Utility of Platelet Parameters in Serologically Proven Dengue Cases with Thrombocytopenia

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Abstract Worldwide, there is a rise in the incidence of dengue infection associated with multiple serotypes. Epidemiological studies have reported a higher incidence of severe dengue in secondary dengue infections. A rapid fall in platelet count associated with an increase in hematocrit above the baseline is one of the warning signs of plasma leakage. This study was undertaken to determine the utility of platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit in dengue fever cases with thrombocytopenia. A hospital-based cross-sectional study was carried out between April and September 2014, among dengue patients with thrombocytopenia using platelet histograms. The study population included all the laboratory confirmed cases of dengue infection with thrombocytopenia admitted at Kasturba Medical College, Manipal, Karnataka during the study period. The blood samples collected from serologically confirmed dengue patients with thrombocytopenia were analyzed using automated analyzer within 2 h of venipuncture. The platelet histograms (MPV, PDW,

Plateletcrit) generated by the Beckman Coulter counter LH755TM and LH780TM series were assessed in dengue fever cases with thrombocytopenia. The mean platelet volume (MPV) was observed to be 9.01 fL (SD = 0.09). The mean platelet distribution width and median plateletcrit were 17.2% (SD = 0.98) and 0.47 (IQR 0.2–0.8) respectively. None of the study participants presented with bleeding manifestations. The present study revealed no significant changes of platelet parameters in dengue cases with thrombocytopenia.

Keywords Dengue · Platelet parameters · Thrombocytopenia

Introduction

Dengue is an acute febrile illness caused by dengue virus (DENV), a mosquito-born Flavivirus. The incidence and geographical distribution of dengue infections have significantly increased in the past few decades and a large number of cases remain undiagnosed and underreported. While 90% of DENV infections are asymptomatic, the majority of symptomatic dengue cases manifest as uncomplicated dengue fever (DF). Nevertheless, a small but significant proportion of patients may progress to dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). India reported about 1, 29,166 dengue cases in the year 2016, with a maximum number of cases from West Bengal and the southern state of Karnataka accounting for 4.7% of the disease burden [1]. Outbreaks have been reported in almost entire India except for few dry or hilly regions where the environmental conditions are un conducive for the mosquito breeding.

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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 [2]. DENV infection is often characterized by leukopenia and may be associated with varying ranges of thrombocytopenia. Studies have documented qualitative and quantitative changes in platelets during DENV infection [3]. The platelet function has a direct impact on the pathology of severe dengue such as DHF and DSS with hemorrhagic manifestations and increased capillary permeability [4]. Meanwhile, platelet count was reported to be a predictive factor for severe dengue and a prognostic indicator of recovery [5]. Automation in hematology has facilitated the researchers to measure the newer parameters such as platelet indices besides the platelet count. These platelet indices provide valuable additional facts about the morphology and maturity of the platelets. The platelet indices, namely plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) are increasingly being explored by researchers in a wide array of clinical disorders. The laboratory-based reference ranges, when well-defined and precise can be vital in the interpretation of the results and can potentially avert unnecessary and expensive follow-ups.

However, there is a paucity of data regarding platelet parameters in dengue patients with thrombocytopenia. In this context, we carried out a study to document the qualitative and quantitative characteristics of platelets in laboratory proven dengue cases with thrombocytopenia.

Methodology

A prospective cross-sectional study was carried out from April to September 2014, at Kasturba Medical College, Manipal. The study population included all the laboratory confirmed (Dengue NS1 Antigen ELISA or DENV-IgM ELISA positive) cases of dengue infection with thrombocytopenia admitted during the study period. The demographic and clinical details of the cases were retrieved from the hospital medical records department using a standard data collection questionnaire. The minimum sample size of 106 was estimated for an anticipated prevalence of thrombocytopenia of 50% in dengue seropositive patients at a relative precision of 10% for 95% confidence level [6]. The dengue cases with platelet count less than 1,50,000/ μ l were enrolled by purposive sampling. All the seropositive dengue patients without thrombocytopenia were excluded from the study. The blood samples were run on automated analyzers (Beckman Coulter counters LH755TM, LH780TM, USA) within 2 h of venipuncture in order to prevent an artefactual EDTA-induced platelet swelling. The Total platelet count (TPC) was confirmed with the

peripheral smear and the platelet histograms (MPV, PDW, Plateletcrit) were compared with the platelet count. The study was approved by the Institutional Ethics Committee, Kasturba Medical College, Manipal University, Manipal (IEC No: 236/2014).

The statistical analysis was performed using SPSS 15.0 for Windows (SPSSTM Inc., Chicago, IL, USA). The descriptive statistics were reported using mean $\pm$ SD for age, with frequency and percentage for the categorical variables. A two-tailed *p* value < 0.05 was considered statistically significant.

Results

A total of 106 cases were included in the study. Among these, 27 (25.5%) were females and 79 (74%) were males. The age-related demographics showed that 47 patients (44.3%) belonged to the age group of 1–25 years, 51 patients (48.4%) in the age group of 26–50 years and 8 (7.5%) were in the age group of 51–75 years. The mean age of the enrolled cases was 27.8 (SD = 13.7). The most predominant symptom in the enrolled cases of dengue fever was headache observed in 60 patients (56.6%). Body ache was reported by 56 cases (52.8%), and arthralgia was the main symptom in 26 patients (24.6%) as shown in Table 1. The gastrointestinal symptoms like vomiting and diarrhoea were reported by 50 patients (47.2%). Maculopapular rash was seen in 35 (33%) cases of which, 13 were associated with itching. None of the patients reported any bleeding manifestations while seizures, weight loss and hypotension were reported by a few of them.

Severe thrombocytopenia ($< 20,000$) was observed in 18 cases (16.9%) with no hemorrhagic manifestations as shown in Table 2. The platelet indices of all the enrolled cases were analyzed and the mean platelet volume (MPV) was observed to be 9.01 fL (SD = 0.09) which was within the normal range of 7–11.5 fL. The mean platelet distribution width (PDW) was found to be 17.2% (SD = 0.98) which was near the upper limit of the laboratory reference range of 11–18%. The median plateletcrit (PCT) was observed to be 0.47 (IQR 0.2–0.8) which was within the standard laboratory reference range of 0.15–0.50%. On peripheral smear examination, three patients had microcytic hypochromic anemia (Hb 7.9, 8.5 and 10 g/dl). None of the smears showed fragmented RBCs.

Discussion

In the present study, the enrolled dengue cases with thrombocytopenia belonged to a wide range of age groups and there was no age-specific disparity in the platelet

Table 1 Clinical profile of dengue fever cases with thrombocytopenia (n = 106)

Clinical features	Number	(%)
Headache		
Yes	60	56.6
No	46	43.4
Body ache		
Yes	56	52.8
No	50	47.2
Abdominal pain		
Yes	29	27.4
No	77	72.6
Arthralgia		
Yes	26	24.6
No	80	75.4
Maculopapular rash		
Yes	35	33.0
No	71	67.0
Vomiting/diarrhoea		
Yes	50	47.2
No	56	52.8
Thrombocytopenia		
Severe (< 20,000)	18	16.9
Moderate (20,000–99,999)	68	64.3
Mild (1,00,000–1,50,000)	20	18.8

Table 2 Platelet parameters of the study population (n = 106)

Platelet parameters	Frequency	Percentage (%)
MPV		
Low (< 7 fL)	3	2.8
Normal (7–11.5 fL)	98	92.5
High (> 11.5 fL)	5	4.7
Mean MPV 9.01 fL (SD 0.09)		
PDW		
Low (< 11%)	0	0
Normal (11–18%)	88	83
High (> 18%)	18	17
Mean PDW 17.2 (SD 0.98)		
PCT		
Low (< 0.15%)	104	98.1
Normal (0.15–0.50%)	2	1.9
High (> 0.50%)	0	0
Median Plateletcrit 0.47 (inter quartile range 0.2–0.8)		

indices. None of the patients experienced any hemorrhagic manifestations. Among the clinical symptoms, headache and myalgia emerged as the most common presenting

complaints. Approximately, one-third of the patients reported nonspecific symptoms like rash and abdominal pain. The serious complications of dengue fever such as hypotension and seizures were seen in sporadic cases. The analysis of the platelet indices revealed minor variations in MPV, PDW and PCT. All the platelet indices were within the normal range and in almost half of the cases, MPV was near the upper limit of the normal range. The mean platelet distribution width (PDW) was observed to be on the upper limit of the normal laboratory reference range and the mean plateletcrit (PCT) was within the normal range. As PCT is a derived product of MPV and platelet count, the variation in each of these parameters could translate into a heterogeneous PCT. In normal individuals, the PDW usually correlates in a linear pattern with MPV [7]. The platelet distribution width is a measure of anisocytosis or the size of the platelets which is highly diverse in communicable as well as non-communicable diseases. The plateletcrit is an index of the biomass of platelets in the peripheral blood.

A few studies carried out among dengue hemorrhagic fever patients reported normal mean platelet volume in thrombocytopenic patients [8, 9]. However, the study by Bashir et al. [10] observed low MPV and low platelet count in dengue cases compared to controls. A study from a tertiary care hospital in Rajasthan, also demonstrated low platelet count, low MPV, low PCT and high PDW in dengue cases [11]. Majority of the patients in the above-mentioned studies had normal platelet count and were classified as dengue fever. In the present cross-sectional study, we included all dengue fever cases with thrombocytopenia and made an attempt to evaluate the changes in platelet parameters. We observed that all the patients did not have any bleeding episodes and had an uneventful recovery with no variation in platelet parameters. Thrombocytopenia in dengue patients was not associated with alteration of platelet indices.

The present study was limited to a tertiary care centre from a small geographic area.

Conclusion

Our study did not reveal any variation in platelet parameters of patients with dengue fever and thrombocytopenia.

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Compliance with Ethical Standards

Conflict of interest The authors of this manuscript have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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