

THROMBOCYTOPENIA; FREQUENCY AND ASSOCIATION AT THE TIME OF DIAGNOSIS IN DENGUE FEVER, PESHAWAR

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ABSTRACT:

OBJECTIVES: To determine the frequency of thrombocytopenia in dengue fever at the time of diagnosis and to see its association with age and gender.

METHODOLOGY: It was a descriptive retrospective study of dengue cases admitted to the Medical Unit of Naseer Teaching Hospital Peshawar during the 2019 outbreak was performed. Only confirmed dengue by serology (IgM) or dengue NS1 (Non-Specific Antigen 1) by Immunochromatographic Technique (ICT) cases were analysed. Complete Blood Count (CBC) was done for all the cases on admission and prevalence of thrombocytopenia on admission was extracted from the records. SPSS version 23 was used to analyse the data and to calculate Odds Ratio of a gender or age group to have thrombocytopenia at the presentation of dengue fever.

RESULTS: A total of 69 confirmed dengue cases were admitted in Naseer Teaching Hospital in the 2019 outbreak. Out of these 69 cases, 51 (73.9%) were males and 18 (26.1%) were females. The ages of these patients ranged from 10-58 years. Fifty-one (51) patients were more than 20 years of age and eighteen (18) were 20 years or less. Thrombocytopenia (platelet count $<150,000 \times 10^9/L$) was present in 57 (82.6%) patients. Patients older than 20 years of age were more likely to have thrombocytopenia at presentation of dengue fever OR=16, ($p=0.0003$), whereas difference amongst genders in this regard was not statistically significant OR=1.07, ($p=0.09$).

CONCLUSION: There is a high frequency of thrombocytopenia (82.6%) in early dengue fever. Patients older than 20 years are more likely to have thrombocytopenia in early dengue fever.

KEYWORDS: Dengue Fever, Acute Febrile Illness, Thrombocytopenia

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mechanisms causing DENV-induced bone marrow suppression in the acute phase are not clear. However, there three main pointing suggestions: (1) direct toxic effects on progenitor cells by DENV; (2) infection of stromal cells; (3) alterations in bone marrow regulation³. Thrombocytopenia in dengue fever may also be due to increased peripheral destruction by mechanisms suggested to be (1) platelet consumption in the coagulopathy process; (2) complement system activation⁴; or (3) augmented peripheral sequestration⁵.⁶. A study by Tomashek et al, have found that even early in the clinical course of an acute febrile illness (AFI), thrombocytopenia is predictive of dengue across all age groups along with the fact that thrombocytopenia, as a predictor of dengue fever, strengthened over time⁷. A study from Karachi, Pakistan has shown that thrombocytopenia was present in 100% patients with early suspected dengue fever⁸. Another study from Lahore, Pakistan showed that using the logistic regression model, platelet count showed statistically significant predictability of dengue haemorrhagic fever⁹. The northern part of Pakistan including Peshawar has been struck with deadly dengue outbreaks in this decade. Complete Blood Count (CBC) is a very cheap baseline test and thrombocytopenia in AFI could therefore give a clue towards its aetiology. We wanted to find out the frequency of thrombocytopenia in early confirmed dengue fever in a teaching hospital in Peshawar,

INTRODUCTION:

Dengue is an arthropod-borne infectious disease caused by a Flavin virus, the dengue virus (DENV). Generally, dengue is a self-limiting acute febrile illness that is followed later by a phase of critical effervescence, characterized by either improvement or progression to a severe form. The features of severe illness are increased vascular permeability, hemodynamic compromise, intravascular volume depletion, hypotension, and shock. Thrombocytopenia is common in both the cases and is related to the clinical outcome. There are different mechanisms postulated to explain DENV-associated thrombocytopenia. They include bone marrow suppression and the peripheral destruction of platelets. Previous studies have shown that early in the dengue fever, there is bone marrow hypocellularity and slowing of megakaryocyte maturation^{1, 2}. The

Pakistan to emphasize the fact that thrombocytopenia early in the course of AFI, utilizing a very cost-effective test (CBC), could be a pointer towards its cause in our region as well. To our knowledge, no local study has tried to find out the association of thrombocytopenia in early dengue fever with age and gender. Through this study, we also investigated this issue to find out specific populations where thrombocytopenia early in AFI could be a strong predictor of dengue fever.

METHODOLOGY:

It was an observational study where retrospective analysis was done for all cases that were admitted with the confirmed diagnosis (NS1 or IgM positive cases) of dengue fever during the outbreak of 2019 (September 1st to November 20th) in Peshawar. Complete blood count including red cell count, haemoglobin, haematocrit, mean corpuscular volume, mean corpuscular haemoglobin concentration, platelets count, total leukocyte count, and differential leukocyte count of all the

patients was performed at the time of diagnosis using automated haematology analyser of the hospital laboratory. Thrombocytopenia was defined as platelet count less than $150 \times 10^9/L$. Data was analysed using SPSS software version 23. Frequencies and percentage were used for qualitative variables like gender and thrombocytopenia. Mean±Standard Deviation was calculated for quantitative or numerical variables like age and platelet count at presentation. Patients younger than 20 years of age were grouped in young age group while those older than 20 years were classified as older age group. Odds ratio (OR) was calculated for association of gender and age groups with thrombocytopenia at the time of diagnosis of dengue fever.

RESULTS:

The demographic and laboratory variables of n=69 confirmed cases of dengue fever admitted to Naseer Teaching Hospital, Peshawar from 1st September to 20th November 2019, are shown in Table 1.

Table 1: Demographic & Laboratory Characteristics of Confirmed Dengue Fever Patients

Parameters	Mean±SD, Number and Percentage
Age	31.30±12.38 years
Gender	
Male	51 (73.9%)
Female	18 (26.1%)
Platelet count	116±65.4×10 ⁹ /L
Thrombocytopenia	
Present	57 (82.6%)
Not Present	12 (17.4%)

*SD=Standard Deviation

All the cases were confirmed dengue fever. Sixty-nine (69) patients were positive for NS1 Dengue antigen and 3 were negative, which were positive for IgM Anti Dengue Antibody. The patients' age ranged from 10 years to 58 years. Platelet count ranged from 30 to $308 \times 10^9/L$. Number of patients in different age categories and the presence or absence of

thrombocytopenia in them is depicted in Figure 1. Patients older than 20 years of age were more likely to have thrombocytopenia at presentation of dengue fever OR=16, ($p=0.0003$). Female patients in early dengue fever had slightly more but statistically non-significant likelihood to have thrombocytopenia at presentation of dengue fever OR=1.07, ($p=0.09$).

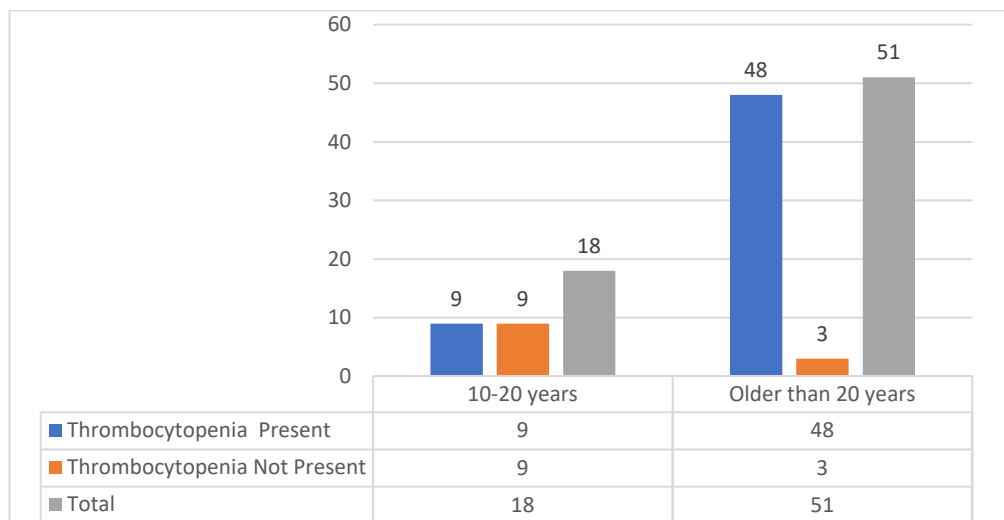


Figure 1: Thrombocytopenia as Diagnosis of Dengue Fever in Two Age Categories

DISCUSSION:

Dengue fever has now become endemic to Pakistan with outbreaks usually reported in every summer over the last decade. It is associated with considerable morbidity and mortality¹⁰. Thrombocytopenia is quite common in dengue fever^{11, 12}, and can give a clue towards the aetiology of acute febrile illness. In this study we tried to find out the frequency of thrombocytopenia in early dengue fever. In our study males dominated as a gender having dengue fever. Such a finding is also present in other national and international studies^{7,13-15}.

Our study showed quite a high frequency of thrombocytopenia i.e. 82.6% right at the time of diagnosis of dengue fever. This finding is quite in line with a study from Saudi Arabia¹⁶, which found out the frequency of thrombocytopenia to be 79.49% amongst 80 patients who were admitted with suspicion of dengue fever, which was later, confirmed by serology. Similarly, in a local study from Punjab¹⁷, a retrospective analysis of 68 proven dengue fever found out the frequency of thrombocytopenia to be 88.8%. In other local studies, the frequency of thrombocytopenia is even higher such

as 90%¹¹, 95%¹², and even 100%⁸. On the other hand, other studies have reported the prevalence of thrombocytopenia to be lower than ours; 60%¹⁶ and 70%¹⁷. However, thrombocytopenia has been demonstrated to be a positive factor for dengue fever early in the course of acute febrile illness in numerous international and national studies⁷⁻⁹. Mean platelet count in our study was $116 \pm 65.4 \times 10^9/L$ (Mean \pm SD). It is near to the one found in a Puerto Rican study⁷, where it was shown to be $121 \times 10^9/L$. Mean platelet count in early dengue fever in another local study from Peshawar has been demonstrated to be $69.29 \pm 50.82 \times 10^9/L$,¹⁵ quite lower than found in ours. We also tried to find out association of gender or age with the presence of thrombocytopenia in early dengue fever. Patients older than 20 years of age were slightly more likely to have thrombocytopenia in early dengue fever in our study (OR=16). Older age (>55 years) has been shown to be a predictor of mortality in dengue fever in a Brazilian study¹⁸. However, in contradiction to our study, an Argentinean study¹⁹, showed low platelets count in dengue fever to be associated with younger age. This is probably related to the fact that this study investigated a much younger (paediatric) age group as well, which we did not. The same study showed female gender to be predictor to worse clinical outcomes.

CONCLUSION:

There is a high prevalence of thrombocytopenia (82.6%) in early

dengue fever. Therefore, a simple test like CBC can be used as a possible screening test for dengue fever in acute febrile illness. Patients older than 20 years of age are more likely to have thrombocytopenia in early dengue fever.

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