Serial Changes in Platelets and Outcomes in Dengue

Manas Thakur[1], Muralidhara Yadiyal[2], Christopher Pais[3], Dattatray Prabhu[4]

ABSTRACT

Introduction: With marked growth of the population, rapid urbanization, inappropriate sanitisation and proliferating trend of mosquitoes, there is substantial increase in dengue infections. The fatality rate due to dengue shock syndrome (DSS) can be brought down to as low as <0.2% with careful management. Understanding the factors which are responsible for progression of the disease to the severe stage and death is essential in determining the triage and management steps.

Material and methods: All patients suspected to have probable dengue / probable dengue fever with warning signs were admitted in government hospital attached to Kasturba Medical College, Mangalore and were given an option of enrolment in the study. After obtaining informed consent, all potentially eligible patients were screened for enrolment. All necessary blood samples needed to confirm dengue fever and other causes of fever were drawn on the first day. Platelet counts were done every day till they reach stable levels or till discharge.

Results: Out of 105 cases (Dengue Fever without complications), platelet counts (median values) were taken as a parameter. It was observed that the platelet counts are at a lowest level on day 2 and day 3 and later on day 4 and day 5 it improved. Friedman's test value = 228.612 and p value <0.001 which was highly significant.

Discussion: Thrombocytopenia is a distinctive feature of dengue and it has been described that its intensity correlates with the degree of viremia and with the magnitude of the immune response. It has been suggested that a progressive decrease in platelets may anticipate the severe form of dengue.

Keywords: Platelets and Outcomes, Dengue

INTRODUCTION

Dengue fever (DF), a viral disease (mosquito-borne), is transmitted by Aedes aegypti. It belongs to Flavivirus genus and has 4 serotypes, i.e. DEN Virus-1, DEN Virus-2, DEN Virus-3 & DEN Virus-4.

If one serotype infects a person, there will be lifelong immunity to that particular serotype. The manifestations are severe if a person gets infected with multiple serotypes. With the marked growth of the population, rapid urbanization, inappropriate sanitisation and proliferating trend of mosquitoes, there is substantial increase in dengue infections. Close observation of patients with judicious use of fluids is very crucial as there is no effective vaccine or antiviral therapy.[1] The fatality rate due to dengue shock syndrome (DSS) can be brought down to as low as <0.2% with careful management.[2] Understanding the factors which are responsible for progression of the disease to the severe stage and death is essential in determining the triage and

management steps.

In a study done by Malathesha et.al[3] it was concluded that peripheral blood parameters are very helpful for disease monitoring and can be useful in prediction of prognosis and most of the cases had raised hematocrit, lymphocytosis with atypical forms (plasmacytoid forms), monocytosis, basophilia & thrombocytopenia.

A study by Jayanthi et.al[4], proved that platelet count can be used to predict the complication and duration of hospital stay and hence better use of resources.

In this study, we attempt to observe the serial changes of platelets in DF and DHF/DSS and to identify any particular pattern in platelet count so as to aid in prognostication of disease.

MATERIAL AND METHODS

All patients suspected to have probable dengue / probable dengue fever with warning signs were admitted in government hospital attached to Kasturba Medical College, Mangalore and were given an option of enrolment in the study. After obtaining informed consent, all potentially eligible patients were screened for enrolment. All necessary blood samples needed to confirm dengue fever and other causes of fever were drawn on the first day. Platelet counts were done every day till they reach stable levels or till discharge (whichever is earlier). Following enrolment in the study, if the confirmatory ELISA-IGM for dengue was reported as negative or if the patient was diagnosed to have other illness or develops conditions mentioned under exclusion criteria, such cases were excluded from the final analysis.

[1]Post graduate, Department of Medicine. Kasturba Medical College, Mangalore. Manipal Academy of Higher Education, Manipal, Karnataka, [2]Associate Professor, Department of Medicine. Kasturba Medical College, Mangalore. Manipal Academy of Higher Education, Manipal, Karnataka, [3]Professor, Department of Medicine. Kasturba Medical College, Mangalore. Manipal Academy of Higher Education, Manipal, Karnataka, [4]Assistant Professor, Department of Anesthesiology. Kasturba Medical College, Mangalore. Manipal Academy of Higher Education, Manipal, Karnataka, India

Corresponding author: Dr Muralidhara Yadiyal, Associate Professor, Department of Medicine. Kasturba Medical College, Mangalore. Manipal Academy of Higher Education, Manipal, Karnataka- 576104, India

STATISTICAL ANALYSIS

The data was entered and analysed using SPSS-17 and was expressed in terms of Mean, Median & Proportion. The association between variables of interest were tested using Chi-Square Test and Students T-test.

RESULTS

Out of 115 patients in the study, 71(62%) were males and 44(38%) were females. Males predominance was seen in our study, probably reflects the working environment and travelling pattern of the males predisposing to mosquito bite and increased risk of dengue infection. Out of 115 Cases, it was found that 2.6% were below the age of 20, 34.8% were in between 21-30, 27% were in between 31-40, 22.6% were in between 41-50 and above 50 years only 13%. It was found

that mostly the young to middle age groups were affected, probably reflects the working environment. Out of 115 cases, 10 cases (8.7%) were DHF/DSS (with complications) and 105 cases (91.3%) were DF (without complications).

Friedman's test

D1-D6 (DAYS OF FEVER); N= Number of cases; IQR (Interquartile range); Data expressed in (mean & median +/- standard deviation); HS = Highly significant.

In the above table, the test was done to detect the differences in the platelet counts of all the 6 days. 115 cases were considered, platelet counts (median values) were taken as a parameter. It was observed that the median values of platelet count on day 2 & day 3 dropped as compared to day 1, and later on day 4 and day 5, it improved. Friedman's test value

	N	Mean	Std. Deviation	Median	IQR	Friedman test value	p value
D1	115	88052.17	57626.27	78000.00	39000-119000	223.215	< 0.001
D2	115	67026.09	48710.47	62000.00	24000-93000		HS
D3	115	49984.35	38966.20	40000.00	19000-68000		
D4	115	57530.43	38916.31	48000.00	25000-77000		
D5	115	87139.13	52756.29	79000.00	52000-101000		
D6	60	116900.00	59938.58	105500.00	72250-143000		
Table-1: Comparison of platelets							

	Wilcoxon signed rank test p value	
D2-D1	< 0.001	HS
D3-D1	< 0.001	HS
D4-D1	< 0.001	HS
D5-D1	0.786	
D6-D1	< 0.001	HS
D3-D2	< 0.001	HS
D4-D2	< 0.001	HS
D5-D2	< 0.001	HS
D6-D2	< 0.001	HS
D4-D3	< 0.001	HS
D5-D3	< 0.001	HS
D6-D3	< 0.001	HS
D5-D4	< 0.001	HS
D6-D4	< 0.001	HS
D6-D5	< 0.001	HS
Table-2: POST HOC Analysis:		

Compli-cations	N	Mean	Std. Deviation	Median	IQR	Friedman Test value	p value
Present							
D1	10	47100.00	35516.66	36000.00	14750-82250	19.257	< 0.001
D2	10	45700.00	29318.37	45000.00	17000-76000		HS
D3	10	38920.00	17565.67	33100.00	28500-48250		
D4	10	51800.00	25292.95	45500.00	37500-70750		
D5	10	70200.00	24665.77	73500.00	49500-90500		
D6	10	92800.00	40317.63	107500.00	55000-120000		
Absent							
D1	105	91952.38	57916.45	82000.00	41500-124500	228.612	< 0.001
D2	105	69057.14	49785.28	63000.00	24500-102500		HS
D3	105	51038.10	40308.41	44000.00	18000-71000		
D4	105	58076.19	40016.03	49000.00	25000-77500		
D5	105	88752.38	54479.14	82000.00	52000-104000		
D6	50	121720.00	62329.94	105500.00	80750-160000		
Table-3: Comparison of platelets in DF (without complications) & DHF/DSS (complications)							

	Complications Present		Complications Absent	
	Wilcoxon signed rank test p value		Wilcoxon signed rank test p value	
D2-D1	0.799		< 0.001	HS
D3-D1	0.415		< 0.001	HS
D4-D1	0.799		< 0.001	HS
D5-D1	0.074		0.429	
D6-D1	0.017	sig.	< 0.001	HS
D3-D2	0.262		< 0.001	HS
D4-D2	0.646		< 0.001	HS
D5-D2	0.047	sig.	< 0.001	HS
D6-D2	0.014	sig.	< 0.001	HS
D4-D3	0.139		< 0.001	HS
D5-D3	< 0.001	HS	< 0.001	HS
D6-D3	< 0.001	HS	< 0.001	HS
D5-D4	0.014	sig.	< 0.001	HS
D6-D4	0.013	sig.	< 0.001	HS
D6-D5	0.013	sig.	< 0.001	HS
Table-4: Post hoc analysis				

= 223.215 and p value < 0.001 which was highly significant.

Wilcoxon signed rank test

The above table shows the post hoc analysis of the platelet counts. It was done as the platelets values were not uniform among all the days. So, the platelet counts (median values) were compared and assessed and showed significant difference (p value< 0.001); highly significant.

Friedman's test

D1-D6 (DAYS OF FEVER); N= Number of cases; IQR (Interquartile range); Data expressed in {mean & median +/- standard deviation}; HS = Highly significant.

In the above table, platelets were taken as a parameter. The values were compared of all the days among dengue fever (with & without complications). The test was done to detect the differences in the platelets of all the 6 days.

Out of 105 cases (Dengue Fever without complications), platelet counts (median values) were taken as a parameter. It was observed that the platelet counts are at a lowest level on day 2 and day 3 and later on day 4 and day 5 it improved. Friedman's test value = 228.612 and p value <0.001 which was highly significant.

Out of 10 cases (Dengue Fever with complications), platelet counts do not show any pattern and are varying randomly, although the day to day variability is highly significant (p value<0.001) from D1-D6. Friedman's test value = 19.257.

Wilcoxon signed rank test:

The above table shows the post hoc analysis of the platelet counts in the cases of DF & DHF/DSS. This was done as the platelets were not uniform among all the days.

In all the 105 cases of DF without complications, day to day variability showed significant difference in most of the cases (p value </= 0.001) but among the 10 cases of DSS/DHF with complications, day to day variability was not significant on all the days.

DISCUSSION

This study was done to observe the daily pattern of changes & outcomes of haematological parameters in dengue fever in an adult population. The present study was a hospital based cross-sectional study in which 115 samples of NS1 & IgM dengue seropositive patients who met the inclusion criteria were followed up for a period of five to six days after obtaining a written informed consent. Daily assessment was done during the hospital stay. Lab investigations were ordered as per pre-set pro-forma and analysis was done.

Out of the 115 cases, male dominance was seen (62%) and the male to female sex ratio was 1.63:1. This finding probably reflects the working environments and outdoor living and travel patterns of males when compared to females in this population, thereby increasing their risk of dengue infection. In a study done by Rachel Daniel et.al[5] 250 cases were considered, out of which male dominance was seen in 52% of the cases and male: female ratio was 1.08:1. A similar study by Ritu karoli et.al[6] included 138 cases, in which 58% were male and male: female ratio was 1.37:1.

In the study by Rachel Daniel et.al[5] 166 cases (66.4%) were diagnosed to have Dengue fever (DF) and 84 cases were diagnosed to have DHF/DSS (33.6%). Similarly, in a study done by Ritu karoli et. al[6], 96 cases (70%) were of DF and 42 cases (30%) were of DHF/DSS. In comparison, my study had 105 cases (91%) of DF and 10 cases (9%) of DHF/DSS. This might be due to an increase in the alertness among medical fraternity and public following the initial epidemic and the availability of diagnostic tools in the hospital have contributed to the increased detection of cases.[7]

Out of 221 cases, 43 (19.4%) showed thrombocytopenia (<150000) in the study done by Malathesha et.al[3] in all the cases without complications (DF). In the present study, out of 105 cases (DF), 89 cases (84%) showed platelets below 150000 on day 1. As the cut off used for the platelet counts are variable in different studies so the results cannot be compared. The drop in platelets may be due to depression of bone marrow observed in acute stage of dengue virus infection.[8] Other explanations can be taken in consideration as there are direct infection of the megakaryocytes by virus leading to increased destruction of the platelets or the presence of antibodies directed against the platelets.[9]

In all the DF cases, there was initial fall in the counts (TLC & Platelets) and later both started improving in the recovery phase. The observation was that the total leucocyte counts starts improving one or two days before the platelet counts.

Thrombocytopenia is a distinctive feature of dengue and it has been described that its intensity correlates with the degree of viremia and with the magnitude of the immune response. It has been suggested that a progressive decrease in platelets may anticipate the severe form of dengue. However, the evidence available in the literature supporting these assertions is scarce.[10]

CONCLUSION

Our study showed a clear picture of thrombocytopenia in all our complicated dengue cases and hence attempting to

increase platelet counts via transfusion in the absence of major bleeding has not conferred protective benefits from bleeding in dengue. Rather, early recognition of dengue, especially severe dengue and DHF, with prompt correction of hemodynamic parameters, remains the cornerstone of avoiding haemorrhage and ensuring good clinical outcomes.

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