Original Research Article

Indian Journal of Emergency Medicine
Volume 6 Number 3, July–September 2020
DOI: http://dx.doi.org/10.21088/ijem.2395.311X.6320.1

Platelet Indices as a Prognostic Marker in Dengue Fever Cases and number of Days to Improvement

Mohan D Kashinkunti[1], Parvatikar Vikas B[2]

Author's Affiliation:
[1]Professor, [2]Resident, Department of General Medicine, SDM College of Medical Sciences and Hospital, Karnataka-580009, India.

Corresponding Author:
Resident Department of General Medicine, SDM College of Medical Sciences and Hospital, Karnataka -580009, India.

E-mail: drvparvatikar@gmail.com

Abstract

Background: Dengue is the most rapidly spreading mosquito-borne viral disease with four serotypes. An estimated 50-100 million cases of dengue fever (DF) and about 250,000-500,000 cases of dengue haemorrhagic fever (DHF) occur every year.In Southeast Asia, the average number of cases of DHF per year has increased from 10,000 in the 1950s to over 200,000 in the 1990s. Thus, dengue virus remains a major cause of morbidity and mortality in tropical areas. Epidemic DF was common in Asia and Pacific region throughout the twentieth century. AIMS & OBJECTIVES: To analyse Mean Platelet Volume and Platelet distribution width as the Predictors of thrombocytopenia and the speed of illness recovery among admitted cases with DF and DHF.To study the early clinical presentation for diagnosis of dengue virus infection. To study the Complications and Prognosis of the illnesses *Materials and Methods*: The Prospective observational study was done on 100 dengue positive cases during the outbreak of dengue infection over a period of 12 months, from Nov 2017 to October 2018. The platelet parameter like Platelet count, Mean platelet volume, Platelet distribution width were noted using BC 3000 plus Mindray Automated Haematology Analyzer and was compared with severity of disease (DF/DHF/DSS). *Results*: Relationship between platelet parameters like platelet count, MPV and PDW were made with severity of the disease (DF/DHF/DSS). No Significant difference was observed between severity of the thrombocytopenia and severity of the disease, (P value 0.080686)Dengue positive cases were associated with low MPV were 13.86% and high PDW values were 43.56%.Even though the increase in the MPV and increase in PDW indicates activation and heralds recovery of platelets, but the correlation between platelet counts and platelet indices like MPV and PDW did not show any significance in our study (p values are 0.710, 0.138 and 0.131 respectively. *Conclusion*: The study focuses the importance of platelet parameters in dengue infection. No significant difference was observed between severity of the thrombocytopenia and severity of the disease (P value 0.080686). Platelet count is thus a predictive parameter of DF/DHF/DSS. Low MPV (13fl) shows sensitivity for dengue fever thus reflecting a predictive marker for diagnosing dengue fever in endemic area.

Keywords: Dengue; Platelets; Mean Platelet Volume; Platelet Distribution width.

How to cite this article:
Mohan D Kashinkunti, Parvatikar Vikas B,Platelet Indices as a Prognostic Marker in Dengue Fever Cases and number of Days to Improvement. Indian J Emerg Med 2020;6(2):137–146

Introduction

Dengue is the most rapidly spreading mosquito-borne viral disease with four serotypes. An estimated 50-100 million cases of dengue fever (DF) and about 250,000-500,000 cases of dengue haemorrhagic fever (DHF) occur every year.[1] In Southeast Asia, the average number of cases of DHF per year has increased from 10,000 in the 1950s to over 200,000 in the 1990s. Thus, dengue virus remains a major cause of morbidity and mortality in tropical areas.[2] Epidemic DF was common in Asia and Pacific region throughout the twentieth century.[3]

India is one of the seven identified Southeast Asian countries reporting frequent outbreaks of the disease, with case fatality rates as high as 3-5%.[4] There have been several outbreaks from rural areas of Karnataka, Haryana, and Maharashtra. Dengue has a wide spectrum of presentation ranging from fever to life-threatening haemorrhage and shock, often with an unpredictable outcome. The spectrum of clinical presentation is variable in different epidemics and in different age groups.[5,6,7] Though many previous studies have reported the clinical profile in dengue patients, studies focusing on predictors of thrombocytopenia using platelet indices like Mean platelet volume(MPV) and Platelet distribution width(PDW) and length of hospital stay are scarce from India and this region. This is important considering the burden of the disease during epidemics, its impact on hospital admissions, and the requirement of platelet transfusion.

Platelet volume, a marker of platelet function and activity is measured as mean platelet volume (MPV) by haematology analysers. MPV can be used as independent predictors of bleeding. It is surrogate marker of bone marrow activity; a high MPV indicates increased Megakaryocyte activity. A low MPV indicates marrow suppression and increased risk of bleeding. Correlation of platelet count and MPV with bleeding and severity of the disease can potentially predict outcome.[8]

Dengue fever (DF) with its severe manifestations such as DHF and DSS has emerged as a major public health problem of international concern. The geographical distribution has greatly expanded over the last 30 years, because of increased potential for breeding of Aedes aegypti. This has been prompted by demographic explosion, rapid growth of urban centres with strain on public services, such as potable water and augmented by rain water harvesting in diverse types of containers resulting in multiple storage practices.

Today, Dengue ranks as the most important mosquito- borne viral disease in the world. Current estimates report that, at least 112 countries are endemic for Dengue and about 40% of the world populations (2.5-3 billion people) are at risk in tropics and sub-tropics. Annually 100 million cases of dengue fever and half a million cases of DHF occur worldwide. Early recognition and prompt initiation of treatment are vital if disease related morbidity and mortality are to be limited.[9]

The present study will be conducted among confirmed dengue NS1/IgM/IgG Positive cases in adults aged >18 years to determine to know association of mean platelet volume (MPV) and platelet distribution width (PDW) with severity, serology and treatment outcome which can be of great help in limiting morbidity and mortality associated with dengue fever and also predict the number of days to recovery, at a tertiary centre in SDMCMSH, Dharwad.

Methodology

Study Design:

A hospital based, Prospective observational study

Study Period:

One year period study from November 2017 to October2018

Method of collection of data:

All patients attending the medical services of SDM College of Medical Sciences & Hospital ,Dharwad from November 2017 to October 2018 and diagnosed to have Dengue Fever will be included in the study, data will be collected through Performa (annexure attached).

Inclusion criteria:

All the patients more than 18 years of age.

All the patients presenting with the complaints of fever (Fever >99.9 F) with thrombocytopenia. (less than 1,50,000/μL) with Dengue serology positive for NS1/IgM/IgG.

Exclusion criteria:

Patients less than 18 years of age.

Patients having afebrile thrombocytopenia.

Congenital thrombocytopenia.

Patients with suspected co-infections like malaria, leptospirosis, enteric fever will be excluded from the study.

Clinical case definition of dengue fever:

Classical dengue fever or break bone fever is an acute febrile viral disease frequently presenting with headaches, bone or joint pain, muscular pains, rash, and leukopenia caused by the Aedes mosquito infected with a dengue virus.

Clinical case definition DHF

Necessary Criteria:

Fever or recent history of acute fever.

Haemorrhagic manifestations.

Low platelet count (100,000/mm3 or less).

Elevated haematocrit (20% or more over baseline).

Low albumin.

Pleural or other effusions.

Clinical case definition of DSS

Four criteria for DHF.

Evidence of circulatory failure manifested indirectly by all of the following.

Rapid and weak pulse.

Narrow pulse pressure (B20 mm Hg) OR.

Hypotension for age.

Cold, clammy skin and altered mental status.

Frank shock is direct evidence of circulatory failure.

Routine investigations done for Febrile illness like - Complete Hemogram, Dengue NS1 and IgM and IgGTest, Malaria, Weil Felix test, Widal Test, Chest radiograph, serum creatinine & Blood urea, SGOT & SGPT, Albumin, Blood Glucose level, Viral markers.

Statistical Analysis:

Data will be analyzed by

Diagrammatic presentation.

Mean+ standard deviation.

Statistical test i.e., Student T- test and Chi Square test.

Results

Seropositive patients were followed clinically for the symptoms of DHF/DSS and were correlated with the respective platelet counts. Dengue fever (DF) cases were noted in 94 cases and dengue haemorrhagic fever (DHF) cases were noted in 7 cases. Significant difference was observed between severity of the thrombocytopenia and severity of the disease, (P value 0.080686)

The Mean Distribution of the Platelets at the time of admission to hospital was 0.926 lakh/mm^3, after 48 hours 0.858 lakh/mm^3 and at the time of the discharge was 1.306 lakh/mm^3.

The Mean of the Mean Platelet Volume (MPV) calculated at the time of the admission is 10.885 fL, during course of hospital stay after 48 hours is 11.326 fL and at the time of discharge is 11.362 fL.

The Mean of the Platelet distribution width (PDW) calculated at the time of the admission is 12.948 fL, during course of hospital stay after 48 hours is 14.038 fL and at the time of discharge is 14.251 fL

The Mean Distribution of the platelets with respect to Dengue Serology was found to be 0.883 lac/mm^3 in NS1 Reactive, 0.814 lac/mm^3in IgM Reactive and 0.846 lac/mm^3 in IgG Status. Not Much Significant difference was found between the different serotypes

The Mean Distribution of the MPV with respect to Dengue Serology was found to be 10.851 fLin NS1 Reactive, 10.782 fLin IgM Reactive and 10.965 fL in IgG Status.

The Mean Distribution of the PDW with respect to Dengue Serology was found to be 12.94%in NS1 Reactive, 12.859%in IgM Reactive and 13.263 %in IgG Status.

Among 101 dengue positive cases, low MPV (<9fl) indicating bone marrow suppression was seen in 13.86 % of the cases, of which 12.76 % were diagnosed as DF while 28.57 % were of DHF and high MPV was seen in 87.23 % were diagnosed as DF and remaining 71.43 % cases showed high MPV (>9fl) were of DHF.

A high PDW (>13fl) which indicates as useful marker for platelet activation was seen in 44% 0f cases, of which 41 cases were DF while 3 cases were DHF remaining 56.44% of cases of which 53 DF and 4 DHF showed low PDW (<13fl).

The Mean days to recovery from illness and increase in the platelet count was 4 days in 28.71 % followed by 3 days in 24.75 % and 5 days in 15.84 % participants. Majority of the participants recovered in 4-5 days of the illness with respect to platelet count improvement.

In the above table the mean of MPV during the time of admission was 10.8845 fL and at the time of discharge were 11.3617 fL and the p value shows 0.021 which is significant, concluding the rising MPV always heralds platelet recovery[10]

In the above table the mean of PDW during the

time of admission was 12.9476 fL and at the time of discharge was 14.2506 fL and the p value shows 0.011 which is significant, concluding the rising PDW indicates platelet activation[11]

Even though the increase in the Mean platelet volume and increase in Platelet distribution width indicates activation and heralds recovery of platelets, but the correlation between platelet counts and platelet indices like MPV and PDW in correlation to the number of days to recovery from illness, did not show any significance in our study (p values are 0.710, 0.138 and 0.131 respectively)

Discussion

Table 1: Platelet count with severity of disease

Platelet Count	DF	DHF	DSS	Total
<20,000	11(73.33%)	4(26.67%)	0(0%)	15(100%)
21,000 to 50,000	22(91.67%)	2(8.33%)	0(0%)	24(100%)
51,000 to 1 lakh	23(95.83%)	1(4.17%)	0(0%)	24(100%)
> 1 Lakh	38(100%)	0(0%)	0(0%)	38(100%)
Total	94(93.07%)	7(6.93)	0(0%)	101(100%)

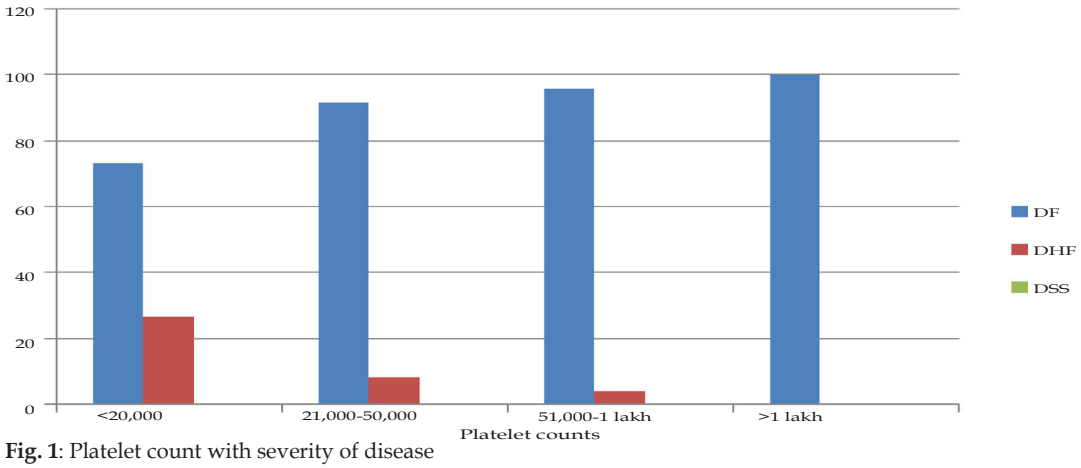

Fig. 1: Platelet count with severity of disease

Table 2: Mean Distribution of Platelets in study participants (N=101)

Mean Platelet count	Lakh
On admission	0.926
After 48 hours	0.859
At discharge	1.306

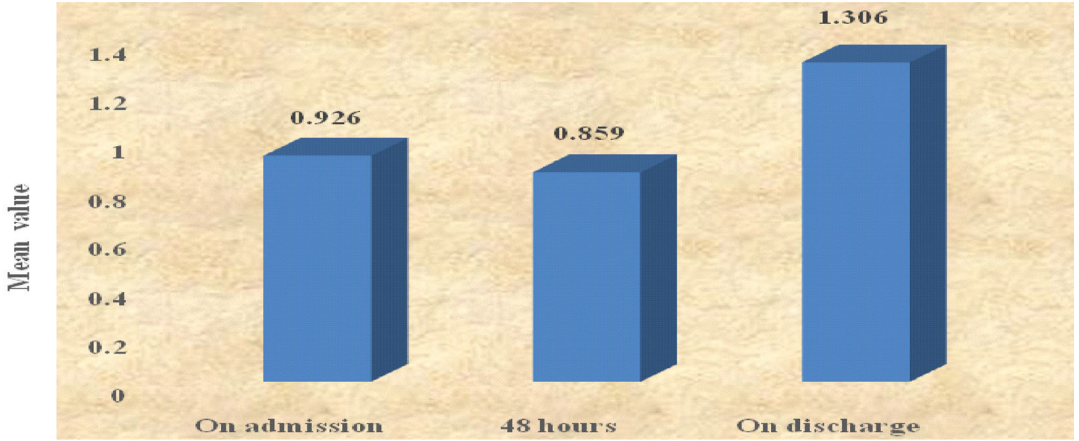

Fig. 2: Mean Distribution of Platelets in study participants (N=101)

Table 3: Mean Distribution of MPV in study participants (N=101)

Mean of MPV	fL
On admission	10.885
After 48 hours	11.326
At discharge	11.362

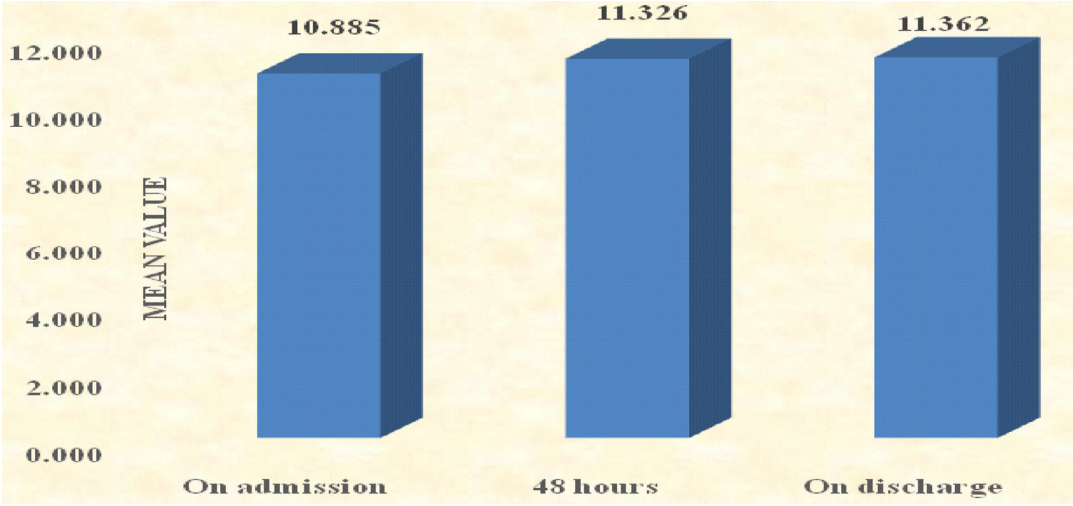

Fig. 3: Mean Distribution of MPV in study participants (N=101)

Table 4: Mean Distribution of PDW (%) in study participants (N=101)

Mean of PDW	fL
On admission	12.948
After 48 hours	14.038
At discharge	14.251

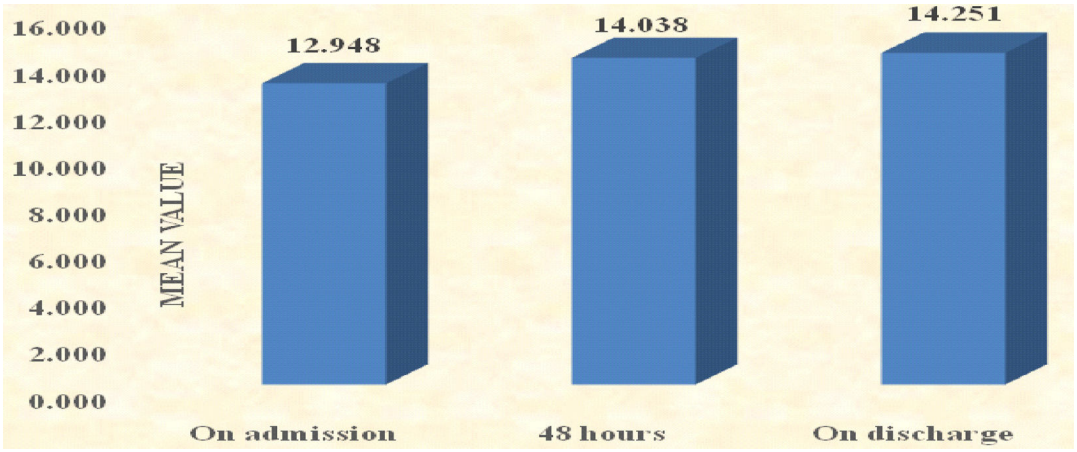

Fig. 4: Mean Distribution of MPV in study participants (N=101)

Table 5: Mean Distribution of Platelets (Lacs) in relation to Dengue serology in study participants (N=101)

	NS1	IgM	IgG
Reactive	0.883	0.814	0.846
Non-Reactive	0.991	0.955	1.077

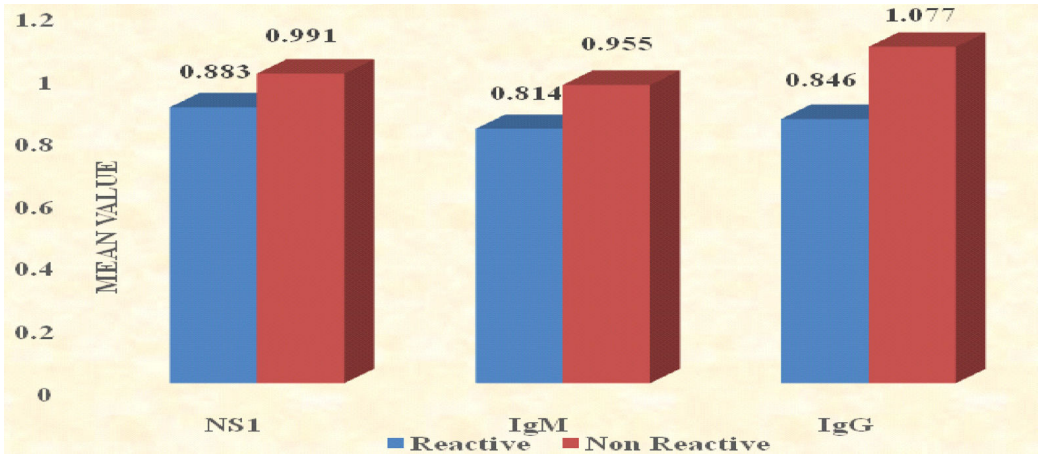

Fig. 5: Mean Distribution of Platelets (Lacs) in relation to Dengue serology in study participants (N=101)

Table 6: Mean Distribution of MPV (fL) in relation to Dengue serologyin study participants (N=101)

	NS1	IgM	IgG
Reactive	10.851	10.782	10.965
Non-Reactive	10.942	10.91	10.753

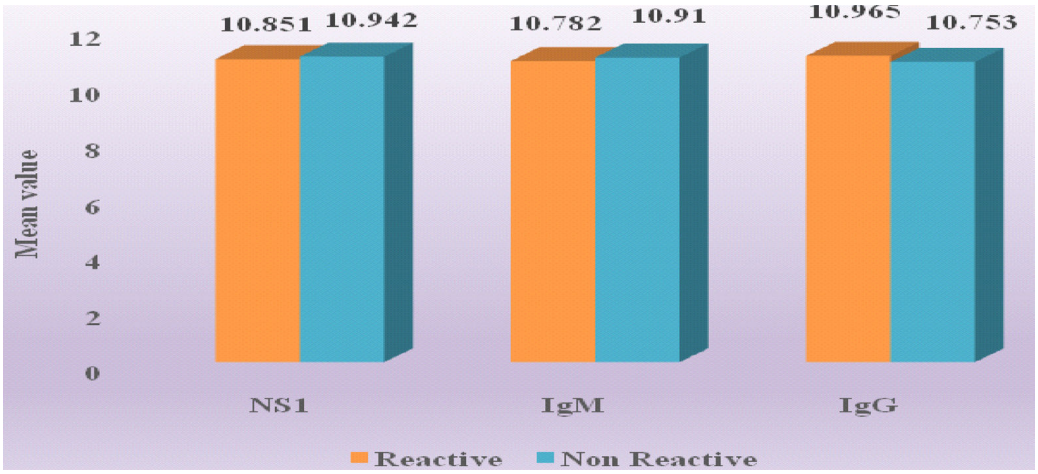

Fig. 6: Mean Distribution of MPV (fL) in relation to Dengue serologyin study participants (N=101)

Table 7: Mean Distribution of PDW (%) in relation to Dengue serology in study participants (N=101)

	NS1	IgM	IgG
Reactive	12.94	12.859	13.263
Non-Reactive	12.961	12.97	12.434

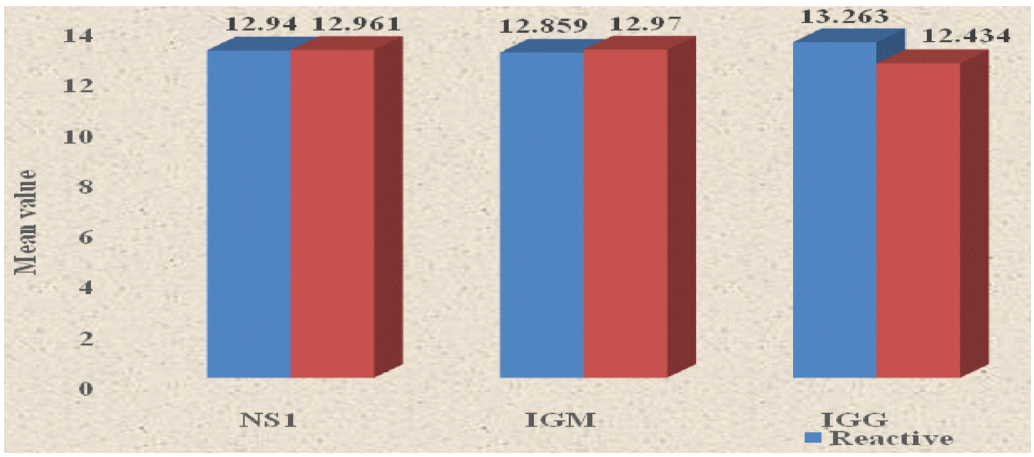

Fig. 7: Mean Distribution of PDW (%) in relation to Dengue serology in study participants (N=101)

Table 8: Platelet indices (MPV) with severity of disease in dengue positive cases

Diagnosis	Low MPV (<9)	High MPV (>9)	Total
DF	12 (12.76%)	82 (87.23%)	94 (93.06%)
DHF	2 (28.57%)	5 (71.43%)	7 (6.94%)
Total	14 (13.86%)	87 (86.14%)	101 (100%)

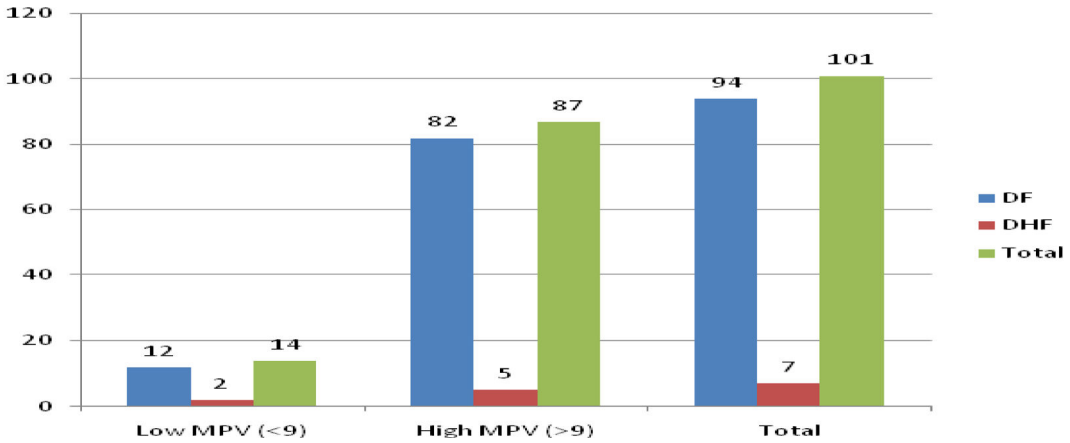

Fig. 8: Platelet indices (MPV) with severity of disease in dengue positive cases

Table 9: Platelet indices (PDW) with severity of disease in dengue positive cases

Diagnosis	Low PDW (<13)	High PDW (>13)	Total
DF	53 (56.38%)	41 (43.62%)	94 (93.06%)
DHF	4 (57.14%)	3 (42.86%)	7 (6.94%)
Total	57 (56.44%)	44 (43.56%)	101 (100%)

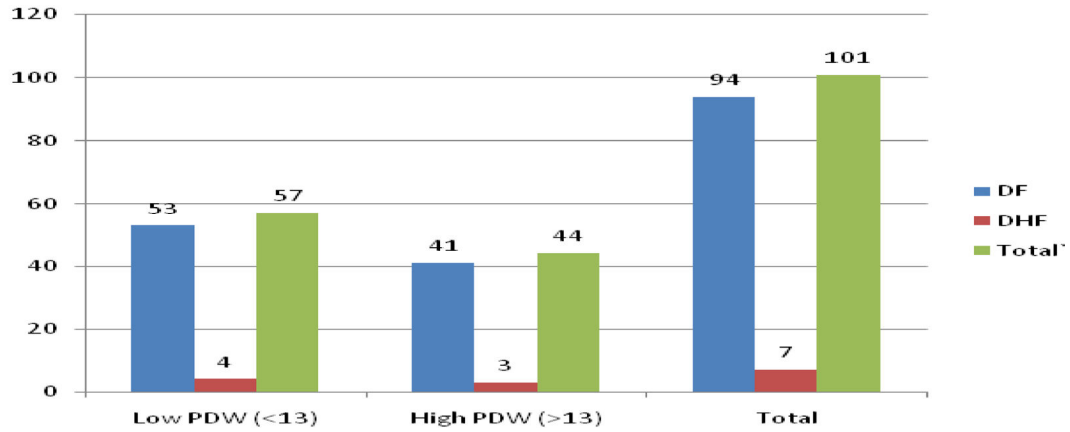

Fig. 9: Platelet indices (PDW) with severity of disease in dengue positive cases

Table 10: No. of Days to improvement in study participants (N=101)

No. of Days	Frequency	Percent
1	1	0.99
2	7	6.93
3	25	24.75
4	29	28.71
5	16	15.84
6	13	12.87
7	4	3.96
8	5	4.95
9	1	0.99
Total	101	101

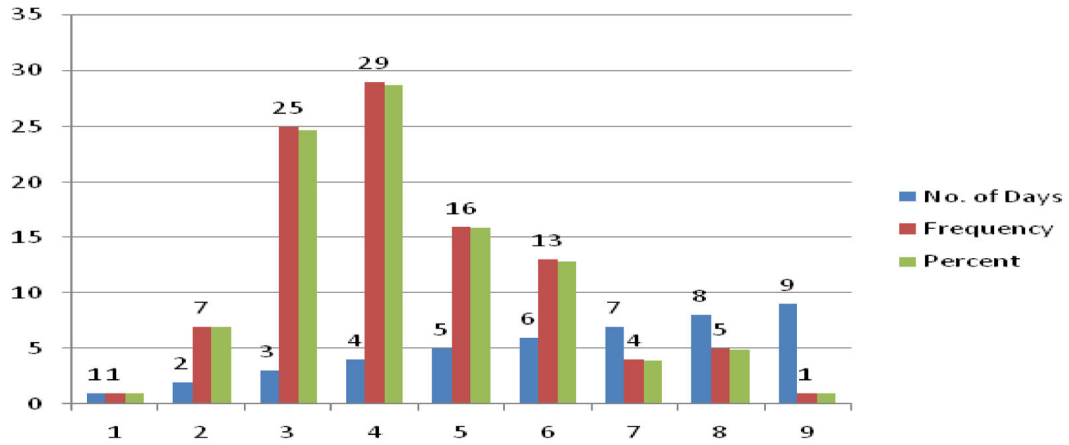

Fig. 10: No. of Days to improvement in study participants (N=101)

Table 11: Correlation to the MPV Value between admission and at the time of discharge (N=101)

	N	Mean	Std Deviation	F	P
On admission	84	10.8845	1.17540		
48 hours	84	11.3262	1.14839		
On discharge	81	11.3617	1.04673	3.925	0.021

Table 12: Correlation to the PDW Value between admission and at the time of discharge (N=101)

	N	Mean	Std Deviation	F	P
On admission	84	12.9476	2.55812		
48 hours	85	14.0376	3.12665		
On discharge	81	14.2506	3.17203	4.634	.011

Table 13: Correlation Number of days to recovery and the percentage increase of the values between admission and at the time of discharge

		N	Mean	Std. Deviation	H	p
	< = 3 days	27	113.505	157.212		
Platelet	4 – 6 days	55	280.251	520.268		
	>6 days	9	718.927	964.479	0.684	0.710
	< = 3 days	24	2.174	10.032		
MPV	4 – 6 days	42	3.973	11.492		
	>6 days	6	14.336	14.860	3.966	0.138
	< = 3 days	24	3.192	16.635		
PDW	4 – 6 days	42	9.954	20.212		
	>6 days	6	25.523	29.975	-60.377	0.131

Dengue fever (DF) is a self-limited viral febrile illness. Dengue Haemorrhagic fever (DHF) is characterized by prominent haemorrhagic manifestations associated with thrombocytopenia and an increased vascular permeability. The clinical diagnosis of DHF especially in the early phase of illness is not easy. Laboratory findings such as thrombocytopenia and a rising haematocrit in DHF cases are usually observed by day 3 or 4 of the illness.[12] The complex mechanism of thrombocytopenia remains unclear. Possible mechanisms of thrombocytopenia could be, direct bone marrow suppression by the virus; anti-dengue antibody-mediated platelet destruction, peripheral consumption of platelets and isolated viral replication in the platelet. Thrombocytopenia leads to bleeding although the platelet count may not directly correlate with the bleeding manifestation recently, novel platelet indices such as MPV and PDW have been investigated as prospective platelet activation markers. Platelet volume, a marker of platelet function and activity

is measured as mean platelet volume (MPV) by haematology analysers. MPV can be used as independent predictors of bleeding. It is surrogate marker of bone marrow activity; a high MPV indicates increased megakaryocyte activity. A low MPV indicates marrow suppression and increased risk of bleeding. Correlation of platelet count and MPV with bleeding and severity of the disease can potentially predict outcome[13]. The aim of the study was finding simple and widely used platelet activation indices (MPV and PDW); focussed on the fact that platelet activation causes morphologic changes of platelets, including both the spherical shape and pseudopodia formation. Platelets with increased number and size of pseudopodia differ in size, possibly affecting platelet distribution width (PDW).[14,15]

According to the study conducted by Jayashree K et. al. there was a significant association between platelet counts and severity of the disease which is similar to our study, thus concluding that platelet count can be used as predictive parameters for diagnosing DF/DHF/DSS.[12]

Similar study was done by Bashir AB et. al. on control and study group and found that the MPV was decreased in cases of study group that is dengue positive cases and was normal in cases of control. PDW was normal in control group while it was increased in dengue infection, which is accordance with our study. Since our study was an observational study only dengue positive cases were taken and control group were not included.[15]

In our study Patients with thrombocytopenia (i.e. platelet count < 1 lakh) 15 patients had platelet count <20,000, 24 patients had platelet count between 21,000- 50,000, 24 patients had platelet count between 51,000-1 lakh and 38 cases had platelet count > 1 lakhs. There was no significant difference in severe thrombocytopenia among different age group. Chi square was done and p value was found to be 0.494193 which signifies that, it is not statistically significant.

Dengue fever (DF) cases were noted in 94 cases and dengue haemorrhagic fever (DHF) cases were noted in 7 cases. Significant difference was observed between severity of the thrombocytopenia and severity of the disease, (P value 0.080686).

Among 101 dengue positive cases, low MPV (<9fl) indicating bone marrow suppression was seen in 13.86 % of the cases, of which 12.76 % were diagnosed as DF while 28.57 % were of DHF and high MPV was seen in 87.23 % were diagnosed as DF and remaining 71.43 % cases showed high MPV (>9fl) were of DHF.

A high PDW (>13fl) which indicates as useful marker for platelet activation was seen in 44% 0f cases, of which 41 cases were DF while 3 cases were DHF remaining 56.44% of cases of which 53 DF and 4 DHF showed low PDW (<13fl).

The Mean days to recovery from illness and increase in the platelet count was 4 days in 28.71 % followed by 3 days in 24.75 % and 5 days in 15.84 % participants. Majority of the participants recovered in 4-5 days of the illness with respect to platelet count improvement.

Even though the increase in the Mean platelet volume and increase in Platelet distribution width indicates activation and heralds recovery of platelets, but the correlation between platelet counts and platelet indices like MPV and PDW in correlation to number of days to recovery, did not show any significance in our study (p values are 0.710, 0.138 and 0.131 respectively)

Conclusion

Even though the increase in the Mean platelet volume and increase in Platelet distribution width indicates activation and heralds recovery of platelets, but the correlation between platelet counts and platelet indices like MPV and PDW in correlation to the number of days to recovery from illness, did not show any significance in our study (p values are 0.710, 0.138 and 0.131 respectively)

The study focuses the importance of platelet parameters in dengue infection. No significant difference was observed between severity of the thrombocytopenia and severity of the disease (P value -0.013). Platelet count is thus a predictive parameter of DF/DHF/DSS. Low MPV (13fl) shows sensitivity for dengue fever thus reflecting a predictive marker for diagnosing dengue fever in endemic area. No significant correlation can be proved with the platelet indices with number of days to recovery from illness.

Acknowledgement:

I am indebted to Dr. Kiran Aithal M.d., Professor and Head, Department of General Medicine, S.D.M. College of Medical Sciences & Hospital Sattur, Dharwad for his constant support, guidance, advice and suggestions during the course of the study.

I am thankful to Professors of General Medicine, whose teachings of practical skills which gave me

confidence.

I thank Assistant Professors & Senior Residents, Department of General Medicine, S.D.M. College of Medical Sciences & Hospital, Sattur, Dharwad for their wisdom and support.

Conflict of Interest: None

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