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Original Article

Pathology Section

Association of Mean Platelet Volume with Severity, Serology & Treatment Outcome in Dengue Fever: Prognostic Utility

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ABSTRACT

Background: Dengue is the most rapidly spreading mosquito-borne viral disease in the world. Dengue fever (DF) with its severe manifestations such as dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) has emerged as a major public health problem of international concern. Thrombocytopenia and bleeding are common complications of dengue fever, hence besides platelet counts, there is a need to assess the role of mean platelet volume.

Aims: Studying association of mean platelet volume (MPV) with severity, serology & treatment outcome to assess its prognostic utility, which can be of great help in limiting morbidity & mortality associated with dengue fever.

Materials and Methods: The present study was conducted in Central Pathology Lab of SMS Medical College & Hospital, Jaipur, Rajasthan from the period of March 2013 till October 2013. Blood samples were collected from 200 patients with NS 1 Antigen positivity experiencing febrile illness, clinically consistent with dengue infection. Evaluation of platelet counts, MPV, IgM and IgG antibodies was done in all these cases.

Statistical Analysis: Categorical data were presented as numbers (percent) and were compared among groups using Chi-square test. Groups compared for demographic data were presented as mean and standard deviation and were compared using student t-test, ANOVA and Post-Hoc Test, Tukey Test using SPSS, version 20 for Windows.

Results: A total of 200 Dengue fever cases were studied. Out of which, 68% cases were of DF, 23% DHF & 9% DSS i.e. classical dengue fever was most common presentation. Maximum (44%) cases were in age group of 15-24 years. Fever was the presenting complaint in all cases (100%). 98% cases of dengue had thrombocytopenia. MPV showed no significant correlation with severity, serology & treatment outcome, thus excluding its role in dengue cases.

Conclusion: Mean platelet volume is not important as prognostic parameter in dengue fever.

Keywords: Acute febrile disease, Dengue haemorrhagic fever (DHF), Dengue shock syndrome (DSS), Thrombocytopenia

INTRODUCTION

Dengue fever (DF) is an acute febrile disease characterized by sudden onset of fever of 3-5 days, intense headache, myalgia, joint pain, retro-orbital pain, anorexia, gastrointestinal disturbances and rash [1]. It is one of the most important mosquito-borne viral diseases in the world [2]. In the last 50 years, incidence has increased 30-fold with increasing geographic expansion to new countries and, in the present decade, from urban to rural settings [2]. Currently dengue causes about 100 million asymptomatic cases and 25 thousand deaths annually. Infection can be asymptomatic or cause a range of severity from mild dengue fever to dengue haemorrhagic fever which can then progress to dengue shock syndrome and death [1].

Incidence of Dengue fever (DF) and its severe manifestations, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) is found to be increasing [3]. At present 2.5-3 billion persons living in tropics and subtropics are susceptible for dengue [4].

Dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) are life threatening reversible vascular complications of DF and are associated with severe thrombocytopenia, bleeding and increased vascular permeability [5]. The decreasing platelet counts have found to predict the severity of the disease [6]. So there is a need to study platelets profile & know its prognostic importance so that adverse outcomes of this rapidly spreading disease can be controlled to a great extent. In addition, the bleeding severity has not been well studied in India, especially in relation to platelet function. A common surrogate marker of bleeding can be mean platelet volume (MPV) which is often used to indicate platelet activation and indirectly bone marrow activity [7]. Not much work has been done on this parameter related to dengue fever. Hence this study has been conducted to know association of mean platelet volume (MPV) with severity, serology and treatment outcome which can be of great help in limiting morbidity and mortality associated with dengue fever.

MATERIALS AND METHODS

The present study was conducted in Central Pathology Lab of SMS Medical College & Hospital, Jaipur, Rajasthan (India) from the period of March 2013 till October 2013. A total of 200 patients admitted to the hospital with the clinical features of dengue fever (selected according to WHO criteria) and NS 1 Antigen positivity in age group between 15-60 years were selected. They were followed from the day of admission till they recovered clinically & were discharged or suffered complications & succumbed to death.

WHO CRITERIA

Clinical Criteria for Diagnosis of Dengue Fever

Dengue fever- Classical dengue fever is an acute febrile viral disease frequently presenting with two or more of the following- headache, bone or joint pain, muscular pain, retro-orbital pain, rash & leucopenia.

Dengue haemorrhagic fever- all must be present:-

1. Fever, or recent history of acute fever.
2. Haemorrhagic manifestations
3. Thrombocytopenia (100,000/mm^3 or less).
4. Evidence of plasma leakage due to increased capillary permeability manifested by one or more of the following:

- >20% rise in haemotocrit for age and sex.
- >20% drop in haemotocrit following treatment with fluids as compared to baseline.
- Signs of plasma leakage (pleural effusion, ascites or hypoproteinaemia).

Dengue shock syndrome- Four criteria for Dengue Haemorrhagic Fever with signs of circulatory failure.

NS1 Antigen in serum was detected by ELISA technique using ELISA kit of Panbio company as per manufacturer's instructions. Following investigations were done- Complete blood counts (CBC), peripheral blood film examination (PBF), IgM and IgG antibody detection. IgM & IgG were detected by kits based on rapid, solid phase *in vitro* immunochromatographic test, of SD (Standard Diagnostics) company. It is based on principle of antigen-antibody reaction. Samples were run in automated Haematology analyser Sysmex XP 100, 3-Part Differential Haematology Analyser by Transasia to obtain complete blood counts. This gives us platelet counts & mean platelet volume. Automated Haematology analysers work mainly on principle of either aperture impedance or light scattering (flow cytometry) technology. Others include fluorescence and light absorption techniques.

Platelets are counted in whole blood using principle of electrical impedance or electro-optical detection techniques. MPV is also derived by electrical impedance technique. Clinical features, platelet counts & mean platelet volume of selected patients were recorded daily. (Normal Mean Platelet Volume – 8-12 fl in Sysmex XP-100 3-Part Differential Haematology Analyser)

STATISTICAL ANALYSIS

Statistical analysis was performed with the SPSS, version 20 for Windows statistical software package (SPSS inc., Chicago, il, USA). The Categorical data were presented as numbers (percent) and were compared among groups using Chi square test. Groups compared for demographic data were presented as mean and standard deviation and were compared using student t-test, ANOVA Test and Post-Hoc Test Tukey Test to find out the most significant group among all the groups. Probability p-value <0.05 was considered statistically significant.

RESULTS

Out of total 200 dengue cases, commonest presentation was dengue fever (DF) (68%) followed by dengue haemorrhagic fever (DHF) (23%) and least were dengue shock syndrome (DSS) (9%). Males were in higher proportion as compared to females (with males 63.5% and 36.5% females) and M:F = 1.7:1. No significant difference was observed according to sex with severity of the cases. Cases of dengue were highest in 15 to 24 age group (younger age group). Proportion of cases decreased as age increased. The mean age of study group was 28.59±10.34 years with range 15 to 60 years [Table/Fig-1].

Fever was the presenting complain in all cases (100%). Except only 4 cases, all (196/200) i.e. 98% dengue cases had thrombocytopenia throughout the course of illness.

Higher proportion (61.11%) (11/18) with 8 to 12 fL MPV were presented with DSS when compared to those with <8 fL MPV. Higher proportion (55.15%) (75/136) of dengue fever and 56.52% (26/46) of DHF cases were in >12 MPV range. However, No significant difference was observed in Mean platelet volume with severity of disease [Table/Fig-2].

The mean MPV in DF, DHF and DSS was 0.39±2.022, 0.59±1.99 and 0.51±2.069 respectively but no significant difference was observed in Mean difference between MPV at the time of Minimal Platelet counts and at the time of discharge among spectrum of Dengue illness. (p=0.837 Not Significant) (ANOVA) [Table/Fig-3].

No significant relation was observed between IgM, IgG antibodies and serology with MPV (fL) (corresponding to minimal platelet counts attained during the course of illness) [Table/Fig-3].

Also, no significant relation was observed between IgM, IgG antibodies and serology with MPV (fL), at the time of discharge [Table/Fig-4].

AGE (in years)	Total		DF		DHF		DSS	
	Number	%	Number	%	Number	%	Number	%
15 -24	88	44	51	37.5	25	54.35	12	66.67
25 -34	62	31	45	33.09	13	28.26	4	22.22
35 -44	28	14	27	19.85	1	2.17	0	0.00
45 -54	15	7.5	7	5.15	6	13.04	2	11.11
>= 55	7	3.5	6	4.41	1	2.17	0	0
	200	100	136	100	46	100	18	100

[Table/Fig-1]: Age group wise distribution with severity
Chi-square = 20.106 with 8 degrees of freedom; Probability p = 0.010, Significant

MPV (fL) (corres-ponding to minimal platelet counts)*	Total	DF		DHF		DSS		Chi-square test
	Number	Number	%	Number	%	Number	%	
<8	2	1	0.74	1	2.17	0	0	2.959 with 4 df; p=0.565 Not Significant (NS)
8 to 12	90	60	44.12	19	41.3	11	61.11	
>12	108	75	55.15	26	56.52	7	38.89	
Total	200	136	100	46	100	18	100	
MPV (fL) at day of discharge	**Number**	**Number**	**%**	**Number**	**%**	**Number**	**%**	
<8	0	0	0	0	0	0	0	0.305 with 2 df; p = 0.859 NS
8 to 12	78	53	38.97	17	37	8	44.4	
>12	122	83	61.03	29	63	10	55.6	
Total	200	136	100	46	100	18	100	

[Table/Fig-2]: Mean platelet volume with severity
*MPV is corresponding to the lowest platelet counts of the patient, attained during his/her course of illness (before day of discharge)
NS - Not Significant df – degree of freedom

SEVERITY	NUMBER	MEAN	STD. DEVIATION	ANOVA
DF	136	.39	2.022	
DHF	46	.59	1.994	
DSS	18	.51	2.069	
Total	200	.45	2.012	0.837 NS

[Table/Fig-3]: Association of mean difference in mean platelet volume with severity of the disease

MPV (fL) (corres-ponding to minimal platelet counts)	Total	IgM		IgG		Sero Negative	Sero-Positive
		-	+	-	+		
<8	2	0	2	0	2	0	2
8 to 12	90	12	78	17	73	4	86
>12	108	9	99	17	91	3	105
Total	200	21	179	34	166	7.00	193
		1.54 with 2 df		0.75 with 2df		0.47 with 2 df	
		0.46 NS		0.75 NS		0.47 NS	
MPV (fL) at day of discharge	**Total**	**IgM**		**IgG**		**Sero Negative**	**Sero-Positive**
		-	+	-	+		
<8	0	0	0	0	0	0	0
8 to 12	78	11	67	15	63	5	73
>12	122	10	112	19	103	2	120
Total	200	21	179	34	166	7	193
		1.19 with 1df		0.23 with 1 df		1.95 with 1 df	
		0.275 NS		0.229 NS		1.95 NS	

[Table/Fig-4]: Mean platelet volume with serology

No significant difference was observed while correlating mean platelet volume with the treatment outcome. No significant difference was observed in Mean between MPV at the time of Minimal Platelet counts and at the time of discharge except in dengue fever cases [Table/Fig-5].

OUTCOME	NUMBER	MEAN of MPV	SD	p-value
DEATH				
MPV corresponding to minimal platelet counts	6	11.42	1.455	0.158 NS
At discharge	6	10.47	0.450	
RECOVERY (DF)				
MPV corresponding to minimal platelet counts	136	11.93	1.557	0.029 S*
At discharge	136	12.32	1.361	
RECOVERY (DHF)				
MPV corresponding to minimal platelet counts	45	11.91	1.831	0.068 NS
At discharge	45	12.51	1.174	
RECOVERY (DSS)				
MPV corresponding to minimal platelet counts	13	11.29	1.740	0.06 NS
At discharge	13	12.47	1.289	

[Table/Fig-5]: Association of mean of MPV with treatment outcome

*S - Significant

DISCUSSION

Dengue fever is a growing public health concern in most tropical countries [1]. In India, epidemics are becoming more frequent [2]. A total of 200 patients admitted to our hospital with the clinical features of dengue fever (according to WHO criteria) and NS1 Antigen positivity were studied.

Incidence of DF, DHF and DSS was 68%, 23% and 9% respectively. The present study included more in (63.5%) male & (36.5%) female patients, M:F=1.7:1 correspontding to the study by K Jayashree et al., (1.39:1) and Dash PK et al., (1.28:1) [6,8]. Cases were highest in 15 to 24 years age group. This was corresponding to the other studies by PM Ukey et al., and D Cecilia et al., in which maximum cases were noted in 15-30 years & 21-30 years respectively [9,10]. Fever was the presenting complain in all cases.

The association of thrombocytopenia with dengue infection has been proved to be significant (p<0.001). A total of 98% patients had thrombocytopenia. Study by M. Anuradha et al., showed thrombocytopenia in 89% of total patients [11].

No significant difference was observed in MPV with severity of diseases. In the study done by Dewi et al., there was no significant difference in MPV between DF, DHF and DSS (9.18±1.5 fL vs. 8.94±1.94 fL vs. 8.57±1.03 fL, p=0.761) [7]. Wiwanitkit et al., found that MPV for patients with DHF is not decreased & appears to be similar to that for the general healthy population [12].

No significant relation was observed between IgM, IgG antibodies and serology (seropositive or seronegative) with MPV (fL) (corresponding to minimal platelet counts attained during the course of illness). No significant relation was observed between them even at the time of discharge.

No significant difference was observed in Mean between MPV at the time of minimal platelet counts and at discharge in dengue cases except in dengue fever cases. This correlated with study done by Dewi et al & Viroj Wiwanitkit et al., [7,12].

CONCLUSION

A total of 200 patients admitted to the hospital with the clinical features of dengue fever (according to WHO criteria) and NS1 Antigen positivity were studied in our study. Present study had an objective of studying mean platelet volume in association with severity, serology & treatment outcome to assess its prognostic utility. MPV showed no significant correlation with severity, serology & treatment outcome, thus excluding its role in dengue cases. Mean platelet volume has not found to be an important prognostic parameter in dengue fever cases.

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