International Journal of Advances in Medicine
Paul D et al. Int J Adv Med. 2023 Mar;10(3):223-227
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20230361

Original Research Article

Evaluation of platelet indices in dengue fever in a tertiary care hospital in Bangladesh

Debatosh Paul[1], Amit K. Pramanik[2]*, Sanchita Biswas[3], Chitra Das[4], Mohammad T. Islam[5]

[1]Department of Laboratory Medicine, [5]Department of Internal Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[2]Department of Transfusion Medicine, Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[3]Department of Paediatrics, Dhaka National Medical College, Dhaka, Bangladesh
[4]Department of Biochemistry, Mymensingh Medical College, Mymensingh, Bangladesh

Received: 30 December 2022
Accepted: 31 January 2023

***Correspondence:**
Dr. Amit K. Pramanik,
E-mail: amit34th@gmail.com

ABSTRACT

Background: Dengue fever is the most rapidly spreading mosquito-borne viral diseases in the world. Some evidence suggests that platelet indices may have diagnostic and prognostic value in Dengue fever. The aim of the study is to evaluate platelet indices and to find their correlation between platelet count in Dengue fever.
Methods: This retrospective cross-sectional study was conducted through the use of stored data in Bangabandhu Sheikh Mujib Medical University (BSMMU) dengue cell from July 2019 to September 2019 at department of laboratory medicine and department of internal medicine, BSMMU, Dhaka. Among them, clinical records of 260 cases are preserved in a structured clinical record form (CRF). After ethical clearance from institutional review board (IRB), form clinical records of 260 cases which were preserved in a structured CRF patients who fulfilled the inclusion and exclusion criteria was selected as study population.
Results: Platelet indices (MPV and PDW) were statistically significant difference among different platelet counts ($p<0.05$). There was significant negative correlation between platelet count and PDW ($r=-0.228$, $p\leq0.001$). There was also negative correlation between platelet count and MPV ($r=-0.106$) which was not statistically significant ($p=0.088$).
Conclusions: Platelet indices are useful parameters in dengue infection. Other than platelet count, PDW and MPV are useful to monitor dengue fever.

Keywords: Dengue fever, Platelet indices, MPV, PDW

INTRODUCTION

Dengue fever is the most common arthropod borne disease caused by dengue virus. It is a vector borne arboviral disease transmitted by predominantly by *Aedes aegypti* and *Aedes albopictus* mosquito. Man and mosquito are reservoir of the infection.[1] Increases in the incidence of dengue outbreaks are seen during the monsoon and post-monsoon seasons. Children and young adults are the population that are most affected.[2] Dengue fever was first reported in Bangladesh in 1964 when it was known as "Dacca fever" and since then it has remained endemic. The seroprevalence was found to be 13% in 1997. In 2000, the reported dengue cases were 5,551 with 93 deaths in different hospitals of Bangladesh. It was then declared as an outbreak of dengue at the national level.[3] Since then the number of hospitalized patients has exceeded 3000 patients in six times: 6232 in 2002, 3934 in 2004, 3162 in 2015, 6060 in 2016, 10148 in 2018 and 81832 by the end of September 2019.[4] The pathogenesis of dengue fever has still not been elucidated completely. Host response is considered to be a significant contributor in the pathogenesis and pathology of dengue.[5] One of the most common laboratory findings in dengue is

thrombocytopenia.[6] 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. Recently, novel platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW) and platelet to large cell ratio (PLCR) have been investigated as prospective platelet activation markers.[7] Platelet volume, a marker of platelet function and activity is measured as MPV by hematology analyzers. 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] PDW directly measures variability in platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology. It is an indicator of platelet anisocytosis. PDW is increased in the presence of platelet anisocytosis. There is a direct relation between MPV and PDW, that is, a high PDW is associated with a high MPV.[9] Platelet indices are reported by most automatic and semi-automatic cell counters used in most hospitals. Despite advances in diagnostic modalities and treatment strategies, there is limited data on dengue fever and its relation with platelet parameters. Platelet indices measurement holds great promise of being this predictor. In this context, this study aims to evaluate the platelet parameters in patients of dengue fever. This may be of great assistance in the management of dengue fever patients in future and at present.

METHODS

This retrospective cross-sectional study was conducted at Department of Laboratory Medicine in collaboration with Department of Internal Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from July 2019 to September 2019. Patients admitted in the dengue cell of BSMMU in the year 2019 from July to September was comprised our study population. Among them, clinical records of 260 cases were preserved in a structured clinical record form (CRF). Only those, with antigen/antibody supported cases was enrolled in the study. A structured CRF was maintained during the management of dengue cases admitted in dengue cell BSMMU during 2019 outbreak. This CRF contains socio-demography, clinical presentation, laboratory reports and management given during that period. Dengue cases were diagnosed as per diagnostic criteria given by the National guideline of management of dengue fever. Severity of illness were categorized accordingly. Disease complications were noted and management given was directed by following the National guideline. After ethical clearance from institutional review board (IRB), form clinical records of 260 cases which are preserved in a structured CRF patients who fulfilled the inclusion and exclusion criteria was selected as study population. All dengue cases with antigen/antibody confirmation were included in this study. Cases with incomplete data was discarded from the analysis.

RESULTS

This retrospective cross-sectional study was carried out to explore platelet indices in Dengue fever. From clinical records of 260 cases were analyzed. Table 1 shows the age distribution of the patients among five platelet groups. Out of 206 patients, maximum cases 76(36.9%) of the patients' platelet range 51,000 to 1,0000, 73 (35.4%) patients within 1,0000 to 1,50000, 64 (31.1%) platelet group more than 1,50000, 35 (17.0%) patients had 21,000 to 50,000 and minimum percentage 12 (5.8%) in platelet count less than 20,000. The mean age of the patients among five platelet groups were not statistically difference.

Table 2 shows the sex distribution on basis of platelet count. Maximum patients 171 (65.8%) were male and rest 89 (34.2%) were female. The prevalence was found to be high in males. No significant difference of sex among different platelet indices ($p>0.05$). Table 3 shows the comparison of platelet indices (MPV and PDW) among different platelet count groups of the study patients. Mean MPV and PDW were statistically significant difference among different platelet indices ($p<0.05$).

Table 1: Comparison of age among different platelet groups of the study patients (N=260).

Age group (years)	Platelet, no. (%)					P value
	<20 (n=12)	21-50 (n=35)	51-1 lac (n=76)	1-1.5 lac (n=73)	>1.5 lac (n=64)	
<20	2 (16.7)	8 (22.9)	22 (28.9)	23 (31.5)	19 (29.7)	
21-30	4 (33.3)	11 (31.4)	23 (30.3)	22 (30.1)	25 (39.1)	
31-40	3 (25.0)	6 (17.1)	13 (17.1)	17 (23.3)	11 (17.2)	
41-50	1 (8.3)	5 (14.3)	12 (15.8)	5 (6.8)	5 (7.8)	
51-60	1 (8.3)	3 (8.6)	3 (3.9)	4 (5.5)	2 (3.1)	
>60	1 (8.3)	2 (5.7)	3 (3.9)	2 (2.7)	2 (3.1)	
Total	12 (100.0)	35 (100.0)	76 (100.0)	73 (100.0)	64 (100.0)	
Mean±SD	35.8±15.6	31.9±16.8	30.8±15.4	28.9±14.8	27.5±13.2	0.333^{ns}

Data were expressed as frequency and percentage and mean±SD, analysis of variance (ANOVA) test was performed to compare among groups, ns=not significant

Table 2: Association of sex among different platelet type of the study patients (N=260).

Sex	Platelet, no. (%)					P value
	<20 (n=12)	21-50 (n=35)	51-1 lac (n=76)	1-1.5 lac (n=73)	>1.5 lac (n=64)	
Male	7 (58.3)	24 (68.6)	49 (64.5)	44 (60.3)	47 (73.4)	0.537^{ns}
Female	5 (41.7)	11 (31.4)	27 (35.5)	29 (39.7)	17 (26.6)	
Total	12 (100.0)	35 (100.0)	76 (100.0)	73 (100.0)	64 (100.0)	

Figures in the parentheses indicate corresponding percentage, Chi-squared test (χ^2) was done to analyze the data, ns=not significant

Table 3: Comparison of platelet indices (MPV and PDW) among different platelet count groups of the study patients (N=260).

Absolute count	Platelet (mean±SD)					P value
	<20 (n=12)	21-50 (n=35)	51-1 lac (n=76)	1-1.5 lac (n=73)	>1.5 lac (n=64)	
MPV	11.75±1.72	11.10±1.61	11.82±1.62	11.78±1.32	11.01±1.31	0.003^{ns}
PDW	67.80±17.82	64.59±11.33	62.48±12.70	61.32±6.68	57.63±7.49	0.002^{s}

Data were expressed as mean±SD, ANOVA test was performed to compare among groups, s=significant, ns=not significant

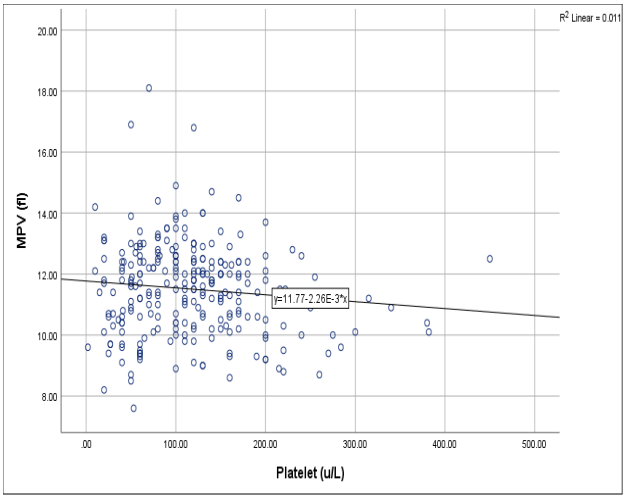

Figure 1: Negative correlation between platelet and MPV (r= -0.106). It was observed that the Pearsons's correlation was not statistically significant (p=0.088).

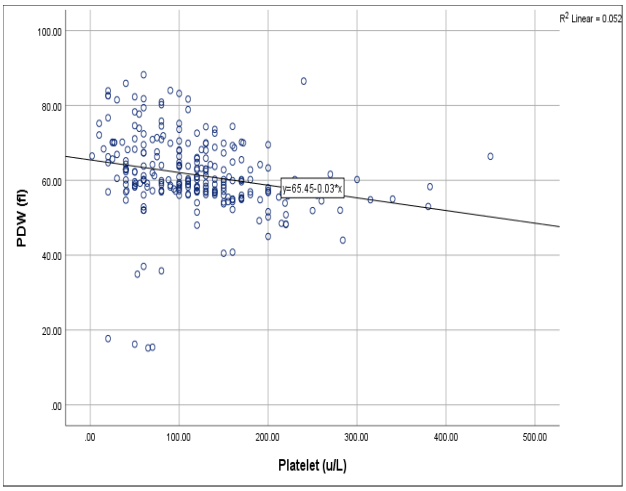

Figure 2: Negative correlation between platelet and PDW (r= -0.228). It was observed that the Pearsons's correlation was statistically significant (p≤0.001).

DISCUSSION

Dengue fever is a growing public health concern in tropical countries like Bangladesh. It is a global re-emerging disease. Various parameters have been used to predict the complications of the Dengue fever. MPV and PDW are used to predict the trend in the platelet count and risk of bleeding manifestations. The aim of this study is to evaluate the platelet parameters in patients of dengue fever.

In present study, the mean age of the patients among five platelet groups were not statistically difference (p=0.333). With decreasing platelet count, age also increasing. In this study, we found majority of patients were found in third decade of life. Majority of patients were in third to fifth decade of life that is from age group 26 to 45 years (54.5%) by another study.[10] Maximum cases in 41 to 50 years (33.1%) and least in 21 to 30 years (21%) was found in a recent study.[11] These results were consistent with our study. There was no significant difference of sex among study subjects in this study (p=0.537). Maximum patients 171 (65.8%) were male and rest 89 (34.2%) were female. The prevalence was found to be high in males. This finding was supported by related previous studies.[10,12]

In present study, comparison of platelet indices that is MPV and PDW between five groups were done. It was observed that MPV and PDW were significantly difference between five groups (p=0.003, p=0.002 respectively). A recent study showed that MPV and PDW were significantly difference between three groups (p=0.033, p=0.03 respectively).[13] Another previous study found that MPV and PDW were significantly difference between three groups (p<0.001, p<0.001 respectively) which was consistent with our study.[11]

In this study, it was found that there was significant negative correlation between platelet count and PDW (r=-0.228, p<0.001). A recent study reported that significant negative correlation between platelet count and PDW (r=-

0.267, p<0.001).[10] Another study found similar result (r=-0.3097, p=0.0017).[12] These results were consistent with our result. It was reported that platelet count was negatively correlated with MPV (r=-0.106) which was not statistically significant (p=0.088). A previous study also found no signifant correlation between platelet count and MPV which was consistent with our study.[14] Another study found significant negative correlation between platelet count and MPV (r=-0.247, p=0.004).[10]

Defect in Dengue fever are multifactorial mechanisms that include thrombopathy, coagulopathy and vasculopathy. Thrombopathy means the thrombocytopenia and platelet dysfunction. Many factors can contribute to the onset of thrombocytopenia in DF, varying from a reactive immune response against platelets to decreased platelet production. The depression in the bone marrow observed in dengue fever in the acute stage may account for thrombocytopenia. In addition, direct infection of megakaryocytes by dengue virus could lead to an increased destruction of platelets.[15] Platelets are involved in hemostasis, tissue repairing, and infection. MPV has been evaluated as a diagnostic tool in different conditions with thrombocytopenia with contradictory results. It has been demonstrated that MPV has sufficient sensitivity and specificity to discriminate aplastic anemia, bone marrow disease, hypoproductive thrombocytopenia, and bone marrow metastasis of solid tumor.[8,16,17] However, it has been reported that although MPV may be used as an initial suggestion of bone marrow disease in thrombocytopenic patient, it has limited sensitivity and specificity.[18] Serially observing the MPV and platelets may guide a clinician in an important subset of patients in DF and severe dengue where the mechanism of thrombocytopenia is largely marrow suppression-initial MPV significantly low and the thrombocytopenia recovery following the MPV. Increased MPV indicates increased platelet diameter, which can be used as a marker of production rate and platelet activation. During activation, platelets' shapes change from biconcave discs to spherical, and a pronounced pseudopod formation occurs that leads to MPV increase during platelet activation.[19] Platelets with increased number and size of pseudopodia differ in size, possibly affecting platelet distribution width (PDW) which increases during platelet activation. 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.[20]

These platelet indices show sensitivity to dengue fever thus reflecting a predictive marker for diagnosing dengue fever in endemic area.

Limitations

As it is retrospective study, there was risk of confounding. The study population was selected from only one tertiary level hospital in Dhaka city. Therefore, sample may not be representative of the selected population of the country. Patients with bleeding manifestation were not sorted.

CONCLUSION

Platelet indices are useful parameters in dengue infection. Other than platelet count, PDW and MPV are useful to monitor dengue fever. Decrease MPV and increase PDW is significant in thrombocytopenia and Platelet indices plays significant role in early predictive diagnosis and severity of dengue in endemic area.

ACKNOWLEDGEMENTS

Authors would like to thank the authority of the Department of Internal Medicine, BSMMU and Department of Laboratory Medicine, BSMMU, for their nice cooperation during sample collection, laboratory procedure and also thankful to the study subjects for their active and enthusiastic participation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Paul D, Pramanik AK, Biswas S, Das C, Islam MT. Evaluation of platelet indices in dengue fever in a tertiary care hospital in Bangladesh. Int J Adv Med 2023;10:223-7.