

Significance of Platelet Parameters as a Screening Test for Dengue Fever

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Abstract

Objective: The objective of this study is to determine the role of various Platelet indices like mean platelet volume, platelet distribution width, and plateletcrit for screening of patients with dengue fever

Methodology: This retrospective observational study was conducted in the Hematology department in association with Dengue General Medical Outdoor of University of Health Sciences, The Children's Hospital Lahore from September 2021 to December 2021 after massive disease load. A total of 125 patients were included. Data was collected using a structured proforma. Samples for Complete blood count were taken on the second day of symptoms onset in EDTA tubes, and analyzed on semi- automated Caltac-A hematology analyzer. Serological tests, including the NS1 antigen test, IgM, and IgG antibodies tests were performed on the fourth day of symptoms onset for confirmation of the screened-out patients. Statistical analysis was conducted using SPSS software. The student t-test was applied and a less than 0.05 p-value was taken to indicate a significant difference.

Results: Among the 125 patients, there were 74 males (59.2%) and 51 females (40.8%). Platelet count on second day was seen below 150,000 in 89 cases (71.2%) while 36 cases (28.8%) had normal platelet count. Out of the total positive NS-1 cases reduced MPV was seen in 88 cases (83.8%), raised PDW was seen in 103 cases (98%) and 81 cases (77.2%) showed reduced plateletcrit. The student t-test revealed that MPV and PDW were significantly higher in NS-1 positive cases ($p < 0.05$), while PCT showed no significant difference ($p = 0.12$).

Conclusion: Platelet parameters MPV, PDW, and PCT show changes at very early phase of dengue fever. Therefore, they prove to be useful markers for screening out patients with dengue fever.

Keywords: Dengue fever, MPV, PDW.

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Introduction

Dengue fever (DF) is an illness that presents acutely with fever and its causative agent is an Arbovirus of the family Flaviviridae. Aedes aegypti, a daytime feeder is the vector that causes the spread of this disease among humans. DEN-1, DEN-2, DEN- 3, and DEN- 4 are the 4 distinct serotypes of the virus; with an incubation period of 4-10 days.¹ Infected individuals are the carriers and multipliers of the virus, ultimately spreading the disease to other individuals. An acute onset of fever usually limits within 3-5 days and is associated with severe headache and myalgias. Pain in the Eyes, diarrhea, and skin rash can be other manifestations of the disease.² Complications of the disease like Disseminated intravascular coagulation, thrombocytopenia, and increased vascular permeability can further lead to life-threatening complications.³ Thus, the disease process can be divided into three stages

including the febrile, critical and recovery phase.

Dengue fever is endemic in more than 100 countries all around the world. Southeast Asia and the western Pacific regions are the major infected areas with 75% of cases.⁴ It is estimated that huge number of cases with mild disease and huge number with complicated disease are witnessed in Asian countries and Pakistan is among them. It was documented in Pakistan in 1994 for the first time later resulted in huge rise in number of cases and it was well recognized in 2005.⁵ Since then, this developing country has witnessed a number of epidemics and faced lots of challenges due to the disease burden.

Platelet parameters basically include mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT). Mean platelet volume (MPV) is a marker of platelet function. When the platelet production is reduced, the newly formed ones are variable in size, thus the MPV is reduced. The association of parameters like platelet count and MPV with bleeding and severity of the disease can also predict the severity of dengue fever.⁶ Another parameter, the Platelet distribution width measure the variation in size of platelets.⁷ It also measures the events occurring with onset of platelet

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activation resulting in variation in morphology.⁸ The plateletcrit (PCT) is used to detect total mass quantitative abnormalities of platelets. An increase in plateletcrit is an indication of platelet aggregates, giant platelets, and regenerating large platelets.⁹

Thrombocytopenia, an important feature, and prognostic marker have always been used to predict the severity of dengue fever.¹⁰ A large number of studies have emphasized its usefulness in determining disease severity. Platelet parameters have recently been investigated and reported in various studies as platelet activation parameters and as prognostic markers.¹¹ However, there is minimal research work on their use in diagnosing dengue fever, which is highlighted in this article.

This study is undertaken with the aim to see the significance of latest platelet indices for early screening of dengue infection. This basic test can help to screen out patients who are very likely to have dengue fever, at a very early stage even before thrombocytopenia is evident and the antigen test is positive. This can be useful, especially during times of epidemics and endemics in regions where serological testing facilities are not available in plenty.

Methodology

Our retrospective observational study was carried out for the period of 4 months from September 2021 to December 2021 in the General Medical dengue outdoors in collaboration with Hematology department of The Children's Hospital & UCHS Lahore. This study was done after approval from the ethical committee of the hospital. 125 patients who fulfilled the Inclusion criteria were enrolled by simple random sampling technique. Cases who presented on the second day of symptoms and with symptoms and signs indicating dengue fever of any pediatric age are included. Whereas, cases with symptoms of dengue fever but also have any previously diagnosed disease that can lead to thrombocytopenia or changes in platelet indices were excluded.

The study methodology was well explained to the participants, and after the informed consent, a pre-designed proforma was filled with relevant data. EDTA samples for performing complete blood counts were collected on the second day of symptoms and these were run on semi- automated Caltac-A hematology

analyzer to obtain the complete parameters. These samples were run on the analyzer within 60 minutes after collection. Peripheral smear examination was done of the samples with platelet count $<150,000/\text{mm}^3$, to confirm thrombocytopenia. The control population was comprised of 50 patients who presented with symptoms of generalized fever but no changes in the platelet parameters. Similar tests were carried out on these patients.

The serological tests including NS1 antigen, IgG, and IgM antibodies were carried out on the fourth day of onset of symptoms to confirm the disease in the suspected cases. Statistical analysis using SPSS software was done. The student t-test was applied and a p-value of less than 0.05 was taken to indicate a significant difference.

Results

A total of 125 patients presented over a period of 4 months in our hospital dengue outdoor. Those having signs and symptoms favoring dengue fever were included after they fulfilled the inclusion criteria. There were 74 males (59.2%) and 51 females (40.8%).

Out of the patients included 32 patients (25.6%) presented with mild symptoms like weakness, body aches, and low-grade fever, 85 patients (68%) had a high-grade fever and 8 patients (6.4%) had severe life-threatening symptoms. In short, 117 patients (93.6%) were in the febrile phase while 8 patients (6.4%) were in the critical phase.

On Day two, platelets were below 150,000 in 89 cases (71.2%) while 36 cases (28.8%) showed count within normal range. Platelet count below 30,000 was noted in 8 cases (71.2%) and in 25(20%) cases had platelets in range of 30 to 100 thousand while there were 56 (44.8%) cases having count in between 100 to 150 thousand. Figure 1. It was observed that there was a positive relationship between the degree of thrombocytopenia with symptoms severity.

Platelet indices like MPV, PDW, and PCT were investigated as indicators of platelet activation. MPV was found to correlate with the severity of dengue fever. MPV was reduced and PDW was notably high in 92 (73.6%) and 107 (85.6%) patients respectively. While PCT was low in 82 cases. Serological testing consisting of NS-1

was carried out on Day 4. Serology was found positive in 105 cases. Figure 2

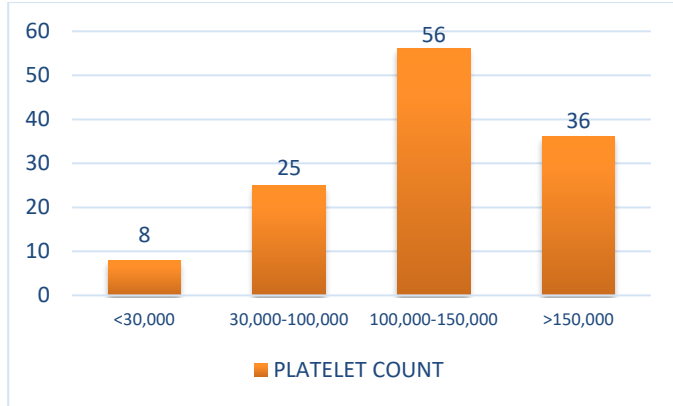


Figure 1: Distribution of Platelet Counts on 2nd day.

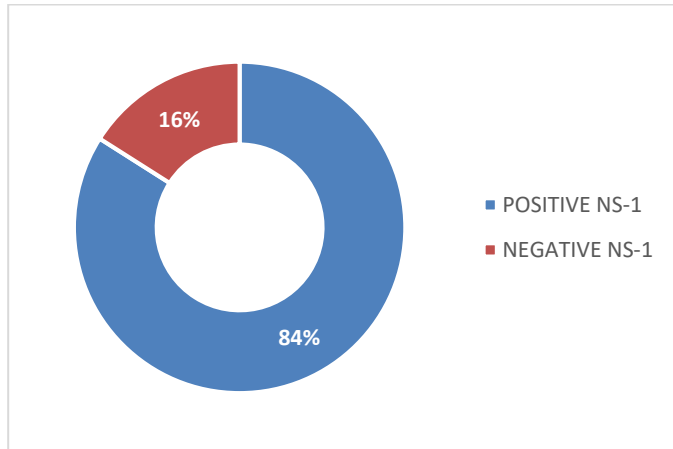


Figure 2. Serological Testing in Dengue Fever Patients.

Out of the total positive NS-1 cases, reduced MPV (mean 14.7) was reported in 88 (83.8% of positive NS-1 cases), normal MPV (mean 10.8) was seen in 11 cases (10.4%) while 6 cases 8.1(5.7%) had high MPV (mean). Table I

Mean Platelet Volume	Frequency of Positive cases	%	Mean
Reduced	88	83.8%	14.7
Normal	11	10.4%	10.8
Raised	6	5.7%	8.1

PDW was significantly raised (mean 16.8fL) in 103 cases (98%) out of the total NS-1 positive cases. Only 2 positive NS-1 patients (1.9%) had normal PDW (mean 11.5fL). Table I Plateletcrit (PCT) was reduced (mean 0.18%) in 81 positive NS-1 cases (77.2%) while 24 cases (22.8%) had normal PCT (mean 0.23%). Table II

Table II: Distribution and Mean Values of PDW & Plateletcrit in Positive NS-1 Cases.

Platelet Distribution	Frequency of Positive NS-1 Cases	(%)	Mean
Raised	103	98	16.8fL
Normal	2	1.9	11.5fL
Plateletcrit			
Reduced	81	77.2%	0.18%
Normal	24	22.8%	0.23%

Also, student t-test was applied to compare platelet parameters between Dengue NS-1 positive and NS-1 negative cases to assess their significance in identifying dengue fever as shown in Table III. The results showed that the MPV was significantly reduced in NS-1 positive cases compared to NS-1 negative cases, significant with a p-value of 0.03. This indicates that MPV could be a valuable parameter for screening dengue fever. Similarly, the PDW was significantly higher in NS-1 positive cases and significant with a p-value of 0.04. However, the Plateletcrit (PCT) did not show a significant difference between the two groups (p=0.12) This implies that PCT may not be a reliable marker for distinguishing between NS-1 positive and NS-1 negative cases.

Table III: Comparison of Platelet Parameters Between NS-1 Positive and Negative Cases.

Parameter	NS-1 Positive Cases	NS-1 Negative Cases	P-value
	Mean $\pm$ Std	Mean $\pm$ SD	
MPV	8.40 $\pm$ 0.14	7.70 $\pm$ 0.14	0.03
PDW	19.05 $\pm$ 0.21	17.65 $\pm$ 0.21	0.04
PCT	0.245 $\pm$ 0.001	0.215 $\pm$ 0.001	0.12

Discussion

Dengue fever is a viral illness with recognized global importance and has shown increasing trend over a short period. There are many publications on the management plans for this illness still there is very little data available on newer parameters to aid in the early diagnosis of this disease.

According to our study, there were 59.2% males and 40.8% females which gives the male: female ratio 1.5:1 which was very similar to the male: female in a study by Aheamad et al i.e., 1.6:1.¹²

Most of the studies conducted previously only included adult patients for example in research carried by Ukey, et al., and Cecilia, et al the patients were between 15-30 years while the uniqueness of our research is that it is conducted on the pediatric population only.^{13,14}

Out of the patients included in our study, 93.6% were in the febrile phase with low to high-grade fever and 6.4% were in the critical phase. Whereas a study conducted by Meena KC et al revealed that 84% of patients presented with symptoms of the febrile phase and 16% of patients presented with severe symptoms in the critical phase.¹⁵ This difference in the presentation can be due to the difference in age groups of the study population. A study by Sumaro conducted in the department of Child health, Cip to Mangunkusumo National Hospital, Jakarta, Indonesia demonstrated 81% of cases with thrombocytopenia. 10 years later in the same institute, a prevalence of 59% thrombocytopenia at presentation was seen. However, our study confirmed 71.2% thrombocytopenia on day 2 of the symptoms. As the day of presentation of patients is not specified in previous studies so this cannot be exactly compared.¹⁶

As well described in the previous studies that serology testing, NS-1, and IgM levels are still the diagnostic tests for the dengue virus. We performed these tests on the fourth day of symptoms which turned out positive in 84% of cases.

Platelet indices like MPV, PDW, and PCT were investigated as probable indicators of platelet activation. Mean platelet volume (MPV) is known to measure platelet function. When these are reduced due to increased destruction, the newly formed ones the variable in size. According to our study, reduced MPV (mean 14.7) was reported in 83.8% of positive NS-1 cases, normal MPV was seen in 11 cases (10.4%) while 6 cases (5.7%) had higher MPV. It was observed that MPV correlates with the severity of the infection and the platelet count. During mild to moderate thrombocytopenia, MPV is normal or reduced. While during severe thrombocytopenia MPV rapidly reduces to severe levels. This observation of a rapid reduction in MPV was also mentioned in studies by Mukker et al¹⁷ and Bashir et al¹⁸ A study by Andhura et al. 2014 also mentions similar findings. Another study done 1n 2020 in India by Ahmad Wayez also specified the reduction in MPV with reducing platelet counts as in dengue fever. It also mentioned that reduced MPV is because of megakaryocyte suppression.²²

Platelet distribution width is a surrogate marker of bone marrow activity that measures platelet anisocytosis. PDW was significantly raised in 98% of the positive cases. A negative correlation between the mean PDW and the

platelet count was found. This finding is similar to those in research by Mukker et al¹⁷ and Bashir, et al. Navya et al. 2016 observed a high PDW greater than 13 fl in 92% of cases in their study.¹⁹ As the platelets increase in the recovery phase, the PDW begins to get within the normal range. Thus, the pattern of PDW can be a predictor of low platelets which indicates dengue fever.

The student t-test compared platelet parameters between Dengue NS-1 positive and NS-1 negative cases to assess their role in identifying dengue fever. MPV was reduced and PDW was significantly higher in NS-1 positive cases, with p-values of 0.03 and 0.04, respectively, suggesting their potential as screening markers. However, PCT showed no significant difference ($p = 0.12$), indicating it may not be a reliable marker for distinguishing between the groups.

Plateletcrit measures the total platelet mass. When PCT was correlated with platelet count at presentation, a positive correlation was found between the two entities. We observed low plateletcrit in 77.2% of the positive cases which indicates that low plateletcrit may be used as a probable indicator of dengue fever.²⁰ Similar finding was mentioned by Navya et al and Mukker et al.^{17,19} Moreover, in a study by Hardeva, et al., in 2016, it was found that plateletcrit was on the lower side of the normal range in dengue fever patients.

These platelet parameters were found to be sensitive to dengue infection thus reflecting as predictive markers which can be beneficial for screening out dengue-positive patients in endemic areas.

However, certain limitations were observed, like patients with known bleeding disorders were excluded, but those with undiagnosed bleeding disorders may have created a bias in the results. Hence, further studies should be done to include individuals with varied manifestations.

Conclusion

Platelet parameters including MPV, PDW, and PCT start showing changes at very early stages of disease. Therefore, they are very helpful for detection of dengue fever at very early stage. As dengue fever is especially a disease of developing countries so these platelet parameters can be useful at times of epidemics when serological testing facilities are not available in great quantities to perform on every dengue-suspected case.

Early diagnosis and timely management can reduce the morbidity and mortality of the disease.

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