FREQUENCY OF THROMBOCYTOPENIA IN CONFIRMED CASES OF MALARIA IN CHILDREN

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ABSTRACT

Objective: To determine the frequency of thrombocytopenia in confirmed cases of malaria in children

Methods: A cross sectional study over a period of six months was done at Department of Pediatrics Mayo Hospital, Lahore from January to June 2018. Using non-probability consecutive sampling, 80 children with confirmed malaria between the ages of two and twelve years, of both genders, were included. A blood sample was taken within 48 hours of admission and their complete blood count was reviewed for the presence of thrombocytopenia after malaria was confirmed on positive peripheral smear. A platelet count below150,000/µl of blood was considered thrombocytopenia. SPSS version 22 was used to enter and analyze the collected data. Data was stratified for age and gender to address the effect modifiers. Presence of thrombocytopenia was presented as frequencies and percentages.

Results: Out of total 80 patients with positive malarial parasite (MP) slide, 65 cases (81.25%) were of *Plasmodium Vivax*,12(15%) were of *Plasmodium Falciparum* while 3 cases (3.75%) were of Mixed infection. 44 patients (55%) were having low platelet count (less than 150,000/µl) while 36 patients (45%) had no thrombocytopenia. Out of 44 patients with thrombocytopenia, 16 patients (20%) had mild thrombocytopenia, 21 patients (26.3%) had moderate thrombocytopenia while 7 patients (8.8%) had severe thrombocytopenia. There was no correlation of thrombocytopenia with age, gender or duration of malaria.

Conclusions: Frequency of thrombocytopenia in confirmed cases of malaria in children is 55%. Presence of thrombocytopenia in febrile patients can raise the possibility of malaria leading to early diagnosis and management.

Keywords: malaria, thrombocytopenia, children

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INTRODUCTION

Malaria is one of the commonest infections of people residing in tropical and sub-tropical areas. It is transmitted by mosquito as a vector of intraerythrocytic protozoa of genus Plasmodium. It has 4 known species; *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, and *Plasmodium malariae*. *Plasmodium vivax* and *Plasmodium falciparum* are the most common infectious agents.[1] Malaria is an acute febrile illness, presenting with symptoms of spiking fever and chills along with splenomegaly and changes in hematological parameters such as anemia and thrombocytopenia.[2] It causes periodic fever which coincides with the degree of parasitemia.[3] High Mortality and morbidity related to malaria is mainly due

to the delayed diagnosis and treatment of this potentially preventable & treatable disease.[4] If this disease is left untreated, affected person may develop severe complications and die.

In 2020, there were an estimated 241 million cases of malaria reported worldwide, and the disease claimed 627,000 lives, mostly young children in sub-Saharan Africa. A COVID-19 pandemic-related disruption in the delivery of diagnosis, prevention, and treatment services was responsible for two thirds of these deaths.[5] Pakistan is one of the countries in the Eastern Mediterranean region with 5.7 million reported malaria cases where malaria is a widespread, regularly occurring disease. In Pakistan, 3.4 million cases were suspected for malaria from January to August of year 2022 whereas 1.7 million cases were confirmed mainly in Sindh and Baluchistan.[6]

Several complications of malaria have been reported particularly in severe cases. Hematological abnormalities noted in malaria include anemia and thrombocytopenia which is directly related to degree of parasitemia.[7] Common mechanisms include coagulation disturbances and sequestration in spleen. Other mechanisms speculated include alteration in bone marrow, platelet destruction and adhesion to erythrocytes and oxidative stress.[8] McMorran et al described that platelets directly kill parasites hence improving host ability to control infection.[9] On the contrary; low platelet count can lead to severe infection.

Frequency of thrombocytopenia is variable in different regions. Variable frequency of thrombocytopenia has been reported in previous studies Latif et al reported 51.3% thrombocytopenia[10], Shah et al reported 47% thrombocytopenia [11] while Ansah et al reported 33% thrombocytopenia in confirmed cases of malaria.[12] According to Gebreweld et al., thrombocytopenia has a 79.5% sensitivity and an 86.3% specificity as a diagnostic biomarker for malaria.[13]

The rationale of this study was to ascertain whether thrombocytopenia and malaria are correlated as very limited data was available in our local population. This simple test can lead to early diagnosis and management of malaria cases thus reducing the burden of mortality and morbidity related to this treatable disease in endemic areas like Pakistan.

METHODS

A cross sectional study over a period of six months was done at Department of Pediatrics Mayo Hospital, Lahore from January to June 2018. After getting approval from the institutional review board, using non-probability consecutive sampling, 80 children with positive peripheral smear for malaria between the ages of two and twelve years, of both genders, were included. (The sample size of 80 patients was estimated by using 95% confidence level & 10% margin of error with expected percentage of thrombocytopenia in children with malaria as 72%). [4] Informed consent was taken from guardians of all children included in the study. A child (symptomatic or asymptomatic) in whom malarial parasite species was detected and identified by microscopy on blood films in laboratory with appropriate expertise was considered as confirmed case of malaria. [14] Patients treated with antibiotics or antimalarial within 48 hours before first blood sample (CBC) collection were excluded. EDTA collection tube (purple top) with proper identification label was used to collect blood sample. Blood sample of each admitted patient after inclusion was drawn according to proper biosafety guidelines and sent to microbiology and hematology laboratory of Pediatric department where thick and thin peripheral smears of blood were examined for the presence of malarial parasite. All slides were examined by experienced lab technician according to standard protocol. After detecting and identifying malarial parasite, patient's CBC was reviewed for presence or absence of thrombocytopenia. The SYSMEX, XN-1000 automated hematology analyzer was employed to ascertain the platelet count, and a peripheral smear examination was performed to verify the results. A platelet count below 150,000/µl of blood was considered thrombocytopenia. It was further classified into mild thrombocytopenia (A platelet count of 100-150,000/µl of blood), moderate thrombocytopenia (A platelet count of 50- 100,000/µl of blood) and severe thrombocytopenia (a platelet count of less than 50,000/µl of blood). Treatment was offered to all patients as per standard hospital protocol. A questionnaire was used to record all data. SPSS version 22 was used to enter and analyze the collected data. Mean ± S.D was computed for quantitative variables such as age whereas qualitative variables such as gender, and thrombocytopenia and its severity were expressed as frequency and percentages. Data was stratified for age, gender and duration of disease for addressing the effect modifiers. After stratification, Chi-square test was applied and for significance a cut off p-value i.e. ≤0.05 was considered.

RESULTS

The mean age of cases was 8.38±3.56 years. There were 37(46.3%) males and 43(53.8%) females. The mean weight of the children was 20.78±3.58 kg. The mean duration of malaria in cases was 14.71±6.93 days. The mean Platelet count was 128622.04±61732.44/ µl of blood. Out of 80 confirmed malaria patients, 65(81.25) cases were of *Plasmodium vivax*, 12(15%) cases were of

Plasmodium falciparum and 3(3.75%) cases were of mixed infection.

There were 44(55%) children with thrombocytopenia and 36(45%) without thrombocytopenia.

36(45%) children had no thrombocytopenia, 16(20%) had mild thrombocytopenia, 21(26.3%) had moderate thrombocytopenia while seven (8.75%) had severe thrombocytopenia (Table 1).

No significant correlation was found between thrombocytopenia and age groups (p-value=0.56) (Table 2), Also, there was no correlation between thrombocytopenia and gender (p-value=0.37) (Table 3) as well as between thrombocytopenia and duration of malaria (p-value=0.51) (Table 4).

Table-1: Severity of Thrombocytopenia in confirmed cases of malaria

Species	Normal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Total
P. vivax	33 (91.67)	14 (87.5)	13 (61.90)	5 (71.43)	65 (81.25)
P. falciparum	3 (8.33)	2 (12.5)	5 (23.81)	2 (28.57)	12 (15)
Mixed Infection	0 (0.0)	0 (0.0)	3 (14.29)	0 (0.0)	3 (3.75)
	36 (100)	16 (100)	21 (100)	7 (100)	80 (100)

Table-2: Thrombocytopenia Stratified for Age Groups

Thrombocytopenia	Age Groups			p-value
	2-6	7-11	12-16	
Present n (%)	15 (55.56)	21 (60)	8 (44.44)	
Absent n (%)	12 (44.44)	14 (40)	10 (55.56)	0.56
Total	27 (100)	35 (100)	18 (100)	

Table-3: Thrombocytopenia Stratified for Gender

Thrombocytopenia	Gender		p-value
	Male	Female	
Present n (%)	19 (51.35)	25(58.14)	
Absent n (%)	18 (48.65)	18(41.86)	
Total	37(100)	43(100)	0.54

Table-4: Thrombocytopenia Stratified for Duration of Malaria

Thrombocytopenia	Duration			p-value
	4-14	15-25	26-36	
Present n (%)	25(58.14)	18(50)	1(100)	
Absent n (%)	18(41.86)	18(50)	0(0.0)	0.51
Total n (%)	43(100)	36(100)	1(100)	

DISCUSSION

In current study, 44(55%) cases of confirmed malaria had thrombocytopenia including *Plasmodium vivax, Plasmodium falciparum* and mixed infections. Our results were comparable to a study conducted in Peshawar, Pakistan by Shah et al which reported frequency of thrombocytopenia in cases of malaria to be 47% but they studied *Plasmodium vivax* Infection only. [11]Another study from Karachi, Pakistan reported 51.3% cases with mild thrombocytopenia, more frequently seen in *Plasmodium falciparum* infection.[12] Another study from Pakistan reported 90% thrombocytopenia in patients with malaria which is much higher frequency as compared to our results.[15]

In an Indian study, Dadhich et al reported that the frequency of thrombocytopenia varies among malaria species and is 68.9% in *Plasmodium vivax*, 72.5% in *Plasmodium falciparum*, and 85% in cases of mixed infection,[16] while we found thrombocytopenia in 49.2% cases of *Plasmodium vivax*, 75% cases of *Plasmodium falciparum* and 100% cases of mixed infections in our study.

In current study, there was no difference in thrombocytopenia between all genders and ages, while in a study of Ghana by Ansah DM et al, the frequency of thrombocytopenia in cases of malaria was 33% but it was more frequent in male children and children below 5 years of age.[12]

In another Indian study done in Rajasthan, thrombocytopenia was found in 83% of malaria patients with more severe thrombocytopenia in *Plasmodium falciparum* infection [17], however in our study, most cases of severe thrombocytopenia were contributed by *Plasmodium Vivax* infection.

As per severity of thrombocytopenia in our study, 16(20%) cases had mild thrombocytopenia, 21(26.25%) had moderate thrombocytopenia while seven (8.75%) had severe thrombocytopenia, which was different from other studies. According to Latif et al, 51% of patients had mild while 31.2% had moderate thrombocytopenia. [10] Gebreweld et al, documented 67% cases of mild to moderate thrombocytopenia whereas there were12.3% cases of severe thrombocytopenia in malaria.[13]

We found that significant number of patients with malaria had thrombocytopenia irrespective of species. We found no significant association of thrombocytopenia with age, gender and duration of illness. However, we could not look for association of thrombocytopenia with severity of illness and its prognostic value to predict the outcome of disease. This was a single center study with a small sample size and also prevalence of different malarial parasites varies in different regions thus these results can't be generalized for whole population of Pakistan.

CONCLUSION

Frequency of thrombocytopenia in confirmed cases of malaria in children is 55%. Presence of thrombocytopenia in

febrile patients can raise the possibility of malaria leading to early diagnosis and management.

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AUTHOR'S CONTRIBUTIONS

NW: Concept, design of work, data collection Manuscript writing, final approval of manuscript, accountable for integrity of research
HN: Data interpretation, data analysis, manuscript writing, editing & revision, final approval of manuscript, accountable for integrity of research
KAH: Data collection, manuscript review, final approval of manuscript, accountable for integrity of research