

Assessment of Platelet Count in Pediatric Patients with Dengue Fever Admitted in A Tertiary Care Hospital of Bangladesh

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ABSTRACT

Background: Dengue is a major vector-borne disease that is prevalent in tropical and sub-tropical countries. A hallmark of dengue fever is thrombocytopenia. This study was conducted to evaluate the platelet count in relation to severity and outcome of dengue infection in a cohort of hospitalized children during 2019 dengue outbreak in Bangladesh.

Materials and methods: This observational study was carried out in the Department of Pediatrics of Chittagong Medical College Hospital, Chattogram, Bangladesh. One hundred and ninety two consecutive serologically positive dengue cases (Age \leq 12 years) admitted from July 2019 to December 2019 were enrolled in the study. Platelet count was done daily from day 3 to 7 days of illness.

Results: Overall the mean age was 7.04 (\pm 3.23) years with male preponderance (59.4%). As per the nadir platelet count 53 (27.7%) patients had counts $>150,000$, 66 patients (34.3%) had count between 100,000 and 150,000, 36 patients (18.7%) had count between 50,000 and 1, 00,000, 13 patients (15.1%) had count between 20,000 and 50,000 while the remaining 6 patients (3.1%) had profound thrombocytopenia. Children with profound thrombocytopenia were likely to had dengue shock syndrome and prolonged hospitalization. There was no fatality in this series.

Conclusion: Though thrombocytopenia was common profound thrombocytopenia was not frequent in the hospitalized pediatric patients with dengue infection.

Key words: Dengue fever; Platelet count; Profound thrombocytopenia.

Introduction

Dengue Fever (DF) is an arboviral disease transmitted by the bite of Aedes mosquitoes. About 390 million dengue infections are estimated to occur annually, of which a quarter of the cases (67–136 million) will manifest clinically, with the overall incidence of dengue having increased 30-fold over the past 50 years^{1,2}. Although the majority of symptomatic infections manifest as a non-specific self-limited febrile illness, a small proportion of patients progress to more severe and occasionally life-threatening disease, which tends to be more

pronounced in children^{3,4}. Recent study demonstrated that, daily monitoring of platelet counts may have an important role to help identify patients at high risk for developing severe dengue⁵.

Dengue is endemic in Bangladesh⁶. Despite large number of dengue cases being reported every year in this country, alarmingly not much of literature is available on clinic-epidemiological profile of cases of DF, especially from pediatric age group^{7,8}. Laboratory and human studies have suggested a direct correlation between activation and depletion of platelets, with a sharp drop occurring on day 4 of fever⁹. It was observed that, profound thrombocytopenia occurred in one-fifth of the adult patients with dengue which was associated with prolonged hospitalization but had no additional higher risk for minor and major hemorrhages¹⁰. Study conducted in pediatric dengue patients reported that, though prevalence of thrombocytopenia is high in this age group associate bleeding manifestations and severe thrombocytopenia are less comparatively to adults¹¹.

There is scarcity of study conducted in pediatric age group in Bangladesh highlighted the issue of platelet count in relation to disease progression and outcome. In this context, this study was performed to evaluate the platelet count, severity and outcome of DF in pediatric patients.

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Date of Submission : 15th May 2021
Date of Acceptance : 8th June 2021

Materials and methods

This observational study was carried out from July to December 2019 in Chittagong Medical College Hospital, 2nd largest tertiary care hospital; of Bangladesh. A total 192 patients with a confirmed diagnosis of DF, aged 0-12 years, admitted in the pediatric ward during this time were included in the study. Patients with concomitant malaria, meningitis and typhoid were excluded. Prior approval was taken from the Ethical Review Committee of Chittagong Medical College and informed consent was obtained from the guardians of the patients.

Detailed history was taken and clinical examination was performed on admission and subsequently during the stay in the hospital. Dengue cases were classified according to WHO revised classification-2009 and National Guideline 2018^{12,13}. Blood samples were obtained as part of standard care for dengue patients from day 3 to 7 days of illness, to measure platelet counts. Platelet nadir was the minimum platelet count observed between days 3 and 7 of illness and profound thrombocytopenia was defined as nadir platelet count of $\leq 20,000/\text{mm}^3$. Patients were managed according to National Guideline 2018 and discharged from hospital when fever subsided and/or vital signs became normal¹³.

Data were expressed as frequencies, means (Standard Deviations). To determine the association of different characteristics with thrombocytopenia, chi-square test was used for categorical variables and ANOVA test was used for continuous variables. Data were analyzed with SPSS-23. p value <0.05 was considered as statistical significant.

Results

Out of the 192 children majority (48.4%) were in the age group of 6–10 years, followed by 0-5 years (34.4%) and 11–12 years (17.2%). Males were predominant with a male to female ratio of 1.46 : 1 and 66.2% of the patients came from rural area. Majority of the patients (66.7%) were classified as DF without warning sign. As per the nadir platelet count majority of the patients (34.3%) had count between 100,000 and 150,000 and only 6 (3.1%) patients had profound thrombocytopenia. All of the patients improved and discharged from the hospital with a mean length of hospital stay of 5.2 days (Table I).

Table I Demographic and clinical characteristics of the dengue cases (n=192)

Variables	Category	Frequency (%) *
Age, years	0-5 years	66 (34.4)
	6-10 years	93 (48.4)
	11-12 years	33 (17.2)
	Mean \pm SD	6.57 \pm 2.74
	Range	1.00-12.00

Sex	Male	114 (59.4)
	Female	78 (40.6)
Residential location	Rural	127 (66.2)
	Urban	65 (33.8)
Classification of DF	DF without warning sign	128 (66.7)
	DF with warning sign	42 (21.9)
	Dengue shock syndrome	22 (11.5)
Nadir platelet count,/ mm^3	$>1,50,000$	53 (27.7)
	1,00,000-1,50,000	66 (34.3)
	50,000-1,00,000	36 (18.7)
	20,000-50,000	31 (16.1)
	$<20,000$	6 (3.1)
In-hospital outcome	LOS (Days)	5.2 (\pm 1.9)
	Need for PICU	18 (9.4)
	Mortality	0 (0)

*Data are expressed as frequency (Percentage) if not otherwise mentioned.

A significant association was observed between the severity of thrombocytopenia and the clinical presentation of DF (p <0.001). All cases with profound thrombocytopenia presented with DSS when compared to those with mild thrombocytopenia. A significant drop in platelet counts was noted as the patient presented with symptoms of DHF/DSS. Greater percentage of patients with moderate thrombocytopenia presented with DF with warning sign. A significant drop in platelet counts was noted as the patient presented with warning sign or shock syndrome (Table II).

Table II Nadir Platelet counts compared with severity of disease at admission

Nadir platelet counts	DF without WS	DF with WS	DSS
$>1,50,000$ mm^3	47 (88.7)	6 (11.3)	0 (0)
1,00,000-1,50,000 mm^3	58 (87.9)	5 (7.6)	3 (4.5)
50,000-1,00,000 mm^3	21 (58.3)	11 (30.6)	4 (11.1)
20,000-50,000 mm^3	2 (6.5)	20 (64.5)	9 (29.0)
$<20,000$ mm^3	0 (0)	0 (0)	6 (100.0)

p <0.001 , obtained from Chi-square test.

WS: Warning sign, DSS: Dengue Shock Syndrome.

In this study platelet count was repeated from day 3 of illness to day 7 of illness. Figure 1 show that, both in patients with non-severe dengue (DF without warning sign and DF with warning sign) and patients with DSS lowest median value of platelet were observed on day 5 of illness. Platelet counts in the patients who developed DSS tended to be lower than in patients who never progressed to DSS from days 3 and 7 of illness.

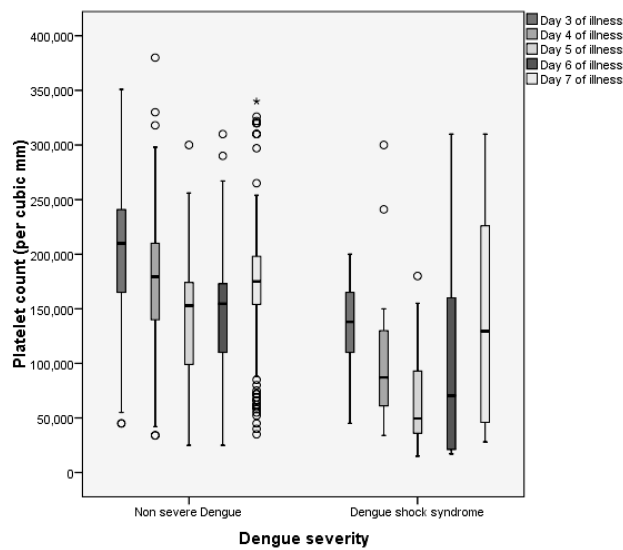


Figure 1 Box plots describing changes in platelet values from day 3 to day 7 of illness, among study participants who developed DSS as well as participants who never developed DSS

All of the six dengue cases who had profound thrombocytopenia developed DSS and needed PICU management. Similarly, LOS was significantly longer among the patients with profound thrombocytopenia. However, there was no mortality in the total 192 dengue admitted cases.

Table III Association between nadir platelet count and outcome of the dengue cases

Variables	Normal (>1,50,000 mm ³) (n=53)	Mild to moderate thrombocytopenia (1,50,000-20,000 mm ³) (n=133)	Profound thrombocytopenia (<20,000 mm ³) (n=6)	p value
LOS (days)	4.04±0.98	4.82±1.41	7.67±0.82	<0.001*
Need for PICU	0 (0)	12 (9.0)	6 (100.0)	<0.001†

Data are expressed as frequency (Percentage) or Mean ±SD as appropriate, LOS: Length of Hospital Stay, PICU: Pediatric Intensive Care Unit. *p value obtained from ANOVA test or †Chi-square test.

Discussion

In the year 2019 Bangladesh has experienced an unprecedented dengue outbreak that has resulted in an enormous increase in the number of cases and mortality as compared to previous years¹⁴⁻¹⁶. Consequently a large number of children with dengue were admitted in Chittagong Medical College Hospital in 2019. So, we believe that this study among the dengue confirmed children admitted in this hospital, would give good insight about the relationship between platelet count, disease severity and outcome of dengue infections in children in our context.

Present study demonstrated that frequency of thrombocytopenia was 78.3%. Among these thrombocytopenic children, mild to moderate thrombocytopenia was seen in 87.7% of the cases and similar pattern was seen in other studies^{11,17-20}. Profound thrombocytopenia was noted in 6 (3.1%) patients only. Other recent studies conducted in adults and children reported the frequency of profound thrombocytopenia 20% and 11.6% respectively^{10,11}. These findings indicate that, though thrombocytopenia was common in dengue infection, the reduction is more prominent among children than adult patients.

In this study platelet count was done daily from day 3 of illness to day 7 of illness. Lowest median value of platelet was observed on day 5 of illness. Between days 3 and 7 of illness, platelet counts in the patients who developed DSS tended to be lower than in patients who never progressed to DSS. The kinetic observation of platelet counts in dengue patients showed a mild to moderate decrease in the 3rd to the 7th day, a significant decrease on day 4, reaching normal levels in the 8th or 9th day of the disease^{10,21}. Recently, Lam et al. identified that incorporating sequential platelet values in a model of established risk factors for DSS improve the ability of the model for prediction of DSS among children with dengue⁵.

Results of the present study observed that, all of the six dengue cases who had profound thrombocytopenia developed DSS and needed PICU management in the current series. Similarly, length of hospital stay was significantly longer among the patients with profound thrombocytopenia. However, there was no mortality in the total 192 dengue admitted cases. Similarly, nil mortality was reported by Praveen et al. indicating thrombocytopenia had no correlation to mortality²². Moreover, patients included in the present study and the previous study were managed in tertiary care hospitals with well established ICU facilities to manage the severe case which might be attributable to this low mortality²².

Limitations

To the best of our knowledge this study is the first to specifically explore the association and outcome of patients with profound thrombocytopenia based on nadir platelet ≤ 20 000/mm³ among Bangladeshi children. However, sample from a single government run tertiary care hospital and limited study period were some of the limiting factors of the current study, which might questioned its generalizability.

Conclusions

In conclusion profound thrombocytopenia was less despite of the high prevalence of thrombocytopenia in children admitted with DF during 2019 outbreak. Patients with profound thrombocytopenia were more likely to have severe diseases and had prolonged hospitalization.

Recommendations

Although the present study highlights important findings on the impact of thrombocytopenia, a larger scale prospective study will be useful to further strengthen these findings.

Acknowledgments

It was a self funded study. The authors would like to thank all survey participants for their involvement, as well as the Physicians of the Pediatric Ward for their collaboration and cooperation.

Disclosure

All the authors declared no competing interest.

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