minimum were 4 cases (4 %) having leucocytosis.

Table-6: Distribution of Cases Based on Platelet Count

Platelet Count	No of Cases	Percentage(%)
<20000	06	6
20000-50000	24	24
50000-100000	28	28
1lac-1.5lac	26	26
>1.5lacs	16	16

Table 7: Mean Platelet Volume (MPV), Plateletcrit (PCT) and Platelet Distribution Width (PDW) in Thrombocytopenic and Non-Thrombocytopenic Patients (categorization based on analyser)

	No of cases	Hct	Platelet count	MPV	PDW	PCT	P-LCR
Thrombocytopenia	84	38.63	0.746 (SD+0.42)	10.32 (SD+2.57)	17.52 (SD +3.587)	0.28 (SD +0.23)	33.14 (SD +9.75)
Non thrombocytopenia	16	36.58	2.453 (SD +0.39)	8.95 (SD+0.45)	14.58 (SD +2.316)	0.52 (SD+0.23)	23.27 (SD +6.29)
P value		0.40	<0.0001	0.0024	0.0314	0.010	0.0085

In the present study out of 100 cases of dengue fever, 84 (84%) cases had thrombocytopenia and 6% cases had severe thrombocytopenia (<20,000/cumm).

Our study, conducted at the Department of Pathology in our tertiary care center, focused on evaluating the hematological abnormalities in patients diagnosed with dengue fever based on NS1 antigen positivity. This research builds upon prior work by Joshi[8], who also investigated NS1 antigen patterns in dengue fever patients.

In our study, the largest proportion of participants (56%) fell within the 18-30 years age group(Table-1). This demographic trend likely reflects the high representation of working individuals, construction site laborers and travelers in our sample. The habitats conducive to Aedes aegypti breeding include domestic containers, stagnant water, ornamental containers, and roof gutters. These findings align with previous studies conducted by Shamsunder Khatroth[9], Yashaswini[10], Mukherjee[11] and PR Relwani[12], indicating consistency in the demographic distribution and mosquito breeding environments observed across different studies.

In our study, the gender distribution showed that 57% of participants were male, while 43% were female, resulting in a male-to-female ratio of 1.32:1(Figure-2). This skew is attributed to the higher representation of males in the working population, who are more exposed to mosquito bites during daytime activities. These findings are consistent with studies conducted by Mukherjee S *et al.,* PR, Relwani *et al* and Ahmed[11,12,13] which also reported similar gender distribution patterns in dengue fever cases.

In our study, all patients (100%) presented with fever, consistent with findings reported by Md Yousuf Khan[14]. The typical fever duration of 2-7 days, as defined by WHO guidelines, was observed in 68% of cases. Severe body ache, a prominent symptom in dengue fever, was reported by 69% of patients in our study. However, retro-orbital pain, often considered a hallmark of dengue fever, was not prominently observed (Table-2).

Other common clinical features included chills and rigor, vomiting and nausea, headache, melena, joint pain, abdominal pain and rashes, aligning closely with findings from various studies conducted across different regions of India. Fever was universally reported as the primary complaint among all 100 cases, consistent with observations by Shradha Khatri[7]. In our present study, hemoglobin (Hb) levels varied widely, ranging from 7 gm% to greater than 15 gm%. Specifically, 48% of cases exhibited Hb levels between 12.1 and 15 gm%, followed by 30% with Hb levels between 9.1 and 12 gm% and 18% with Hb levels exceeding 15 gm%. A smaller percentage (4%) had Hb levels ranging from 7 to 9 gm%.(Table-3). These findings contrast with those reported by Meena[16], where Hb levels ranged from 7.5-17.5 g/dl, with a mean Hb value of 12.62 g/dl. They noted that Hb levels above 15 gm% were observed in 6% of their cases.

In our current study, 56% of cases presented with a hematocrit of 30-39.9%, while 34% had a hematocrit between 40-49.9%. A smaller proportion (2%) showed elevated hematocrit levels (>50%) upon presentation. The majority of patients exhibited hemoglobin levels ranging from 9.1-15 gm/dl alongside hematocrit levels spanning 30-49.9%(Table-3). Similar findings were reported by Shamsunder Khatroth 9 and Meena[16]. These studies also observed hemoconcentration due to plasma leakage, resulting in increased concentrations of red blood cells and other components, thereby elevating hematocrit levels. Joshi[8] study on the hematocrit spectrum in dengue reported a range of 20.8-59.6%, with an average hematocrit of 40.2%, which is comparable to our findings (mean Hct- 38.3%).

In our present study, leukopenia was observed in 38% of cases(Table-5). Ahmed et al13reported a similar incidence of leukopenia at 43% in their study. Leukopenia typically results from viral replication within white blood cells, particularly monocytes and lymphocytes, leading to a decrease in circulating white blood cell counts. Prathyusha[17], in their study, demonstrated that as leukopenia severity increases, there is a higher incidence of hemorrhagic manifestations. However, our study did not find a significant association between leukopenia and hemorrhagic manifestations. Similar findings were reported by Md Yousuf Khan[14].

In our current study, a significant number of cases with leukopenia exhibited reactive atypical lymphocytes on peripheral blood smear. These lymphocytes often displayed characteristics such as dark basophilic cytoplasm and large nuclei, while some exhibited a plasmacytoid morphology. Similar findings were reported in studies conducted by Viswanath[20], Kadadavar S S *et al* and Choudhary[21,22].

In our current study, the majority of patients (84%) demonstrated thrombocytopenia. Among those affected, 16% had counts exceeding 150,000/cumm, 26% had platelet counts between 100,000 and

150,000/cumm, 24% exhibited thrombocytopenia with platelet counts ranging from 20,000 to 50,000/cumm, and 6% had thrombocytopenia with counts below 20,000/cumm (Table 6). These findings are consistent with those reported by Shamsunder Khatroth and Yashaswini[9,10].

Thrombocytopenia in dengue fever is primarily caused by direct viral effects on bone marrow, leading to decreased platelet production. Additionally, the immune system, particularly through antibody responses, contributes to increased platelet destruction.

Platelet Indices: Mean Platelet Volume (MPV) ,Platelet Distribution Width (PDW) and Plateletcrit.

In our study, we categorized cases based on platelet count assessed by automated analyzer into thrombocytopenic and non-thrombocytopenic groups(Table-7). The normal range for mean platelet volume (MPV) is typically between 8.6 and 15.5 fL. We found that the mean MPV in thrombocytopenic patients (10.32 Fl±2.578) was significantly higher compared to non-thrombocytopenic patients (8.95 fL ± 0.39459) (P=0.0024). Similar findings were also noted by Aashna[18] with mean MPV in thrombocytopenic patients [10.36 (±1.96)] was found to be significantly higher than in non-thrombocytopenic patients [9.61 (±1.39)] (P=0.002).

In our study, the normal range for platelet distribution width (PDW) is typically between 8.3% and 25%. We observed that the mean PDW in thrombocytopenic patients (17.52%±3.58) was significantly higher compared to non-thrombocytopenic patients (14.58% ±2.316) (P=0.0314). Additionally, the mean PDW in thrombocytopenic patients(17.94%±0.98) was found to be significantly higher than in non-thrombocytopenic patients (16.41%±0.82) (P=0.002). The normal value of PCT is in between 0.22% and 0.32%.

In the present study thrombocytopaenia patients have low PCT as the baseline value and the mean PCT was 0.16%±0.1 had a statistically significant association (P=0.010) [Table]. Low plateletcrit was also observed by Asha *et al* and Shradha Khatri[19,7] in their studies.

In our study, the normal range for platelet-large cell ratio (P-LCR) is typically between 15% and 35%. We found that 32% of patients had elevated P-LCR values, 66% had normal P-LCR values and 2% had values below the baseline. The mean P-LCR value was 31.5%±9.9%. Patients with high P-LCR values were significantly associated with the need for platelet transfusion (P=0.0085). This association was particularly notable in patients with thrombocytopenia requiring transfusion, and the findings were statistically significant [Table]. Similar results were reported by Asha[19].

CONCLUSION

In our present study, we found no significant correlation between thrombocytopenia and hemorrhagic manifestations, contradicting findings from previous literature. Our research also identified leukopenia with reactive lymphocytes early in the disease., however, we observed no significant correlation with the risk of complications, regardless of previous dengue fever history. It's important to note that bleeding manifestations are not solely attributed to thrombocytopenia., altered coagulation parameters and platelet dysfunction also play significant roles in this regard. Additional platelet indices such as Mean Platelet Volume (MPV), Plateletcrit and Platelet Distribution Width (PDW) provided by analyzers can provide insights into the pathogenesis of altered platelet counts, particularly in cases of thrombocytopenia.

Platelet transfusion is not universally necessary in all cases of thrombocytopenia., decisions should be tailored to the patient's condition. Assessing additional hematological parameters like immature platelet fraction (IPF) levels can aid clinicians in treatment strategies. Elevated IPF levels may indicate disease progression, prompting closer monitoring or aggressive treatments. A decrease in IPF suggests bone marrow recovery and increased mature platelet production, showing a positive treatment response. Further daily evaluations and larger studies are needed for confirmation.

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