Original Article

Thrombocytopenia with Malaria

Frequency and Severity of Thrombocytopenia in Children with Malaria Caused by Different Species of Plasmodium

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ABSTRACT

Objective: To determine the frequency and severity of thrombocytopenia in malaria.
Study Design: Descriptive / **c**ross sectional study
Place and Duration of Study: This study was conducted at the Department of Pediatrics, Liaquat University Hospital, Hyderabad from 24th June 2014 to 23rd December 2014.
Materials and Methods: All children presenting in pediatricsdepartment of Liaquat University Hospital Hyderabad with fever (>101 °F) or history of fever (>101 °F) for 3 days duration were evaluated for malaria parasite through thick and thin blood smear. Then all malaria positive patients were assessed for platelet count. Thrombocytopenia (if present) was classified according to the reference ranges and categories.
Results: Total 154 children of malaria were included in this study mean age + SD (range) was 5.76 + 3.63 (6 months to 12 years). 118 cases were plasmodium vivax positive while 34 were suffering from plasmodium falciparum malaria, whereas 02 children had mixed (p. vivax and p. falciparum) infection. Out of 154 children of malaria, 100(65.0%) had decreased platelets count. Of these, 71(71.0%, n = 100) had mild thrombocytopenia, 26(26.0%, n = 100) had moderate thrombocytopenia, while severe thrombocytopenia was observed in 3(3.0%, n = 100).
Conclusion: This study concluded that various degree of thrombocytopenia is common with malaria which if severe then may be associated with prolongs bleeding time leading to life threatening bleeding. Early diagnosis and prompt precautions and management by intervention such as immediate transfusion of platelets can prevent fatal outcome.
Key Words: P. falciparum, p. vivax, malaria, platelets,thrombocytopenia

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INTRODUCTION

Malaria has been recognized as a human disease for thousands of years. Over 40% of world population lives in malaria endemic area including Southeast Asia, India, Pakistan, Bangladesh, Africa, areas of middle east, Central and South America with significant economic burden. Pakistan being a part of endemic belt has an incidence of one case per thousand populations. The reported prevalence of malaria in Pakistan is 43% and such high prevalence is due to extreme poverty and lack of education regarding preventive measures. In Pakistan estimated fifty thousand deaths each year mostly in infants, children and pregnant women with maximum mortality are associated with Plasmodium falciparum malaria.[1, 2]

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Malaria is caused by the bite of a female Anophelesmosquito that is infected with species of the protozoan genus Plasmodium. There are four most common species affecting humans as P falciparum, P vivax, P. ovale, P malariae. Considering the gravity of the complications of this potentially treatable disease, it is important to diagnose and treat this disease timely. Microscopy remains the Gold standard for the diagnosis of malaria. All clinically suspected malaria patients must be diagnosed by repeated smear examinations or rapid antigen detection tests.[3,4]

Hematological abnormalities have been observed in patients with malaria, which ranges from asymptomatic thrombocytopenia to fulminant disseminated intravascular coagulation (DIC), anemia and thrombocytopenia being the most common.[5, 6, 7]

The mechanism of thrombocytopenia in malaria is unknown; postulated mechanisms reported is macrophage activation leading to platelet destruction, increased levels of cytokines, immunological destruction due to antiplatelet IgG and oxidative stress. It has been observed that 70% patients infected with either P. vivax or P. falciparum malaria develop thrombocytopenia during infective period, whereas regarding the severity; the mild thrombocytopenia was observed in 68% patients, moderate thrombocytopenia

in 24% patients and severe thrombocytopenia in 8% patients.[8,9]

Severity of Thrombocytopenia: [7]

1. Mild thrombocytopenia <150,000 to >50,000/l.
2. Moderate thrombocytopenia <50,000 to >20,000/l.
3. Severe thrombocytopenia <20,000/l.

Therefore this study is designed to evaluate the frequency and severity of thrombocytopenia in malarial patients, which if associated with prolong bleeding time then become major medical emergency, require immediate platelet transfusion for preventing fatal outcomes.

MATERIALS AND METHODS

This Cross sectional descriptive study was conducted in Department of Pediatrics, of Liaquat University Hospital Hyderabad from 24th June 2014 to 23rd December 2014. A total 154 patients of malaria from non - probability purposive sampling were selected.

Inclusion criteria:

- The age ranges 06 months to 12 years (as malaria in children <6 months age is less frequent and secondly thrombocytopenia in children <6 months age is mostly due to sepsis, whereas >12 year of age children were out of pediatric range.
- Fever (>101 ^{o}F) at the time of presentation or history of fever (>101 ^{o}F) for 3 days duration and positive malarial parasites by thick or thin blood smears
- Both genders.

Exclusion criteria:

- Patients who had taken anti-malarial therapy.
- Patients with typhoid fever, prior history of tuberculosis, Diabetes mellitus, connective tissue disease, chronic liver disease, neoplasm (because they represent as chronic fever cases).
- Known case of idiopathic thrombocytopenic purpura, known case of aplastic anemia, myelodysplastic syndrome, osteopetrosis.
- Patients on drug therapy (fansidar, septran, thiazides and chemotherapeutic agents that can lead to thrombocytopenia).

Data Collection Procedure: After approval by ethical committee of Liaquat University of Medical and Health Sciences and written informed consent from attendant of the patients regarding purpose and procedures, this study was carried out. All children presenting in pediatric department of Liaquat University Hospital Hyderabad with fever (>101 ^{o}F) measured via mercury containing standard thermometer which was kept in an armpit for a minimum of two minutes by a trained staff nurse or history of fever (>101 ^{o}F) for 3 days duration and fulfilled the inclusion as well as exclusion criteria of the study were evaluated for malarial parasite through thick and thin blood smear by using a standard sterile needle (blood Lancet) skin was punctured at fingertip of ring finger and a drop of blood was used to prepare thick and thin blood film by expert laboratory technician. Then all malaria positive subjects were assessed for platelet count by taking 2ml venous blood in complete blood picture bottle and sent to pathology laboratory for analysis through Medionic cell counter method. Thrombocytopenia (if present) was classified according to the reference ranges and categories.All the data of the study were recorded on the pre-designed proforma.

Data Analysis: The data of all patients were entered and analyzed in the statistical program SPSS version 16.0. Qualitative data (frequency and percentage) such as gender, age in groups, species of plasmodium, frequency of thrombocytopenia and its severitywere presented as n (%). Mean and standard deviation of continuous variables like age in years, platelet counts was calculated.

RESULTS

One hundred and fifty four patients of malaria were enrolled in this study based on inclusion and exclusion criteria. Males were 95 (61.7%) and 59(38.3%) were female shown in Table No. 1

Of these 154 children of malaria, mean age + SD (range) was 5.76 + 3.63 (6 months to 12 years). Majority of the children i.e. 58(37.7%) were seen in the age group 1 to < 5 years, 55 (35.7%) were ranged from 5 to < 10 years, 36(23.4%) were observed between 10 to 12 years of age group and only 05(3.2%) children were 6 months to <1 year of age. Table No. 2

Out of 154 cases, 118 cases were plasmodium vivax positive, 78(66.1%) were male and 40(33.9%) were female. Thirty four children were suffering from plasmodium falciparum malaria, 16(47.1%) were male and 18(52.9%) were female whereas 02 children had mixed (p. vivax and p. falciparum) infection, 1(50.0%) was male and 1(50.0%) female. Table No. 3

Out of 154 children of Malaria, 100(65%) had decreased platelets count indicative of thrombocytopenia, 59 (59%) were male and 41 (41%) were female. 54 had normal platelets count. Out of 100 thrombocytopenic patients, 71(71.0%) were found mild thrombocytopenic.

Of these, 48(67.6%) were suffering from p. vivax, 22(31.0%) had p. falciparum malaria and 1 (1.4%) had mixed infection (p. vivax and p. falciparum). 26(26.0%) had moderate thrombocytopenia. Of these, 18(69.2%) children were p. vivax positive, 7(26.9%) were p. falciparum positive and only 1(3.8%) child had mixed infection (vivax and falciparum). Severe thrombocytopenia was observed in 3(3.0%). Of these, 2(66.6%) were p. falciparum and 1(33.3%) were p. vivax malarial children. Table 4

Majority of the thrombocytopenia was observed in 67(67.0%) children of p. vivax while 31(31.0%) children had p. falciparum malaria, 2(2.0%) children

had mixed (p. falciparum + p. vivax) malaria. In vivax malaria, mild and moderate degree of thrombocytopenia was more common whereas in falciparum malaria severe thrombocytopenia was commonly seen. In the present study, out of 118 cases of p.vivax, 67(56.8%) had thrombocytopenia while out of 34 cases of p. falciparum malaria, 31(91.2%) had thrombocytopenia and 2 children had mixed infection (vivax + falciparum), both had thrombocytopenia. Table 5.

Table No. 1: Gender Distribution (n = 154)

Gender	Frequency	Percentage
Male	95	61.7%
Female	59	38.3%

Table No. 2: Frequency of age groups of study participants (n = 154)

Age groups	Frequ-ency	%age	Mean + SD
6 months to < 1 year	05	3.2%	0.60 + 0.29
1 to < 5 years	58	37.7%	2.32 + 1.0
5 to < 10 years	55	35.7%	6.42 + 1.38
10 to 12 years	36	23.4%	11.0 + 0.86

Table No.3: Species of plasmodium in gender (n = 154)

Malaria	Gender		Total
	Male n = 95	Female n = 59	
Vivax	78(66.1%)	40(33.9%)	118(100.0%)
Falciparum	16(47.1%)	18(52.9%)	34(100.0%)
Vivax & Falciparum	1(50.0%)	1(50.0%)	2(100.0%)

Table No.4: Plasmodium malaria in patients with and without thrombocytopenia (n = 154)

P. Malaria	Thrombo-cytopenia n = 100	Without thrombo-cytopenia N = 54	Total
Vivax	67(56.8%)	51(43.2%)	118(100.0%)
Falciparum	31(91.2%)	3(8.8%)	34(100.0%)
Vivax & Falciparum	2(100.0%)	0	2(100.0%)

Table No.5: Severeity of thrombocytopenia with plasmodium malaria (n = 154)

P. Malaria	Mild n = 71	Moderate n = 26	Severe N = 3	Total
Vivax	48(67.6%)	18(69.2%)	1(33.3%)	67(67.0%)
Falciparum	22(31.0%)	7(26.9%)	2(66.7%)	31(31.0%)
Vivax & Falciparum	1(1.4%)	1(3.8%)	0	2(2.0%)

DISCUSSION

Malaria affects an estimated 300 million people and causes more than a million deaths per year worldwide. Acute malaria is often associated with mild or moderate thrombocytopenia in non-immune adults.[10]

Thrombocytopenia occurs in 60-80%cases of malaria and is considered to be an important predictor of severity in childhood malaria.Finding of thrombocytopenia is an important clue to the diagnosis of malaria in patients with acute febrile illness in endemic areas as suggested by previous investigator.[11, 12, 13]

In this study, 61.7% were male and 38.3% were female similar results were seen in the study conducted by Jalal-Ud-Din et al in Ayub Medical College, Abbottabad who revealed that male children had higher incidence of malaria than female (male = 71.25% vs. female = 28.75%); probable reasons is because males are having more exposed to mosquito bite than female.[14]

In this series, the mean age of children was 5.76 years (n = 154) which is comparable to study conducted by Katira B et al. who reported 5.1 years.

Out of 154 cases, 118(76.6%) were plasmodium vivax positive, 78(66.1%) were male and 40(33.9%) were female. Thirty four(22.1%) were suffering from plasmodium falciparum malaria, 16(47.1%) were male and 18(52.9%) were female whereas 02(1.3%) children were mixed (p. vivax and p. falciparum) positive, 1(50.0%) was male and 1(50.0%) female. Yasinzai MI et alreported that P. vivax was present in 88.69% cases, 73.20%were male and 26.80% were female, whereas infection of P. falciparum was observed in 11.30%, 74.5% in male and 25.5% in female. In the present study, the results of p. vivax malaria correlate well to the study of Yasinzai MI et al but the difference of p. falciparum malaria may be because of large sample size of population and study duration. [15,16]

In the present study, the incidence of P. vivax was observed to be higher (76.6%, n = 154) as compared with that of P. falciparum (22.1%, n = 154). Similarly, Yasinzai, M.I et al. found higher incidence of p. vivax 88.69% and p. falciparum 11.3%. Jan and Kiani (2001) while studying malarial parasites in Kashmiri refugees settled in Muzaffarabad reported high incidence of P. vivax than of P. falciparum also reported same. Jalal-Ud-Din et al. showed the same observation i.e. Plasmodium vivax was 92.21% and Plasmodium falciparum was 7.79% [14,16,17]

In this study 100(65.0%) children suffering from malaria showed some degree of thrombocytopenia these observations are comparable with studies done by Ansari S. et al. who revealed 69.18%, similarly, Memon AR et al. in their study conducted in Dow University of Health Sciences & Civil hospital Karachi

showed 70% thrombocytopenia. In another cross sectional study of Shaikh QH et al. conducted in JPMC Karachi, thrombocytopenia was 80.6%.[10, 12,18]

Khan SJ et al. reported 58.0% cases of thrombocytopenia.[74]Mehmood and Yasir observed 58.0%.[19, 20]

In this study, higher prevalence of thrombocytopenia was seen in male than female i.e.(59% vs. 41%) out of 100 cases. Similarly, Phulpoto JA et al. showed 74% male in majority than 26% female, whereas Memon AR revealed that 76% male and 24% female patients had thrombocytopenia. These results indicated that the thrombocytopenia is more common in male than female cases of malaria.[4, 10]

Another observation in the present study was that out of 118 cases of p.vivax, 67(56.8%) had thrombocytopenia while Morales et al. reported percentage of patients (44%) affected by P. vivax malaria while in study of Shaikh QH et al.[78] showed 93.33% thrombocytopenic in p. vivax cases. Abro AH et al. documented the figure of 81.0% thrombocytopenia in p. vivax cases. Difference in observations may be due to difference in study populations, environmental, sample size, duration of study and other social factors.[21, 22, 23]

Out of 34 cases of p. falciparum malaria, 31(91.2%) children had thrombocytopenia. Memon AR et al. accounted 93% of thrombocytopenia in patients having malaria due to p. falciparum. Another observation made by Abro AH showed 87% thrombocytopenia in cases of p. falciparum malaria whereas Mahmood A et al. reported the 75.18% percentage of thrombocytopenia in p. falciparum malaria. These results nearly correlate to the present findings. [10, 20, 23]

The results of the present study revealed that mild thrombocytopenia was in 71.0% out of 200 cases of thrombocytopenia, moderate thrombocytopenia 26.0% and severe thrombocytopenia was in 3.0% children. However, the similar results were seen in the study of Memon AR i.e. 70% mild, 22% moderate and 8% severe thrombocytopenia, these results nearly correlate to the present study. [10]

CONCLUSION

This study concluded that mild to moderate and some degree of severe thrombocytopenia is common with malaria which may lead to prolong bleeding time, which is a medical emergency and can be life threatening e.g. intracranial bleeding, so timely recognition by assessing bleeding time in each thrombocytopenic malaria patient and management by intervention such as immediate transfusion of platelets can prevent fatal outcome.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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