Original Article

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Correlation of Mean Platelet Volume and Hemorrhagic Manifestations in Dengue Fever: An Observational study

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ABSTRACT

Background: *Platelet count has been used extensively to assess the severity of dengue fever, direct treatment and forecast prognosis. However, because of its exclusive use, the potential of alternative platelet indices, such as Mean Platelet Volume (MPV) has not been investigated. The association of MPV with hemorrhagic manifestations in patients with dengue fever is observed through this research.*

Materials and methods: *This prospective observational study was conducted in a tertiary care hospital in Chattogram, Bangladesh for a period of six months. A total of 100 patients with confirmed dengue infection who fulfilled the inclusion criteria were followed from the day of admission to recovery. Clinical and laboratory findings, including platelet parameters were noted. Mann Whitney U Test was performed for correlation identification between MPV and hemorrhagic manifestations in Dengue Fever.*

Results: *Out of 26 patients hemorrhagic manifestation. Around 50% of the patients with had a low MPV (<9fL) whereas among 74 patients without bleeding manifestation - higher MPV (>10fL) was noted in 96% of patients. A significant correlation was observed between low MPV and hemorrhagic manifestation (p value <0.001).*

Conclusion: *Mean platelet volume has the potential to serve as an additional laboratory marker to predict hemorrhagic manifestation in patients with dengue fever.*

Key words: Dengue; Hemorrhage; MPV; Outcome; Platelet.

Introduction

Dengue Fever (DF) is an arboviral disease caused by one of the four serotypes of Dengue virus (DEN 1-4) belonging to the family Flaviviridae. The primary vector for the disease is Aedes aegypti mosquito, which is widely spread in the tropical and subtropical regions. It is an imperative public health challenge globally with more than 2.5 billion people at risk of infection in the tropics and subtropics.[1] Annually, an estimated 390 million (284-528 million) dengue infection occurs in around 129 countries, of which 70% of the burden contributor is in Asia.[1] The disease ranges from a mild subclinical infection to acute febrile illness to full blown shock.

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In 2009, the WHO revised the classification of the disease from 1997 dengue case guidelines (Dengue fever, dengue hemorrhagic fever and dengue shock syndrome). The current scheme is based on the levels of severity, i.e. dengue without warning signs, dengue with warning signs (Abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy, restlessness, hepatomegaly and increased haematocrit concurrent with a rapid decrease in platelet count) and severe dengue.[2] The modification was done as dengue affects different age groups and a wide geographical area. The course of DF depends on numerous underlying factors such as age, comorbid conditions, infecting serotype and secondary infection with other serotypes/organisms. Of all the clinical features, the disease severity and mortality appear to depend maximum on the occurrence of bleeding manifestations, which can vary from minor petechiae and gum bleeding to life-threatening internal hemorrhage and such manifestations are assumed as a result of underlying thrombocytopenia.[3] The exact mechanisms of thrombocytopenia in DF remain unclear, although many theories have been postulated for it.[4,5]

The platelet count has been used to predict the course of DF in a patient since long, so as to predict the likelihood of bleeding, severity of illness and prognosticate patient recovery. Nevertheless, there are various drawbacks associated with this parameter.

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Foremost, apart from the platelet count, effective hemostasis also depends on the platelet activity. Relying solely on platelet count to predict bleeding outcomes can be premature. Secondly, analytical errors by the automated analyzers result in falsely low platelet counts in routine practice, due to either giant platelets or platelet aggregates in the blood. Such analytical errors are common during stages of inflammation. Furthermore, an artefactual rise in automated platelet count due to bacterial overgrowth in the sample may mask underlying thrombocytopenia and lead to inaccurate results.[6] This may lead to unnecessary platelet transfusions, which have their own associated risks and cost implications.

Recently, novel platelet indices such as Mean Platelet Volume (MPV) have been investigated as prospective platelet activation markers.[7] Mean Platelet Volume is a surrogate marker of bone marrow activity, a high MPV indicates increased megakaryocyte activity. A low MPV indicates marrow suppression. Platelets with increased number and size of pseudopodia differ in size, possibly affecting platelet function.[7]

The exclusive dependence on platelet count as a management criterion for DF has prevented the potential efficacy of other indices like Mean Platelet Volume (MPV) from being explored and recognized. These indices are calculated and given by every 3-part differential cell counter, but are often not reported, possibly because their utility in clinical practice has not been well-established. Based on these concepts, the platelet indices and the lack of substantial evidence in their utility, this study was formulated to recognize whether this indices can be used as better alternatives or as adjuncts to platelet count in the evaluation of severity in dengue patients.

Attempt was taken explore the association of MPV with hemorrhagic manifestations in patients with dengue fever.

Materials and methods

This study was a hospital based observational study. The patients who presented with dengue fever with thrombocytopenia in the Department of Medicine, Marine City Medical College & Hospital, Chattogram, Bangladesh from August 2023 to January 2024 were taken in study. The informed consent was obtained from each patient prior to commencement of this study. The detailed history and examination was carried out and each patient was investigated as per designed proforma.

Inclusion criteria

- Patients with a positive dengue serology (Non-Structural protein 1 antigen-NS1or IgM)
- Platelet count <50 thousand/cumm.

Exclusion criteria

- IgG positive cases
- Inherited Disorders of thrombocytopenia
- Patients who received platelets transfusion during the study
- Patients on antiplatelet medications.

Cases with confirmed dengue infection were followed from the day of admission till they either recovered clinically and were discharged or suffered from complications. Demographic details, clinical features and warning signs were noted.

Laboratory findings including platelet parameters (Count and MPV) were recorded using Mythic-22AL Automated Hematology Analyzer on venous samples collected in Ethylene-Diamine Tetra-Acetic Acid (EDTA) vials. The samples were analyzed within one hour of sample collection.

The patients were divided into 2 categories i.e. with hemorrhage and without hemorrhage. The indices were compared between these groups to look for any association with MPV irrespective of their platelet count.

Data was collected and entered into Microsoft Office Excel Sheet 2019. Statistical analysis was performed using the latest SPSS version 23 software, including descriptive analysis. Mann Whitney U Test was performed on the presence of hemorrhage and MPV irrespective of Platelet Count. Any p value of <0.05 was considered significant.

Results

Table I Sex distributions(n=100)

	Frequency	Percent (%)
Female	42	42.0
Male	58	58.0
Total	100	100.0

Table I reflects gender distributions where male was 58(58%) and female was 42(42%)

Table II Age group (n=100)

	Frequency	Percent (%)
<20 years	44	44.0
21-30 years	18	18.0
31-40	20	20.0
41-50 years	6	6.0
>51 years	12	12.0
Total	100	100.0

Table II depicts age group distributions where younger age groups were affected more than the older ones, less than 20 years were 44%.

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Table III Clinical Data (n=100)

Variables	Number	Percent (%)
Fever	100	100
Aches and pain	98	98
Eye pain	8	8
Headache	22	22
Vomiting	68	68
Diarrhoea	10	10
Rash	20	20
Bleeding	26	26
Elevated liver enzymes	26	26

Its observed from above table that different symptoms where all patients had fever, 98(98%) patients suffering from aches and pain, 44(44%) had headaches and 68(68%) had vomiting. Other symptoms were rash, bleeding, diarrhea and eye pain.

Table IV Serological test (n=100)

Tests	Number	Percent (%)
NS1	61	61
IgM	37	37
NS1 & IgM	2	2

Table IV showing 61(61%) patients were positive for dengue NS-1 antigen, 37(37%) patients were positive for dengue IgM by ELISA and 2(2%) patients were positive for both NS1 and IgM.

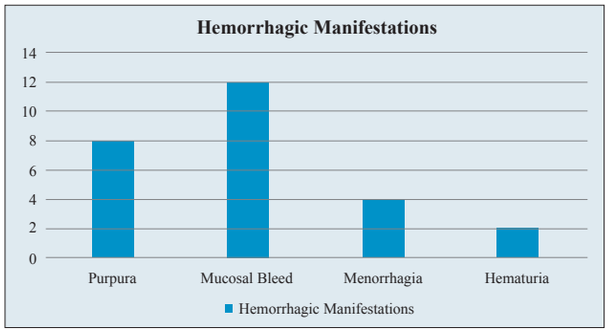

Figure 1 Hemorrhagic manifestations (n=100)

Out of 100 patients, 8 (30.77%) patients had purpura, 12 (46.15%) patients had mucosal bleeding, 4 (15.38%) patients had menorrhagia and 2 (7.69%) had hematuria.

Table V Comparison of hemorrhagic manifestation with MPV (n=100)

MPV (Femtoliter)	Hemorrhagic Manifestation		Mann Whitney U Test (p Value)
	Yes (n=26)	No (n=74)	
	9.78	11.46	<0.001

The patients who had hemorrhagic manifestation those 26 patients MPV was 9.78 fL whereas the rest 74 patients MPV was detected as 11.46 fL

Discussion

Dengue infection is associated with an increase in the vascular permeability and thrombocytopenia. The latter is also recognized by the WHO as a marker of clinical severity. The exact cause of thrombocytopenia in DF has not been elucidated. Possible pathogenesis includes direct suppression of the bone marrow by the virus, anti-dengue antibody mediated damage, peripheral consumption of platelets due to high levels of platelet-activating factor, isolated viral replication in the platelet or abnormal pooling of blood.[8] Studies have shown that DF is characterized by increased platelet activation (As evidenced by increased expression of p- selectin on the platelet surface) increased apoptosis (As shown by increased phosphatidylserine levels) and complement mediated destruction; all of which account for thrombocytopenia.[9]

Similar to these data, a case-control research by Bashir et al. on 334 patients with DF revealed lower levels of MPV and platelet count with increased value of PDW.[10] It also exhibited that MPV <9 fL and PDW >13 fl had very high sensitivity for DF. A considerable sensitivity and specificity was recorded by Hardeva et al. for low platelet count and MPV values, and high PDW, which can be used as a predictor of the severity of dengue infection.[11] Krishnamurthy et al. and Kumar et al. also observed similar findings in their respective research.[12,13]

It has been well established that a low platelet count is associated with increased risk of developing bleeding and other complications.[14] This is also in accordance with this observations. However this research having a combination of markers for relation is more efficient than relying on a single parameter alone. Platelet activation leads to a change in shape from biconcave to spheroid and causes the formation of pseudopodia, which affects the values of MPV and PDW.[15,16] Observing MPV and platelet count trends together can help interpret the major contributory cause of thrombocytopenia in a patient and thus, accordingly aid in assessing the need for transfusion. Plateletcrit is identical to hematocrit, which incorporates MPV and platelet count, and can predict the requirement of platelet transfusion.[15] In a research on MPV and plateletcrit, it was observed that low MPV was associated with high chances of bleeding and low plateletcrit value can identify the need of platelet transfusion.[17]

An increasing MPV suggests a rapid marrow response (a left shift) with the release of newly synthesized, large platelets that increase the overall MPV.[18] In this scenario, the low platelet count is largely due to

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increased peripheral destruction. The combined presence of low platelet count and high MPV represents adequate marrow functioning and platelet recovery.[15] A wait-full watch may suffice in such a case, hence averting the need for transfusion.[19]

The study was done to determine whether the Mean Platelet Volume can be used as predictor of hemorrhagic diathesis in patients with thrombocytopenia due to dengue fever. This was achieved by comparing the said parameter with the bleeding manifestations observed.

The lowest platelet count noted was 4, 000/Cumm and highest was 50,000/Cumm, with the mean value being 28,000/Cumm. The mean MPV in the study population was 10.44±1.82 fL.It was obvious that bleeding manifestations were seen with lower platelet counts. However, there were other factors adding to this. As evidenced by the analysis, a lower mean platelet volume was associated with increased risk of bleeding. The mean MPV for the patients with bleeding manifestations was found to be 9.78 fL ($p < 0.001$) as opposed to 11.46 fL ($p < 0.001$) in those without bleeding manifestations.

Conclusion

Overall, around 50% of the patients with bleeding manifestations had a low MPV (<9fL) whereas higher MPV (>10fL) was noted in 96% of patients without any hemorrhagic manifestations. Normal range of MPV is 7.5 to 11.5 femtoliters (fL). So, this can aid for the management of severe catagory of dengue patients, reducing the morbidity and morality.

Disclosure

The authors declare no conflict of interest.

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