Original Article

Platelet Indices and the Severity of Dengue Infection in Children

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ABSTRACT

Aim: Dengue is becoming endemic in India. The reported case-fatality rate in India is 3-5%. Thrombocytopenia is the most common finding. Platelet indices are gaining importance in the illness. To study the platelet indices in children with dengue infection and to note their relationship with the severity of disease.

Materials and Methods: Observational record-based study done over 12 months at a medical college hospital in costal Karnataka. Platelet parameters were noted from the hospital-based data system and compared with the severity of disease (Bleeding score, Severity score, Warning signs and Duration of stay).

Results: Out of 125 dengue positive patients studied, 83% had mean platelet volume below 9fl, 68% had platelet distribution width below 18, 64% had plateletcrit (PCT) below 0.1%, 57% had a platelet count fall below 1 lakh during their illness. PCT showed a significant correlation (p=0.001) with decreasing and increasing trends of the platelet count and a similar relation to the severity of the disease. Patients had a longer duration of stay (>4days) when platelet counts decreased to less than 1 lakh during their illness compared to those with more than 1 lakh (73% vs 35%). Platelet counts below 1 lakh were noted in 85% (37 of 44) of patients with warning signs as compared to 41% (34 of 81) of patients without warning signs.

Conclusion: Platelet indices are decreased in dengue infection. A decreased platelet count and PCT correlate with the severity of the infection.

Keywords: Platelet indices, dengue infection, severity

Introduction

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 (1) and an estimated 390 million dengue infections occur annually in around 125 countries worldwide (2). 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. It is a vector borne arboviral disease transmitted by Aedes mosquitoes (3).

One of the most common laboratory findings in dengue is thrombocytopenia (3). Possible mechanisms of thrombocytopenia could be, direct bone marrow suppression by the virus, anti-dengue antibody-mediated platelet destruction, peripheral consumption of the platelets and isolated viral replication in the platelets. Thrombocytopenia leads to bleeding although the platelet count may not directly correlate with the bleeding manifestations (4). Bleeding in dengue can vary from minor petechiae to severe haemorrhage causing the death of the patient (5).

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Platelet indices like mean platelet volume (MPV), platelet distribution width (PDW) and Plateletcrit (PCT) are being investigated as prospective platelet activation indicators. 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. The normal range for MPV is 8.9-11.8 fL (6). 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. 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 = platelet count × MPV/10.000. The normal range for PCT is 0.22-0.24% (5).

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 in the paediatric population and its relation with platelet parameters. This study aims to fill in some of these gaps by describing the severity of dengue infection in children, particularly with relation to platelet indices.

Materials and Methods

It is an observational record based study done over a period of 12 months between July 2017 to July 2018. 125 cases coming under the inclusion criteria admitted as an inpatient in our Medical college Hospital were included in the study. The approval was obtained from the Father Mullers Medical College Institutional Ethics committee and the waiver of consent was approved with approval number: FMMCIEC/CCM/453/2018.

All children aged less than 15 years (1 month to 15 years) presenting with features of suspected or probable dengue as per WHO guidelines with positive serology (NS1 or immunoglobulin M (IgM) positive by rapid card test or ELISA) were included in the study. Children who were IgM or NS1 negative (those who cannot be proven as "probable or confirmed dengue") and children with a pre-existing chronic disease which may interfere with the assessment of the complications of dengue infection were excluded from the study.

Demographic features, clinical features, warning signs and duration of stay were noted from inpatient records. Serology and platelet parameters were noted from the hospital-based data system. Bleeding score, severity score, warning signs and duration of stay were the parameters used to assess the severity of illness.

The study population was divided into two categories with respect to each platelet indices. Normal reference ranges were used in categorizing the study population. A platelet count of 1 lakh, PCT of 0.22, MPV of 9fl and PDW of 18 were considered as cut off points (4-7) to categorize the cases into two subgroups. Severity parameters were compared between the 2 subgroups with respect to each platelet indices.

Severe abdominal pain, persistent vomiting, bleeding gums, vomiting blood, rapid breathing, and fatigue/restlessness were considered as warning signs as described by the World Health Organization. Based on the site and type of bleeding (data obtained from inpatient case records), a bleeding score was assigned to each patient as depicted in Table I (8). Each patient was classified into one of the four vascular leakage categories as depicted in Table II according to the overall severity of hemo-concentration and/or the development of shock (9).

Statistical Analysis

Data was entered into Microsoft Office Excel Sheet 2010. Statistical analysis was done using SSPS-21 software. Statistical analysis of the data included descriptive analysis and differences between groups (based on dengue severity scores) as Pearson's correlation or chi-square tests. Any p value of <0.05 was considered as significant.

Results

A total of one hundred and twenty-five cases were

Table I. Bleeding scores

Bleeding score	Description
0	No bleeding
1	Petechiae
2	Epistaxis or gingival bleeding, menorrhagia
3	Gastrointestinal bleeding
4	Intracranial bleed, intrapulmonary bleed

Table II. Severity scores

Severity score	Description
1	10% or less change in hematocrit
2	10% to 20% change in hematocrit
3	20% or more change in hematocrit and/or evidence of fluid accumulation on a radiograph or ultrasound image.
4	Dengue shock syndrome

included in the study. Among these, 42% (52) were females and 58% (73) were males. The age-related demographics showed that 17% (21) of patients belonged to the age group of 6 months to 5 years, 34% (42) patients were in the age group of 5-10 years and 49% (62) were in the age group of 10-15 years. Serological parameters showed that 77% (96) of patients were positive for NS1, 12% (15) were positive for IgM, 11% (14) were positive for NS1 and IgM. Platelet indices of all the enrolled cases were analysed and minimum values noted during the stay were considered for grouping.

Out of one hundred and twenty-five cases considered, 57% had their platelet count fall to less than 100.000 (10.4% to less than 25.000; 9.6% between 25.000-50.000; 36.8% between 50.000-100.000) compared to 43% of cases in whom the platelet count persisted above 100.000 during their illness. 78% of our cases had PCT fall to less than 0.22 (10.4% were less than 0.025; 14.4% ranged between 0.025-0.05; 39% were between 0.05-0.1; 14.2% ranged from 0.1 to 0.22) compared to 22% of them who had PCT persistently above 0.22 during their illness. MPV had fallen to less than 9fl in 83% (29% were less than 8 fl and 54% were between 8-9 fl) of cases compared to 17% of cases who had MPV persistently above 9fl during their illness. PDW was less than 18 in 68 % (29% were less than 17 and 39% ranged from 17 to 18) of cases whereas 32% of cases had PDW persistently above 18 during their illness.

A significant positive correlation (p<0.01, r=0.93) was noted between rising and falling trends of platelet counts with PCT. A negative correlation (p<0.05, r=-0.350) was noted between falling and rising trends of platelet count and MPV. Similarly, a negative correlation was noted between falling and rising trends of PCT and MPV (p<0.01, r=-0.390).

Out of one hundred and twenty-five cases considered in our study, 69% had no bleeding manifestations (bleeding score of 0) while 31% had bleeding scores of 1 and above (28% had a score of 1 and 3% had a score of 2). In respect to severity scores, 68% had severity scores of 1 while 32% had severity scores of 2 and above during their illness. Warning signs were present in 35% of the cases while 65% of cases had no warning signs. In relation to the duration of stay, 44% of the population were discharged within 3 days while 56% had a hospital stay of 4 days or more.

Severity parameters were compared between the 2 subgroups as described in the methodology. The tabulated data is depicted in Table I. As shown in the Table, a higher proportion of the population with a platelet count less than 1 lakh and PCT less than 0.22 had higher disease severity parameters during their illness compared to the other group in the corresponding platelet indices categories. Low MPV and PDW did not show any effects on the severity of disease. However, a higher proportion of the population with PDW more than 18 had higher disease severity parameters (Table III).

Discussion

Platelet counts have no role in determining the need for transfusion in dengue. Transfused platelets are as likely to be destroyed by the antibodies as one's own

Table III. Comparison of severity parameters in platelet indices categories

Parameters	Platelet count		Plateletcrit		MPV		PDW	
	<1 lakh	>1 lakh	<0.2	>0.2	<9 fL	>9 fL	<18	>18
Bleeding scores								
0 (No bleeding)	51%	93%	36%	96%	68%	71%	79%	48%
1 or above	49%	7%	64%	4%	32%	29%	21%	52%
Severity score								
1	56%	83%	49%	88%	67%	71%	79%	45%
2 or above	44%	17%	51%	12%	33%	29%	21%	55%
Warning signs								
Present	49%	11%	67%	7%	35%	24%	25%	50%
Absent	51%	89%	33%	93%	65%	76%	75%	50%
Duration of stay								
<3 days	25%	67%	28%	82%	44%	38%	48%	32%
>4 days	75%	33%	72%	18%	56%	62%	52%	68%

MPV: Mean platelet volume, PDW: Platelet distribution width

platelets and hence platelet transfusions have a limited role in the management of dengue (7). 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. 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. 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 (11). In our study, we found that MPV was decreased in the early stages of dengue and low MPV with thrombocytopenia was associated with higher disease severity parameters and bleeding. These findings indicate that bone marrow suppression by dengue virus could be one of the causes of thrombocytopenia and bleeding in dengue infection.

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). In our study, the PDW increased during the recovery phase indicating increased production from the bone marrow and release into circulation. Part of our study population had a PDW of more than 18% indicating that hyper-destruction could be a mechanism of thrombocytopenia in dengue infection. No relation was found between PDW and the severity of disease in our study. PCT, a product of platelet count and MPV had similar effects on the illness as MPV and platelet count. Low PCT was associated with higher disease severity and bleeding.

Wiwanitkit (13) observed that MPV in patients with Dengue hemorrhagic fever was not decreased and was similar to the healthy population. A study by Bashir et al. (14) observed that patients with dengue fever had lower levels of MPV and platelet count; however, PDW values were increased in patients with dengue fever. Navya et al. (15) 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. Hardeva et al. (16) recorded 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. Similar findings were noted by Krishnamurthy et al. (17) and Kumar et al. (18).

In our study, we found that platelet indices are depressed during dengue illness. Our analysis showed a significant correlation between low platelet count, MPV and PCT with different severity parameters. Low MPV and increased PDW during the course of the illness suggested that hypo-production and hyper-destruction are the two possible mechanisms of thrombocytopenia in dengue infection.

Study Limitations

This is a record-based retrospective study so the clinical parameters collected were from records rather than direct observation which would have led to bias in assigning bleeding scores and severity scores.

Conclusion

Platelet indices are decreased in dengue infection. Decreased platelet count, MPV and PCT correlate with the severity of the infection. No significance was noted with PDW and the severity of the disease.

Ethics

Ethics Committee Approval: The approval was obtained from the Father Mullers Medical College Institutional Ethics committee and the waiver of consent was approved with approval number: FMMCIEC/CCM/453/2018.

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: C.S.B., K.S.A., Concept: C.S.B., K.S.A., Data Collection or Processing: C.S.B., K.S.A., Analysis or Interpretation: C.S.B., K.S.A., Literature Search: C.S.B., K.S.A., Writing: C.S.B., K.S.A.

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