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Original Research Article

A study of relationship between various platelet indices and outcome of dengue fever in pediatric patients

Roopa Mangshetty*, Apurva A. B., Shweta Harwal

Department of Pediatrics, M. R. Medical College, Kalaburagi, Karnataka, India

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***Correspondence:**
Dr. Roopa Mangshetty,
E-mail: rmangshetty@gmail.com

ABSTRACT

Background: The study analyzed clinical characteristics and platelet indices in 200 children (1 month to 15 years) diagnosed with dengue fever, admitted to affiliated hospitals. It aimed to explore the relationship between platelet indices and disease severity in pediatric patients of teaching hospitals affiliated with MRMC College with a confirmed diagnosis of dengue fever.
Methods: In this study, the majority of patients were aged (10-15) years, with a small percentage (3.5%) being infants. Females accounted for 50% of the cases. Fever was the most common symptom, followed by headache, abdominal pain, and myalgia. Rash occurred in (14.5%) of cases. Among 200 cases, 80 exhibited warning signs, with varying positivity for NS1 and IgM. All patients required fluid therapy, and (77.5%) needed ICU care. Platelet count and Plateletcrit decreased initially but improved later, while PDW, MPV, and PLCR increased and then decreased. NS1-positive cases had lower platelet count and Plateletcrit but higher PLCR and MPV compared to IgM-positive cases.
Results: The study found that lower platelet count and Plateletcrit, as well as higher mean platelet volume, were associated with more severe disease outcomes, including longer hospital stays, increased intensive care unit care, and higher fluid therapy requirements. However, there was no significant correlation between other platelet indices (PLCR and PDW) and disease severity indicators.
Conclusions: In conclusion, this study provided valuable insights into the clinical features and platelet indices of patients with dengue fever. Understanding the relationship between these indices and disease severity can help in predicting the progression of the illness and improving patient management strategies.

Keywords: Platelet indices, Dengue fever, Pediatric patients

INTRODUCTION

Dengue is a tropical viral disease caused by dengue virus (DEN-1, DEN2, DEN-3, DEN-4). They are arbovirus belonging to the genus flavivirus of the family Flaviviridae. Mode of transmission is through the bite of Aedes aegypti mosquitoe.[1,2] Dengue fever (DF) and its severe forms dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) have become major international public health concerns. Over the past three decades, there has been a dramatic global increase in the frequency of dengue fever (DF), DHF and DSS and their epidemics, with a concomitant increase in disease incidence. There is no specific treatment for dengue, but appropriate medical care frequently saves the lives of patients with the more serious dengue hemorrhagic fever. The most effective way to prevent dengue virus transmission is to combat the disease-carrying mosquitoes. Dengue should be suspected when a high fever (40°C/104°F) is accompanied by 2 of

the following symptoms during the febrile phase (2-7 days): severe headache, Retro-orbital pain, muscle and joint pains, nausea, vomiting, swollen glands, Rash. Pathogenesis: Children acquiring sequential dengue infections have enhancing antibodies is the strongest risk factor for development of severe disease Absence of cross-reactive neutralizing antibodies is another factor. When dengue virus immune complexes attach to macrophage fc receptors, a signal is sent that suppresses innate immunity resulting in enhanced viral production During acute stage of dengue infection, there is rapid activation of complement system. These complement factors, virus itself or NS1 may interact with endothelial cells and platelets to produced increased vascular permeability. Blood clotting and fibrinolytic systems are activated and factor XII is depressed. Mild degree of DIC, liver damage and thrombocytopenia may operate synergistically. Capillary damage allows fluid, electrolytes, small proteins and in some RBCs to leak into extravascular space. There may be internal redistribution of fluid, together with deficits caused by fasting, thirsting and vomiting, hemoconcentration, hypovolemia, increased cardiac output, tissue hypoxia, metabolic acidosis, hyponatremia. Rare instances death may occur as result of GI/ intracranial haemorrhage.[3]

Diagnosis

The infection is detected by demonstrating the dengue antigens, dengue specific IgM/IgG antibodies or by isolating Non-Structural Protein 1 (NS1). Few things that are worth mentioning**:** Any form of platelet activation causes morphological changes in the platelet, resulting in pseudopodia formation and associated structural changes in the platelet. This may be reflected in the platelet distribution width (PDW).[4,5,6] Platelet indices like MPV, PDW and P-LCR have been investigated as prospective platelet activation indicators[7] Platelet volume, a marker of platelet function and activity is obtained as mean platelet volume. MPV is a useful independent predictor of bleeding. It is surrogate indicator of bone marrow activity. Correlation of parameters like platelet count and MPV with bleeding and severity of the disease can be a predictor of disease outcome.[8] Plateletcrit is a measurement of total platelet mass. Plateletcrit is useful for detecting platelet quantitative abnormalities. PCT is the volume occupied by platelets in the blood as a percentage and calculated by the formula;

$$PCT = platelet\ count \times MPV/10{,}000.$$

The normal range for PCT is 0.22- 0.24%.[9-12]

Objectives

Objectives of current study were to study the clinical features of patients with dengue illness and to study the relationship between various platelet indices and morbidity parameters of dengue fever.

METHODS

Prospective observational study conducted at: Department of pediatrics Basaveshwar teaching and general hospital and Sangameshwar teaching and general hospital for a period of 18 months from 1 March 2021 to 31 August 2022.

Sample size and sampling procedure

Sample size was 200 and Simple random sampling technique was used.

Inclusion criteria

Patient tested positive for Dengue IgM or IgG, NS1 and Patients of age group between 1 month to 15 years were included.

Exclusion criteria

Patients with proven causes of thrombocytopenia (TCP) were excluded.

Procedure

In the study 200 subjects with dengue were included. Institutional ethical clearance was obtained prior to the start of study and Informed consent was obtained from all the parents prior to the recruitment and Assent was obtained in children aged >14 years. Data was collected using structured questionnaire consisting of demographic details, clinical profile, anthropometry profile and laboratory profile. All the children who participated in the study underwent following investigation under standard protocols: complete blood profile, urine routine, hematocrit, PDW, P-LCR. Dengue serology NS1, IgM and IgG. Children were followed up for Outcome such as duration of ICU stay, Hospital stay and other morbidity.

Statistical analysis

Data was analyzed using IBMSPSS 20.0 version software. For qualitative data analysis Chi Square Test was applied. For quantitative data analysis T test and Anova Test were applied, p value <0.05, was considered as statistically significant.

RESULTS

In the study 200 children positive for Dengue were included in the study. It was observed that 24.5% were in the age group 2-5 years, 36% of subjects were in the age group 6-10 years and 30.5% were in the age group 11-15 years. 50.5% were males and 49.5% were females. The most common clinical feature observed in the study was fever, which was present in all cases (100%).

Table 1: Profile of children with dengue.

Parameters	Aspect	N	%
Age distribution (years)	6-10	72	36
	11-15	61	30.5
	2-5	49	24.5
Gender distribution	Males	101	50.5
	Females	99	49.5
Clinical features	Fever	200	100
	Headache	80	40
	Pain abdomen	62	31
	Myalgia	49	24.5
	Rash	29	14.5
Warning signs	Present	80	40
	Not present	120	60
Laboratory test results	NS1 positive	91	45.5
	IgM positive	97	48.5
	Combined NS1 and IgM positive	12	6

Table 2: Distribution of Platelet Counts (Lakh) on various days of follow-up.

Parameter	Time	N	Minimum	Maximum	Mean	SD
Platelets	Day 1	194	16000	90000.00	74912	6998.24
	Day 2	174	23000	84000.00	70845	6378.30
	Day 3	126	21000	44000.00	59664	4776.73
	Day 4	87	26000	93000.00	40589	12537.27
	Day 5	43	16000	650000	35540	7286.6
	Day 6	15	22000	254000	71000	12800
	Day 7	6	46000	247000	98000	5980
	Day 8	4	65000	215000	159000	6300

Table 3: Comparison of lab parameters with serology.

Parameter	NS1+ve Cases	IgM+ve Cases	IgM+ve and NS1+ve Cases
Mean platelet count	0.92	1.58	1.18
Mean plateletcrit	0.10	0.17	0.11
Mean PDW	15.93	15.97	15.95
Mean P-LCR	32.12	30.82	31.19
Mean MPV	10.14	9.93	9.82

Table 4: Relationship of morbidity parameters with platelet count.

Parameters	Platelet count (Lakh)						P value
	Low <1.5		Normal (1.5-4)		High (>4.01)		
	Mean	SD	Mean	SD	Mean	SD	
Age	8.41	4.00	8.20	4.43	4.00	2.83	0.322
Fluid therapy	2.78	1.34	1.90	1.20	1.00	0.00	0.001
Hospital stays	4.28	2.24	3.63	1.52	2.00	0.00	0.043
ICU care	**N**	**%**	**N**	**%**	**N**	**%**	
No	93	72.1	56	88.9	2	100.0	0.024
Yes	36	27.9	7	11.1	0	0.0	

Other common features were: Headache (40%), Pain Abdomen (31%), Myalgia (24.5%) and Rash (14.5%). Warning Signs: Out of the 200 cases, 40% (80 cases) had warning signs, while 60% (120 cases) did not have any warning signs. The laboratory test showed that NS1 Positive: 91 cases (45.5%), IgM Positive: 97 cases (48.5%) and Combined NS1 and IgM Positive: 12 cases (6%) (Table 1). In the present study mean platelet count on day 1 was 74912±6998.24, on day 2, day 3, day 4 and day 5 there was decrease in Platelet count and from Day 6 onwards there was increase in platelet count and on day 8 mean platelet count was 159000±6300.

Table 5: Relationship of morbidity parameters vs. plateletcrit.

Parameters	Plateletcrit (%)						P value
	Low <0.108		Normal (0.108-0.282)		High (>0.282)		
	Mean	SD	Mean	SD	Mean	SD	
Age	8.30	4.090	8.69	4.099	5.60	4.061	0.079
Fluid therapy	3.04	1.309	1.97	1.121	1.69	1.316	0.000
Hospital stays	4.57	2.123	3.58	1.859	3.46	1.613	0.002
ICU care	**N**	**%**	**N**	**%**	**N**	**%**	
No	61	64.2	83	90.2	11	84.6	<0.001
Yes	34	35.8	9	9.8	2	15.4	

Similar observation was made for plateletcrit i.e., it decreased from day 1 to day 5 and later increased from day 6 onwards (Figure 1).

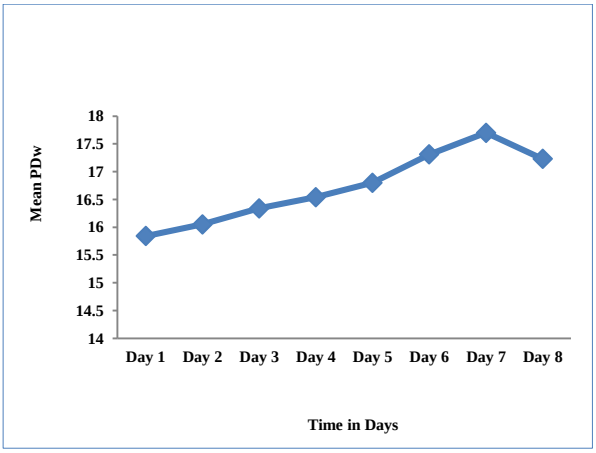

Figure 1: Distribution of PDW.

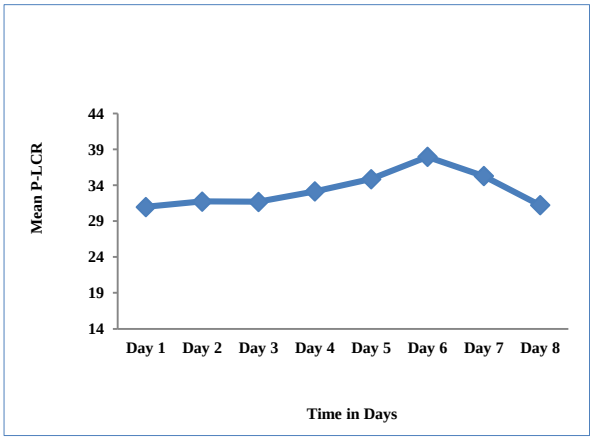

Figure 2: Distribution of P-LCR (%).

Mean PDW and P-LCR increased from Day 1 till Day 6 and Day 7 respectively and later it started decreasing (Figure 2, Figure 3). The mean platelet count was lowest (0.92) in NS1 positive patients. Mean PC was 1.58 in IgM positive cases. And 1.18 in IgM+ve and NS1+ve cases. Mean Plateletcrit was also found to be lowest (0.10) in NS1. it was 0.17 and 0.11 in IgM+ve and NS1+ve cases respectively. The mean PDW was 15.93 in NS1+ve cases, 15.97 in IgM+ve cases and 15.95 in IgM+ve and NS1+ve cases. The mean P-LCR was 32.12 in NS1+ve cases, 30.82 in IgM+ve cases and 31.19 in IgM+ve and NS1+ve cases and mean MPV was 10.14 in NS1+ve cases, 9.93 in IgM+ve cases and 9.82 in IgM+veand NS1+ve cases (Table 3). In this study population 45 cases required ICU care and 155 did not require ICU care.

The mean duration of fluid therapy was 2.78+1.34 days, 1.90+1.20 days and 1.00+0.00 days in cases with Platelet count of <1.5 Lakh, 1.5-4.0 lakh and >4.0 lakh respectively. The mean duration of hospital stay was 4.28 +2.24 days, 3.63+1.52 days and 2.00+0.00 days in cases with Platelet count of <1.5 Lakh, 1.5-4.0 Lakh and >4.0 Lakh respectively. 27.9% cases with a platelet count <1.5 Lakh required ICU stay, whereas only 11.1% and 0% cases with a mean Platelet count of 1.5-4.0 Lakh and >4.0 Lakh respectively required ICU stay. There was a significant association between the platelet count and all three morbidity parameters with a p value <0.05.

The mean duration of fluid therapy was 3.04±1.309 days, 1.97±1.121 days and 1.69±1.316 in cases with plateletcrit <0.108, 0.108 to 0.282, and >0.282 respectively. The mean duration of hospital stay was 4.57±2.123 days, 3.58±1.859 days and 3.46+ 1.613 in cases with plateletcrit <0.108, 0.108 to 0.282, and >0.282 respectively. 35.8% cases with a low PCT of <0.108 required ICU care. Whereas 9.8% and 15.4% cases with a mean PCT of 0.108 to 0.282, and >0.282respectively required ICU care. There was a significant association between the platelet count and all three morbidity parameters with a p value <0.05 (Table 5).

The mean duration of fluid therapy was 2.45±1.383 days and 1.80±0.837 days in cases with MPV of 6.58-12 and >12 respectively. The mean duration of hospital stay was 3.95±2.084 days, 4.00±2.236 days in cases with MPV of 6.58-12 and >12 respectively. 20.6% cases with a P-LCR 11-45 and none of them with a P-LCR >45 required ICU stay. There was a significant association between the MPV and all three morbidity parameters with a p value <0.05. The mean duration of fluid therapy was 1.95±1.08 days, 2.897±1.42 days and 3.17±1.27 in cases with IgM+ve, NS1+ve and IgM+ve and NS1+ve respectively. The mean duration of hospital stay was 3.54±2.27 days, 4.46±1.7 days and 4.75±1.42 in cases with IgM+ve, NS1+ve and IgM+veand NS1+ve cases respectively

12.4% cases with NS1+ve cases required ICU care, whereas 30.8% and 41.7% cases with IgM+ve, NS1+ve and IgM+ve and NS1+ve cases respectively required ICU care. There was a significant association between the platelet count and all three morbidity parameters with a p value <0.05.

DISCUSSION

When all study subjects (200) were evaluated, we observed that the mean age was 8.34 years+4.13. In our study all patients required fluid therapy. The mean duration of fluid therapy was 2.47+1.34 days. The mean duration of hospital stay was 4.04+2.03 days, which was similar to study conducted by Mohan et al 4.16+2.52.[13] Among 200 cases 45 cases (22.5%) required ICU care. Whereas in a study done by Mohan et al among 210 cases, 46 cases (22%) required ICU care.[13] In our study, out of 200 cases, 50.5% were males and 49.5% were females similar to Mohan et al in western Rajasthan in 2020 had slight male preponderance males 55.23% compared to females 44.76%. The majority (36%) children were under 6-10 years. Whereas 24.5% are under 2-5 yrs and 30.5% are under 11-15 yrs. Whereas a study by Khan et al found majority (46.1%) of the children belonged to the age group of 10-14 years.[14] In our study, out of 200 cases, 91(45.5%) cases were NS1 Positive, 97 (48.5%) were IgM positive and 12 (6%) were combined NS1 and IgM positive. A study done by Wayez in Aligarh in 2019 showed that out of 106 cases, 71 (66.9%) were NS1 positive; 35 cases (33.1%) were both NS1 and IgM positive.[15] In our study It was found that the Mean Platelet count dropped from day 1 to day 5, whereas it improved after that.

Study done by Jacob et al showed similar variation in platelet count which showed decrease from D1 to D2 and increase from D2 to D3 our study it was found that the mean MPV shows a gradual increase from day 1 to day 6, after which it started to fall.[16] Study done by Jacob et al showed that there is an increase in MP initially followed by decrease or normalization. In our study It was found that the mean PDW increased from day 1 to day 6 dropped thereafter. Study done by Jacob et al showed that there is a gradual decrease followed by increase.[16]

Limitations

This study was done in children and since there is no available study regarding the platelet indices and it is relation to the change in platelet trend in dengue. But the study was done in the adult and so the reference values of IPF and MPV are of adult reference range. One of the limitations of the study is that there are no reference values of platelet indices in children. This study was done at tertiary care center, which receives cases treated at other hospital or in a private clinic, because of the above treatment when the children come to our hospital even at the day two of critical phase or even after the critical phase got over and in recovery phase.

CONCLUSION

The mean platelet count and mean plateletcrit dropped from day 1 to day 5, after which it started to improve. The mean PDW, MPV and PLCR increased for the first few days after which they dropped as the patient improved. The mean platelet count and mean plateletcrit was low in NS1 positive cases, and high in IgM positive cases. The mean P-LCR and mean MPV was high in NS1 positive cases, and low in IgM positive cases. We found significant correlation of platelet count, plateletcrit and MPV with the morbidity parameters. With a low mean platelet count and plateletcrit, the duration of hospital stays, ICU care and Fluid therapy increased. With a higher MPV, the duration of hospital stays, ICU care and Fluid therapy increased. However, there was no correlation of other two platelet indices P-LCR and PDW with the morbidity parameters in our study.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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