

ORIGINAL ARTICLE

A Cross Sectional Study on the Plateletcrit and Platelet Indices in Different Forms of Dengue FeverSADAQAT HUSSAIN¹, UNAIZA SHARIF², ABDUL KABEER BAIG³, SEHRISH RAJA⁴, MUHAMMAD KHURRAM⁵, SAIRA MAHMOOD⁶^{1,2}Civil Medical Officer, THQ Abbaspur AJK³Registrar Medicine, Khadim Ali Memorial Hospital Jhelum,⁴Postgraduate Trainee Medical Unit 2, Holy Family Hospital Rawalpindi⁵Dean of medicine, Rawalpindi Medical University,⁶Postgraduate Trainee Medical Unit 2, Holy Family Hospital RawalpindiCorresponding author: Sadaqat Hussain, Email: Sadaqathussain321@gmail.com, Cell: 03457451213**ABSTRACT**

Background: Dengue fever is a viral disease caused by four different serotypes of dengue viruses from DENV, transmitted mostly by the *Aedes aegypti* mosquito. The disease has history of many outbreaks mostly in tropic and sub-tropic countries, costing many lives annually, with millions in mild to complicated forms, bringing stress to health systems and economies of poor countries. Dengue epidemic occurred in Pakistan in 2010 with 257 deaths during the epidemic and prevalence of 16580 cases in Rawalpindi, repeated epidemic in 2015, 2017, 2018 and 2019 with higher prevalence.

Objective: To determine the frequency of dengue hemorrhagic fever in patients of dengue fever and to compare mean plateletcrit and platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever.

Materials And Methods: The design of this study was an observational cross sectional study design. This study was conducted in the Department of Infectious Diseases, Holy Family Hospital, Rawalpindi and the duration of this study was 6 months after the approval of synopsis i.e 1st May 2021 to 30th Oct 2021. Patients fulfilling selection criteria were enrolled in the study from emergency of Department of Infectious Diseases, Holy Family Hospital Rawalpindi. Informed consent was taken. Then patients were evaluated and divided for severity score (annexure I). Reports were assessed for Platelet indices including platelet count, mean platelet volume, platelet distribution width (as per operational definition). All this information were recorded on proforma (attached).

Results: Total 150 participants were enrolled in the study as per the inclusion criteria. Mean age in the study was 38.42±13.74 whereas there were 94 (62.7%) male and 56 (37.3%) female patients who were included in the study according to the inclusion criteria. Among 150 patients, 28 (18.7%) patients were presented with dengue hemorrhagic fever in patients of dengue fever. Mean Platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever in the study was 0.26±1.62 vs 0.08±0.02 (p-value 0.552) whereas mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever in the study was 64.19±41.11 vs 78.10±32.74 (p-value 0.097).

Practical Implication: To determine the frequency of dengue hemorrhagic fever in patients of dengue fever and to compare mean plateletcrit and platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever

Conclusion: The study concluded that different indices of platelets within different forms of dengue fever to assess the severity of the disease process may serve as an early indicator of disease progress and severity which will help to decide early intervention.

Keywords: Dengue Fever, Hemorrhagic, Platelet, Indices, Serotypes, Epidemic, Participants

INTRODUCTION

Dengue fever is a viral disease caused by four different serotypes of dengue viruses from DENV, transmitted mostly by the *Aedes aegypti* mosquito¹. The disease has history of many outbreaks mostly in tropic and sub-tropic countries, costing many lives annually, with millions in mild to complicated forms, bringing stress to health systems and economies of poor countries. The incidence is recently increasing and expanding from urban to rural setting²⁻⁴. Dengue fever presents from simple viral illness to more complicated forms of dengue hemorrhagic fever and dengue shock syndrome. With incubation period of 3 to 7 days; diagnosed clinically and by serological tests; antibodies against dengue virus and NS-1 protein⁵. Dengue epidemic occurred in Pakistan in 2010 with 257 deaths during the epidemic and prevalence of 16580 cases in Rawalpindi, repeated epidemic in 2015, 2017, 2018 and 2019 with higher prevalence^{6,7,8}.

With need of more efficient method of early detection and prevention of complicated dengue fever. Thrombocytopenia is used as indicator of severity of dengue fever; work has been done on platelet count and other indices like mean platelet volume⁹, platelet distribution width comparing with different values of platelets in dengue fever. Mean platelet volume is a marker of platelet activation and is used as a predictor of bleeding¹⁰⁻¹².

A recent study in 2018 showed that MPV (9.2±0.09 vs. 13.8±1.3fL, p value of <0.001) and PDW (57±13.8 vs. 54.4±6.9, with p value of 0.001) were significantly altered in patients with dengue fever with different values of platelets, 20000 vs (13,14,6), 100000. Another study reported that there were 32% patients who had dengue hemorrhagic fever (severity score >2) while remaining had only dengue fever⁽¹⁵⁾. The platelet count was low in 56%

patients with dengue fever while in 44% patients with dengue hemorrhagic fever, the plateletcrit was low in 49% patients with dengue fever while in 51% patients with dengue hemorrhagic fever, the mean platelet volume was low in 67% patients with dengue fever while in 33% patients with dengue hemorrhagic fever and the platelet distribution width was low in 45% patients with dengue fever while in 55% patients with dengue hemorrhagic fever⁽¹⁶⁾.

Rationale of this study is to determine frequency of dengue hemorrhagic fever in patients of dengue fever and then compare mean plateletcrit and platelet indices in patients with or without dengue hemorrhagic fever^(17,18). There is a need to establish relation in different indices of platelets within different forms of dengue fever, to assess the severity of the disease process and as a predictive value⁽¹⁹⁾; may serve as an early indicator of disease progress and severity and help to decide early intervention⁽²⁰⁾. Very few studies had been conducted before regarding this issue and mostly patients had deranged platelet profile. So, we want to conduct this study to evidence for local population.

MATERIALS AND METHODS

Study Design: Observational cross-sectional study

Study Setting: Department of Infectious Diseases, Holy Family Hospital, Rawalpindi

Duration of study: Minimum 6 months after the approval of synopsis i.e 1st May 2021 to 30th Oct 2021.

Sample size: Sample size of 150 cases is calculated with 95% confidence level, 7.5% margin of error and taking expected percentage of dengue hemorrhagic fever i.e. 32% in patients diagnosed for dengue fever.

Sampling technique: non-probability, consecutive sampling.

Selection criteria:

Inclusion criteria: Patients of age 16-75 years, both genders, diagnosed with dengue fever (as per operational definition).

Exclusion criteria: Patient with unconscious state, with abnormal blood clotting profile (PT>15sec), thalassemia, von Willebrand disease, leukemia (on medical record)

Data collection procedure: 150 Patients fulfilling selection criteria were enrolled in the study from emergency of Department of Infectious Diseases, Holy Family Hospital Rawalpindi. Informed consent was taken. Demographics like name, age, gender, BMI, smoking (>5 pack years) diabetes (BSR>200 mg/dl), hypertension (BP>140/90 mmHg) was noted. Blood sample was drawn by using 3cc disposable syringe and sent to the laboratory of the hospital for assessment of complete blood count including hematocrit level to determine the severity of dengue fever. Then patients were evaluated and divided for severity score (annexure I). Reports were assessed for Platelet indices including platelet count, mean platelet volume, platelet distribution width (as per operational definition). All this information was recorded on proforma (attached).

Data Analysis: Data analysis was on SPSS version 21. Quantitative variables like age, BMI, severity score, platelet indices were expressed in terms of mean ± standard deviation. Qualitative variables like gender, smoking, hypertension, diabetes, type of dengue fever (dengue fever, dengue hemorrhagic fever), normal and deranged levels of platelet indices was expressed in terms of frequency and percentage. Normal and deranged levels of platelet indices was compared in patients with or without dengue hemorrhagic fever by using chi-square test. P-value < 0.05 was considered as significant. Data was stratified for age, gender, BMI, smoking, diabetes, and hypertension. Post-stratification, chi-square test was applied to compare the frequency of dengue hemorrhagic fever in stratified groups and then normal and deranged levels of platelet indices will be compared in patients with or without dengue hemorrhagic fever by using chi-square test. P-value < 0.05 was considered as significant.

RESULT

Data was entered and analyzed in SPSS version 21.0. Total 150 participants were enrolled in the study as per the inclusion criteria. Descriptive statistics of age of patient was also calculated in terms of mean and standard deviation. Mean age in the study was 38.42±13.74, as shown in Table.1. Distribution of gender of patient was also calculated in terms of frequency and percentage of male and female patients. There were 94 (62.7) male and 56 (37.3) female patients who were included in the study according to the inclusion criteria, as shown in Table.2. Descriptive statistics of body mass index (BMI) was calculated in terms of mean and standard deviation. Mean body mass index among patients was 26.42±4.41, as shown in Table.3. Severity score was assessed in the study. Patients were presented with severity score 1 to 4 whereas mean severity score was 2.01±0.97, as shown in Table.4.

Frequency and percentage of smoking, hypertension and diabetes were assessed in the study. Among 150 patients, majority of the patients were presented with hypertension 28 (18.7), following by smoking 20 (13.3) and diabetes 16 (10.7), as shown in Table.5. Frequency and percentage of normal and deranged levels of platelet indices were analyzed in the study, as shown in Table.6, whereas descriptive statistics in terms of mean and standard deviation values were calculated of platelet indices as shown in Table.7.

The objective of the study is to determine the frequency of dengue hemorrhagic fever in patients of dengue fever. Among 150 patients, 28 (18.7%) patients were presented with dengue hemorrhagic fever in patients of dengue fever, as shown in Table.8. The secondary objective is to compare mean plateletcrit and mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever. Mean Plateletcrit indices in patients with or without dengue hemorrhagic fever due to dengue

fever in the study was 0.26±1.62 vs 0.08±0.02 (p-value 0.552) whereas mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever in the study was 64.19±41.11 vs 78.10±32.74 (p-value 0.097), as shown in Table.9.

Effect modifier like age stratification was done and compared with mean plateletcrit and mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever. Among age group 16-50 years with platelet < 100,000, there were 96 (100.0) vs 26 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, among PCT < 0.2; there were 81 (84.4) vs 26 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, as shown in Table. 10. Effect modifier like gender stratification was done and compared with mean plateletcrit and mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever. Among male patients with platelet < 100,000, there were 87 (100.0) vs 7 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, among PCT < 0.2; there were 35 (100.0) vs 21 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, as shown in Table. 11. Effect modifier like body mass index (BMI) stratification was done and compared with mean plateletcrit and mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever. Among patients BMI (21-23) with platelet < 100,000, there were 44 (100.0) vs 10 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, among PCT < 0.2; there were 37 (84.1) vs 10 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, as shown in Table. 12. Effect modifier like smoking stratification was done and compared with mean plateletcrit and mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever. Among smoker patients with platelet < 100,000, there were 20 (100.0) vs 0 (0.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, among PCT < 0.2; there were 17 (85.3) vs 0 (0.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, as shown in Table. 13.

Effect modifier like diabetes stratification was done and compared with mean plateletcrit and mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever. Among diabetic patients with platelet < 100,000, there were 15 (100.0) vs 1 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, among PCT < 0.2; there were 12 (80.0) vs 1 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, as shown in Table. 14. Effect modifier like hypertension stratification was done and compared with mean plateletcrit and mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever. Among hypertensive patients with platelet < 100,000, there were 24 (100.0) vs 4 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, among PCT < 0.2; there were 20 (83.3) vs 4 (100.0) patients with or without dengue hemorrhagic fever due to dengue fever in the study, as shown in Table. 15

Table 1: Descriptive Statistics of Age (years)

	N	Minimum	Maximum	Mean	Std. Deviation
age (years)	150	16.00	72.00	38.42	13.74

Table 2: Gender Distribution of Patients

	Frequency	Percentage
Male	94	62.7
Female	56	37.3
Total	150	100.0

Table 3: Descriptive Statistics of Body Mass Index (BMI)

	N	Minimum	Maximum	Mean	Std. Deviation
Body Mass Index (BMI)	150	21.00	34.00	26.42	4.71

Table 4: Descriptive Statistics of Severity Score

	n	Minimum	Maximum	Mean	Std. Deviation
Severity Score	150	1	4	2.01	0.97

Table 5: Frequency & Percentage of Smoking, HTN & Diabetes

		n (%)
Smoking	Yes	20 (13.3)
	No	130 (86.7)
Hypertension	Yes	28 (18.7)
	No	122 (81.3)
Diabetes	Yes	16 (10.7)
	No	134 (89.3)

Table 6: Frequency & percentage of Normal & Deranged levels of Platelet Indices

		n (%)
Platelet	< 100,000 (deranged)	150 (100.0)
	> 100,000 (normal)	0 (0.0)
PCT	< 0.2	132 (88.0)
	> 0.2	18 (12.0)
MPV	< 9	32 (21.3)
	> 9	118 (78.7)
PDW	< 18	146 (97.3)
	> 18	4 (2.7)

Table 7: Descriptive Statistics of Platelet Indices

Platelet Indices	n	Minimum	Maximum	Mean	Std. Deviation
Platelet	150	9.0	193.0	66.79	39.95
PCT	150	.01	18.00	0.23	1.46
MPV	150	7.90	17.00	9.79	1.14
PDW	150	10.10	20.40	15.66	1.78

Table 8: Frequency & percentage Dengue Hemorrhagic Fever in patients of dengue fever

	Frequency	Percentage
dengue fever	122	81.3
dengue hemorrhagic fever	28	18.7
Total	150	100.0

Table 9: Comparison Of Mean Platecrit & Platelet Indices In Patients With Or Without Dengue Hemorrhagic Fever Due To Dengue Fever

Type of Dengue Fever	n	Mean	Std. Deviation	p-value	
Platecrit	dengue fever	122	26	1.62	0.552
	With dengue hemorrhagic fever	28	.08	0.02	
Platelet	dengue fever	122	64.19	41.11	0.097
	With dengue hemorrhagic fever	28	78.10	32.74	

Table 10: Effect Modifier Like Age Stratification and Compared With Mean Platecrit & Platelet Indices In Patients With Or Without Dengue Hemorrhagic Fever Due To Dengue Fever

Age groups	Normal and Deranged levels of Platelet Indices		Dengue Fever	Dengue Hemorrhagic Fever	Total	p-value
16-50	Platelet	< 100,000	96 (100.0)	26 (100.0)	122 (100.0)	NA
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
51-75	Platelet	< 100,000	26 (100.0)	2 (100.0)	28 (100.0)	NA
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
16-50	PCT	< 0.2	81 (84.4)	26 (100.0)	107 (87.7)	0.031
		> 0.2	15 (15.6)	0 (0.0)	15 (12.3)	
51-75	PCT	< 0.2	23 (88.5)	2 (100.0)	25 (89.3)	0.611
		> 0.2	3 (11.5)	0 (0.0)	3 (10.7)	
16-50	MPV	< 9	21 (21.9)	5 (19.2)	26 (21.3)	0.770
		> 9	75 (78.1)	21 (80.8)	96 (78.7)	
51-75	MPV	< 9	5 (19.2)	1 (50.0)	6 (21.4)	0.307
		> 9	21 (80.8)	1 (50.0)	22 (78.6)	
16-50	PDW	< 18	96 (100.0)	24 (92.3)	120 (98.4)	0.006
		> 18	0 (0.0)	2 (7.7)	2 (1.6)	
51-75	PDW	< 18	24 (92.3)	2 (100.0)	26 (92.9)	0.684
		> 18	2 (7.7)	0 (0.0)	2 (7.1)	

Table 11: Effect Modifier Like Gender Stratification And Compared With Mean Platecrit & Platelet Indices In Patients With Or Without Dengue Hemorrhagic Fever Due To Dengue Fever

Gender	Normal and Deranged levels of Platelet Indices		Dengue Fever	Dengue Hemorrhagic Fever	Total	p-value
Male	Platelet	< 100,000	87 (100.0)	7 (100.0)	94 (100.0)	NA
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
Female	Platelet	< 100,000	35 (100.0)	21 (100.0)	56 (100.0)	NA
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
Male	PCT	< 0.2	74 (85.1)	7 (100.0)	81 (86.2)	0.271
		> 0.2	13 (14.9)	0 (0.0)	13 (13.8)	
Female	PCT	< 0.2	30 (85.7)	21 (100.0)	51 (91.1)	0.070
		> 0.2	5 (14.3)	0 (0.0)	5 (8.9)	
Male	MPV	< 9	18 (20.7)	2 (28.6)	20 (21.3)	0.624
		> 9	69 (79.3)	7 (100.0)	74 (78.7)	
Female	MPV	< 9	8 (22.9)	4 (19.0)	12 (21.4)	0.737
		> 9	27 (77.1)	17 (100.0)	44 (78.6)	
Male	PDW	< 18	87 (100.0)	7 (100.0)	94 (100.0)	0.592
		> 18	0 (0.0)	0 (0.0)	0 (0.0)	
Female	PDW	< 18	33 (94.3)	19 (90.5)	52 (92.9)	0.103
		> 18	2 (5.7)	2 (9.5)	4 (7.1)	

Table 12: Effect Modifier Like BMI Stratification and Compared With Mean Platecrit & Platelet Indices In Patients With Or Without Dengue Hemorrhagic Fever Due To Dengue Fever

BMI	Normal and Deranged levels of Platelet Indices		Dengue Fever	Dengue Hemorrhagic Fever	Total	p-value
21 - 23	Platelet	< 100,000	44 (100.0)	10 (100.0)	54 (100.0)	NA
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
> 24	Platelet	< 100,000	78 (100.0)	18 (100.0)	96 (100.0)	NA
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
21 - 23	PCT	< 0.2	37 (84.1)	10 (100.0)	47 (87.0)	0.176
		> 0.2	7 (15.9)	0 (0.0)	7 (13.0)	
> 24	PCT	< 0.2	67 (85.9)	18 (100.0)	85 (85.5)	0.090
		> 0.2	11 (14.1)	0 (0.0)	11 (11.5)	
21 - 23	MPV	< 9	8 (18.2)	1 (10.0)	9 (16.7)	0.531
		> 9	36 (81.8)	9 (90.0)	45 (83.3)	
> 24	MPV	< 9	18 (23.1)	5 (27.8)	23 (24.0)	0.674
		> 9	60 (76.9)	13 (72.2)	73 (76.0)	
21 - 23	PDW	< 18	43 (97.7)	10 (100.0)	53 (98.1)	0.630

		> 18	1 (2.3)	0 (0.0)	1 (1.9)	
> 24	PDW	< 18	77 (98.7)	16 (88.9)	93 (96.9)	0.031
		> 18	1 (1.3)	2 (11.1)	3 (3.1)	

Table 13: Effect Modifier Like Smoking Stratification and Compared With Mean Platecrit & Platelet Indices In Patients With Or Without Dengue Hemorrhagic Fever Due To Dengue Fever

Smoking	Normal and Deranged levels of Platelet Indices	Dengue Fever	Dengue Hemorrhagic Fever	Total	p-value	
Yes	Platelet	< 100,000	20 (100.0)	0 (0.0)	20 (100.0)	-
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
No	Platelet	< 100,000	102 (100.0)	28 (100.0)	130 (100.0)	-
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
Yes	PCT	< 0.2	17 (85.0)	0 (0.0)	17 (85.0)	0.031
		> 0.2	3 (15.0)	0 (0.0)	3 (15.0)	
No	PCT	< 0.2	87 (85.3)	28 (100.0)	115 (88.5)	0.030
		> 0.2	15 (14.7)	0 (0.0)	15 (11.5)	
Yes	MPV	< 9	2 (10.0)	0 (0.0)	2 (10.0)	-
		> 9	18 (90.0)	0 (0.0)	18 (90.0)	
No	MPV	< 9	24 (23.5)	6 (21.4)	30 (23.1)	0.815
		> 9	78 (76.5)	22 (78.6)	100 (76.9)	
Yes	PDW	< 18	20 (100.0)	0 (0.0)	20 (100.0)	-
		> 18	0 (0.0)	0 (0.0)	0 (0.0)	
No	PDW	< 18	100 (98.0)	26 (92.9)	126 (96.9)	0.160
		> 18	2 (2.0)	2 (7.1)	4 (3.1)	

Table 14: Effect Modifier Like Diabetes Stratification and Compared With Mean Platecrit & Platelet Indices In Patients With Or Without Dengue Hemorrhagic Fever Due To Dengue Fever

Diabetes	Normal and Deranged levels of Platelet Indices	Dengue Fever	Dengue Hemorrhagic Fever	Total	p-value	
yes	Platelet	< 100,000	15 (100.0)	1 (100.0)	16 (100.0)	-
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
no	Platelet	< 100,000	107 (100.0)	27 (100.0)	134 (100.0)	-
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
yes	PCT	< 0.2	12 (80.0)	1 (100.0)	13 (81.3)	0.620
		> 0.2	3 (20.0)	0 (0.0)	3 (18.8)	
no	PCT	< 0.2	92 (86.0)	27 (100.0)	119 (88.8)	0.039
		> 0.2	15 (14.0)	0 (0.0)	15 (11.2)	
yes	MPV	< 9	4 (26.7)	1 (100.0)	5 (31.3)	0.126
		> 9	11 (73.3)	0 (0.0)	11 (68.8)	
no	MPV	< 9	22 (20.6)	5 (18.5)	27 (20.0)	0.813
		> 9	85 (79.4)	22 (81.5)	107 (79.9)	
yes	PDW	< 18	13 (86.7)	1 (100.0)	14 (87.5)	0.696
		> 18	2 (13.3)	0 (0.0)	2 (12.5)	
no	PDW	< 18	107 (100.0)	25 (92.6)	132 (98.5)	0.005
		> 18	0 (0.0)	2 (7.4)	2 (1.5)	

Table 15: Effect Modifier Like Hypertension Stratification And Compared With Mean Platecrit & Platelet Indices In Patients With Or Without Dengue Hemorrhagic Fever Due To Dengue Fever

Hypertension	Normal and Deranged levels of Platelet Indices	Dengue Fever	Dengue Hemorrhagic Fever	Total	p-value	
yes	Platelet	< 100,000	24 (100.0)	4 (100.0)	28 (100.0)	NA
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
no	Platelet	< 100,000	98 (100.0)	24 (100.0)	122 (100.0)	NA
		> 100,000	0 (0.0)	0 (0.0)	0 (0.0)	
yes	PCT	< 0.2	20 (83.3)	4 (100.0)	24 (85.7)	0.378
		> 0.2	4 (16.7)	0 (0.0)	4 (14.3)	
no	PCT	< 0.2	84 (85.7)	24 (100.0)	108 (88.5)	0.049
		> 0.2	14 (14.3)	0 (0.0)	14 (11.5)	
yes	MPV	< 9	6 (25.0)	2 (50.0)	8 (28.6)	0.306
		> 9	18 (75.0)	2 (50.0)	20 (71.4)	
no	MPV	< 9	20 (20.4)	4 (16.7)	24 (19.7)	0.679
		> 9	78 (79.6)	20 (83.3)	98 (80.3)	
yes	PDW	< 18	22 (91.7)	4 (100.0)	26 (92.9)	0.549
		> 18	2 (8.3)	0 (0.0)	2 (7.1)	
no	PDW	< 18	98 (100.0)	22 (91.7)	120 (98.4)	0.004
		> 18	0 (0.0)	2 (8.3)	2 (1.6)	

DISCUSSION

Dengue illness remains a significant clinical and public health challenge globally. More than 2.5 billion people in the tropics and subtropics are at risk of infection and an estimated 390 million dengue infections occur annually in around 125 countries worldwide (21). Platelet indices like mean platelet volume (MPV), platelet distribution width (PDW) and Plateletcrit (PCT) are being investigated as prospective platelet activation indicators (22). MPV is a useful independent predictor of bleeding. It is a surrogate indicator of bone marrow activity. Low MPV indicates bone marrow suppression and suggests a risk of bleeding (23,24). The normal range for MPV is 8.9-11.8 fL. PDW is a marker of volume variability in platelet size and is elevated in the presence of platelet anisocytosis. It directly measures variability in platelet size and

changes occurring with platelet activation, and also suggests the heterogeneity in platelet morphology (25). The normal range for PDW is 10.0%-17.9% (7). PCT is the volume occupied by platelets in the blood as a percentage and calculated by the formula $PCT = \text{platelet count} \times MPV / 10,000$. The normal range for PCT is 0.22-0.24% (26).

Platelet indices give information on whether the platelet destruction is ongoing (necessitating an impending platelet transfusion) or whether the bone marrow is responsive and so platelet transfusions can be put on hold (27,15). Low platelet count, low MPV, low PCT and high PDW may be used as probable indicators for dengue in endemic areas and also as a predictor of the severity of the dengue infection. In the acute stage of dengue fever, thrombocytopenia is due to bone marrow depression. Low MPV with low platelets implies marrow suppression as a

mechanism of thrombocytopenia⁽⁸⁾. Increasing MPV with ongoing thrombocytopenia represents peripheral destruction⁽¹⁰⁾ and signals a need for a platelet transfusion while an increase in MPV together with a stable platelet count possibly indicates recovery. Decreased MPV with severe thrombocytopenia with hemorrhagic tendencies could be an ominous sign in dengue and could indicate the need for a red cell transfusion⁽²⁸⁾.

PDW is higher in hyper-destructive patients when compared with hypo-productive thrombocytopenic patients. The high PDW in platelet destruction could be explained by the fact that newly produced platelets are larger than circulating platelets, which tend to decrease in size with age in circulation similar to reticulocytes with respect to red blood cells. As a result, in patients with thrombocytopenia secondary to peripheral destruction, the PDW is increased reflecting active bone marrow compensation with the release of young platelets⁽¹²⁾. Another study reported that patients with dengue fever had lower levels of MPV and platelet count; however, PDW values were increased in patients with dengue fever. It was observed that platelet count was a predictive parameter of dengue fever and they also showed that low MPV and high PDW sensitivity were related to dengue fever⁽¹⁵⁾. A significant association between platelet counts and the severity of the disease. Low platelet count, low MPV, low PCT and high PDW show considerable sensitivity and specificity for dengue fever and can be used as a predictor of the severity of dengue infection⁽¹⁶⁻¹⁸⁾.

Data was entered and analyzed in SPSS version 21.0. Total 150 participants were enrolled in the study as per the inclusion criteria. Mean age (weeks) in the study was 38.42+13.74 whereas there were 94 (62.7%) male and 56 (37.3%) female patients who were included in the study according to the inclusion criteria⁽²⁹⁾. Mean body mass index among patients was 26.42+4.41. Patients were presented with severity score 1 to 4 whereas mean severity score was 2.01+0.97. Frequency and percentage of smoking, hypertension and diabetes were assessed in the study. Among 150 patients, majority of the patients were presented with hypertension 28 (18.7), following by smoking 20 (13.3) and diabetes 16 (10.7). Among 150 patients, 28 (18.7%) patients were presented with dengue hemorrhagic fever in patients of dengue fever. Mean Platecrit indices in patients with or without dengue hemorrhagic fever due to dengue fever in the study was 0.26+1.62 vs 0.08+0.02 (p-value 0.552) whereas mean platelet indices in patients with or without dengue hemorrhagic fever due to dengue fever in the study was 64.19+41.11 vs 78.10+32.74 (p-value 0.097).

CONCLUSION

The study concluded that different indices of platelets within different forms of dengue fever to assess the severity of the disease process may serve as an early indicator of disease progress and severity which will help to decide early intervention.

REFERENCES

- Mukker P, Kiran S. Platelet indices evaluation in patients with dengue fever. *Int J Res Med Sci* 2018;6(6):2054.
- Kantharaj A. Role of red cell and platelet indices as a predictive tool for transfusions in dengue. *Global Journal of Transfusion Medicine* 2018;3(2):103.
- Bashir A, Saeed O, Mohammed B, Ageep A. Role of platelet indices in patients with dengue infection in Red Sea State, Sudan. *Int J Sci Res* 2015;4(1):1573-6.
- Sharma K, Yadav A. Association of mean platelet volume with severity, serology & treatment outcome in dengue fever: prognostic utility. *Journal of clinical and diagnostic research: JCDR* 2015;9(11):EC01.
- Khatri S, Sabeena S, Arunkumar G, Mathew M. Utility of platelet parameters in serologically proven dengue cases with thrombocytopenia. *Indian Journal of ematology and Blood Transfusion* 2018;34(4):703-6.
- WHO. Dengue fever. 2021 [cited 2021]; Available from: <http://www.emro.who.int/pak/programmes/dengue-fever.html>.
- Chiranth S, Avabratha KS. Platelet Indices and the Severity of Dengue Infection in Children. *The Journal of Pediatric Research* 2019;6(3):242-7.
- R. Chen and N. Vasilakis, "Dengue-Quo Tu et Quo Vadis?" *Viruses*, vol. 3, no. 9, pp. 1562–1608, 2011.
- B. R. Murphy and S. S. Whitehead, "Immune response to dengue virus and prospects for a vaccine," *Annual Review of Immunology*, vol. 29, pp. 587–619, 2011.
- D. J. Gubler, "Dengue/dengue haemorrhagic fever: history and current status," *Novartis Foundation Symposium*, vol. 277, pp. 3– 16, 2006.
- S. Bhatt, P.W. Gething, O. J. Brady et al., "The global distribution and burden of dengue," *Nature*, vol. 496, no. 7446, pp. 504–507, 2013.
- O. J. Brady, P. W. Gething, S. Bhatt et al., "Refining the global spatial limits of dengue virus transmission by evidence-based consensus," *PLoS Neglected Tropical Diseases*, vol. 6, no. 8, Article ID e1760, 2012
- G. N. Malavige, S. Fernando, D. J. Fernando, and S. L. Seneviratne, "Dengue viral infections," *Postgraduate Medical Journal*, vol. 80, no. 948, pp. 588–601, 2004.
- R. Perera, M. Khaliq, and R. J. Kuhn, "Closing the door on flaviviruses: entry as a target for antiviral drug design," *Antiviral Research*, vol. 80, no. 1, pp. 11–22, 2008.
- Y. Modis, S. Ogata, D. Clements, and S. C. Harrison, "Variable surface epitopes in the crystal structure of dengue virus type 3 envelope glycoprotein," *Journal of Virology*, vol. 79, no. 2, pp. 1223–1231, 2005.
- R. de Alwis, M. Beltramello, W. B. Messer et al., "In-depth analysis of the antibody response of individuals exposed to primary dengue virus infection," *PLoS Neglected Tropical Diseases*, vol. 5, no. 6, Article ID e1188, 2011.
- S. Watanabe, K. W. K. Chan, J. Wang, L. Rivino, S.-M. Lok, and S. G. Vasudevan, "Dengue virus infection with highly neutralizing levels of cross-reactive antibodies causes acute lethal small intestinal pathology without a high level of viremia in mice," *Journal of Virology*, vol. 89, no. 11, pp. 5847–5861, 2015.
- W. Dejnirattisai, A. Jumnainsong, N. Onsrirakul et al., "Crossreacting antibodies enhance dengue virus infection in humans," *Science*, vol. 328, no. 5979, pp. 745–748, 2010.
- S.-J. L. Wu, G. Grouard-Vogel, W. Sun et al., "Human skin Langerhans cells are targets of dengue virus infection," *Nature Medicine*, vol. 6, no. 7, pp. 816–820, 2000.
- A. Molina-Cruz, L. Gupta, J. Richardson, K. Bennett, W. Black IV, and C. Barillas-Mury, "Effect of mosquito midgut trypsin activity on dengue-2 virus infection and dissemination in *Aedes aegypti*," *The American Journal of Tropical Medicine and Hygiene*, vol. 72, no. 5, pp. 631–637, 2005.
- M. I. Salazar, J. H. Richardson, I. S'anchez-Vargas, K. E. Olson, and B. J. Beaty, "Dengue virus type 2: replication and tropisms in orally infected *Aedes aegypti* mosquitoes," *BMC Microbiology*. 2007;7(9):205-213
- S. Swaminathan and N. Khanna, "Experimental dengue vaccines," *Molecular Vaccines: From Prophylaxis to Therapy*, vol. 1, pp. 135–151, 2013.
- J. Barniol, R. Gaczkowski, E. V. Barbato et al., "Usefulness and applicability of the revised dengue case classification by disease: multi-centre study in 18 countries," *BMC Infectious Diseases*, vol. 11, article 106, 2011.
- F. Narvaez, G. Gutierrez, M. A. P'erez et al., "Evaluation of the traditional and revised WHO classifications of dengue disease severity," *PLoS Neglected Tropical Diseases*, vol. 5, no. 11, Article ID e1397, 2011.
- M. G. Guzman, L. Hermida, L. Bernardo, R. Ramirez, and G. Guill'en, "Domain III of the envelope protein as a dengue vaccine target," *Expert Review of Vaccines*, vol. 9, no. 2, pp. 137– 147, 2010.
- S.-W. Wan, C.-F. Lin, S. Wang et al., "Current progress in dengue vaccines," *Journal of Biomedical Science*, vol. 20, no. 1, article 37, 2013.
- N. Bhamarapravati and Y. Sutee, "Live attenuated tetravalent dengue vaccine," *Vaccine*, vol. 18, supplement 2, pp. 44–47, 2000.
- W. Sun, D. Cunningham, S. S. Wasserman et al., "Phase 2 clinical trial of three formulations of tetravalent live-attenuated dengue vaccine in flavivirus-naïve adults," *Human Vaccines*, vol. 5, no. 1, pp. 33–40, 2009.
- V. Watanaveeradej, S. Simasathien, A. Nisalak et al., "Safety and immunogenicity of a tetravalent live-attenuated dengue vaccine in flavivirus-naïve infants," *The American Journal of Tropical Medicine and Hygiene*. 2011; 85 (2):341–351