



RESEARCH ARTICLE

ASSOCIATION OF THROMBOCYTOPENIA AND PROLONG BLEEDING TIME IN CHILDREN
SUFFERING FROM MALARIA

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ABSTRACT

Objective: To determine the association of thrombocytopenia and prolong bleeding time in children suffering from malaria.

Study design: Cross sectional descriptive study

Setting: Department of pediatrics Liaquat University Hospital Hyderabad.

Duration: Six month from 24th June 2014 to 23rd December 2014

Subjects and methods: All children presenting in pediatrics department 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 then further evaluated for their bleeding time (BT) by Duke's method and observation were noted.

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). Prolonged bleeding time was observed in those children who had thrombocytopenia. Out of 100 cases of thrombocytopenia, prolonged bleeding time (> 8 minutes) was seen in 8(8.0%, n = 100) cases. Of these, 5(62.5%, n = 8) children had moderate thrombocytopenia while 3(37.5%, n = 8) had severe thrombocytopenia.

Conclusion: This study concluded that various degree of thrombocytopenia is common with malaria from asymptomatic to prolong bleeding time leading to life threatening bleeding require early diagnosis and prompt management.

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INTRODUCTION

Malaria remains a major cause of morbidity and mortality in tropical regions of world and accounts for at least 1 million deaths every year. 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. Malaria is caused by Plasmodium specie. There are four different types of Plasmodia

(*P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*) that infect humans by bite of female Anopheles mosquito. (Francischetti *et al.*, 2008; WHO, 2009) Malaria is preventable and treatable disease if diagnosed in time; otherwise it may be fatal due to complications like hematological and cerebral. Therefore all clinically suspected cases must be diagnosed with peripheral blood smear which is of gold standard due to presence of trophozoites and schizonts of Plasmodium vivax. The rapid malaria antigen test was negative for *P. falciparum*, but positive for *P. vivax* both associated with complications. (Bal *et al.*, 2012; Fajardo and Tallent, 1974) Anemia and thrombocytopenia are the most frequent malaria-associated hematological complications. Hematological abnormalities may range from asymptomatic thrombocytopenia to fulminant disseminated intravascular coagulation (DIC), Mild thrombocytopenia is common in both falciparum and vivax

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malaria, severe thrombocytopenia and bleeding manifestations have been seen in *P. falciparum* malaria. Thrombocytopenia in malaria has been attributed to both non-immunological and immunological mechanisms of unknown etiology. Presence of *P. vivax* within platelets by electron microscopy, suggesting direct lytic effect of parasite on platelets or postulated mechanisms reported is macrophage activation leading to platelet destruction, increased levels of cytokines, immunological destruction due to antiplatelet IgG and oxidative stress. (Thapa *et al.*, 2009; Katira and Shah, 2006)

Severity of thrombocytopenia: (Kocher *et al.*, 2009)

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 determine the association of thrombocytopenia and prolong bleeding time in children suffering from malaria which if severe then become acute emergency, require immediate platelet transfusion for prevention of 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
- Fever (>101 °F) at the time of presentation or history of fever (>101 °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.
- 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 °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 °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 Medionix cell counter method. Thrombocytopenia (if present) was classified according to the reference ranges and categories. The malaria infected thrombocytopenic patients were further evaluated for their bleeding time (BT) by Duke method i.e. the patients were pricked with a special needle or lancet, on the earlobe or fingertip, after aseptic measures, then wipes the blood every 30 seconds with a filter paper until bleeding ceases were labeled as normal or prolonged according to standard cut off range. 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 severity were 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 females. 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.1 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. 2 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 3 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 1. Frequency of age groups of study participants (n = 154)

Age groups	Frequency	Percentage	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 2. 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 3. Plasmodium malaria in patients with and without thrombocytopenia (n = 154)

P. Malaria	Thrombocytopenia n = 100	Without thrombocytopenia 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 4. Severity 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%)

Table 5. Prolonged bleeding time in thrombocytopenic children with plasmodium malaria n = 8

P. Malaria	Frequency	Percentage
P. vivax	04	50.0%
P. Falciparum	03	37.5%
Mixed (<i>p. vivax + p. falciparum</i>)	01	12.5%

Table 4 The mean bleeding time + SD of thrombocytopenic malaria children was 4.19 + 1.84 minutes (n = 100). Prolonged bleeding time was observed in those children who had thrombocytopenia (n = 100) while in the other cases (n = 54) no bleeding time was assessed. Out of 100 cases of thrombocytopenia, prolonged bleeding time (> 8 minutes) was seen in 8(8.0%, n = 100) cases. Of these, 5(62.5%, n = 8) children had moderate thrombocytopenia while 3(37.5%, n = 8) had severe thrombocytopenia. No prolonged bleeding time was observed in those children who had mild thrombocytopenia shown in Table 5.

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. (Agarwal *et al.*, 2005; Kumar and Shashirekha, 2006) 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. (Memon and Afsar, 2006; Ansari *et al.*, 2009) 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. 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. (Jalal-Ud-Din *et al.*, 2006; Katira and Shah, 2006) 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 al.* reported 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 *et al.* but the difference of *p. falciparum* malaria may be because of large sample size of population and study duration. (Yasinzai and Kakarsulemankhel, 2008) 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 *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% (Jalal-Ud-Din *et al.*, 2006; Yasinzai and Kakarsulemankhel, 2008; Jan and Kiani, 2001) In this study 100(65.0%) children suffering from malaria showed some degree of thrombocytopenia these observations are comparable with studies done by Ansari *et al.* who revealed 69.18%, similarly, Memon *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%. (Memon and Afsar, 2006; Ansari *et al.*, 2009; Shaikh *et al.*, 2009) Khan SJ *et al.* reported 58.0% cases of thrombocytopenia. Mehmood and Yasir observed 58.0%. (Khan *et al.*, 2008; Mahmood and Yasir, 2005) In this study, higher prevalence of thrombocytopenia was seen in male than female i.e. (59% vs. 41%) out of 100 cases. Similarly, Phulpoto *et al.* showed 74% male in majority than 26% female, whereas Memon 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. (Memon and Afsar, 2006; Phulpoto and Shaikh, 2010)

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 *et al.* showed 93.33% thrombocytopenic in *p. vivax* cases. Abro

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. (Rodriguez-Morales et al., 2005; Shaikh et al., 2009; Abro et al., 2008) Out of 34 cases of p. falciparum malaria, 31(91.2%) children had thrombocytopenia. Memon et al. accounted 93% of thrombocytopenia in patients having malaria due to p. falciparum. Another observation made by Abro showed 87% thrombocytopenia in cases of p. falciparum malaria whereas Mahmood et al. reported the 75.18% percentage of thrombocytopenia in p. falciparum malaria. These results nearly correlate to the present findings. (Memon and Afsar, 2006; Abro et al., 2008; Mahmood and Yasir, 2005) The results of the present study revealed that mild thrombocytopenia was in 71.0% out of 100 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. (Memon and Afsar, 2006) In the present study, frequency of prolonged bleeding time in thrombocytopenic malaria children (n = 100) was 8.0%, the same observation 9.6% was carried out in the study of Siddig M et al. whereas 7.1% by Koh et al. These findings are nearly correlate well to the present study. (Siddig et al., 2004; Koh et al., 2004; Uttra et al., 2010)

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.

REFERENCES

Abro AH, Ustadi AM, Younis NJ, Abdou AS, Hamed DA, Ahmed AlhajSaleh. 2008. Malaria and hematological changes. *Pak J Med Sci.*, 24(2):287-91.

Agarwal A, Rath S, Shashiraj. 2005. Plasmodium vivax malaria presenting with severe thrombocytopenia. *J Trop Pediatr.*, 51:120-1.

Ansari S, Khoharo HK, Abro A, Akhund IA, Qureshi F. 2009. Thrombocytopenia in plasmodium falciparum malaria. *J Ayub Med Coll Abbottabad.*, 21(2):145-7.

Bal BS, Duggal A, Khurana S, Kaur J, Duggal A. 2012. Haematological abnormalities in Plasmodium vivax malaria. *JiIACM*, 13(3): 236-8

Fajardo LF. and Tallent C. 1974. Malarial parasites within human platelets. *JAMA*, 229: 1205.

Francischetti, I. M. B., Seydel, K. B., & Monteiro, R. Q. 2008. Blood Coagulation, Inflammation and Malaria. *Microcirculation*, 15(2), 81-107.

Jalal-Ud-Din, Khan SA, Ally SH. 2006. Malaria in children: study of 160 cases at a private clinic in Mansehra. *J Ayub Med Coll Abbottabad.*, 18(3):44-5.

Jan, A.H. and T.A. Kiani. 2001. Haematozoan parasites in Kashmiri refugees. *Pakistan J. Med. Res.*, 40:10-2

Katira B. and Shah I. 2006. Thrombocytopenia in plasmodium vivax infected children. *J Vector Borne Dis.*, 43(3):147-9.

Katira B. and Shah I. 2006. Thrombocytopenia in Plasmodium vivax infected children. *J Vector Borne Dis.*, 43(3):147-9

Khan SJ, Khan FR, Usman M, Zahid S. 2008. Malaria can lead to Thrombocytopenia. *Rawal Med J.*, 33(2):183-5.

Kocher et al. 2009. Severe Plasmodium vivax malaria: A report on serial cases from Bikaner in North Western India. *Am J Trop Med Hyg.*, 80: 194-8

Koh KH, Chew PH, Kiyu A. 2004. A retrospective study of malaria infections in an intensive care unit of a general hospital in Malaysia. *Singapore Med J.*, Jan;45(1):28-3

Kumar A, Shashirekha. 2006. Thrombocytopenia – an indicator of acute vivax malaria. *Indian J Pathol Microbiol.*, 49:505-8.

Mahmood A. and Yasir M. 2005. Thrombocytopenia: A predictor of Malaria among febrile patients in Liberia. *Infect Dis J.*, 14:41-4.

Memon AR and Afsar S. 2006. Thrombocytopenia in hospitalized malaria patients. *Pak J Med Sci.*, 22(2):141-3.

Phulpoto JA. and Shaikh AH. 2010. Frequency of thrombocytopenia in Malaria patients. *Med Channel*, 16(4):511-513.

Rodriguez-Morales AJ, Sanchez E, Vargas M, et al. 2005. Occurrence of thrombocytopenia in Plasmodium vivax malaria. *Clin Infect Dis.*, 41:130-1.

Shaikh QH, Ahmad SM, Abbasi A, Malik SA, Sahito AA, Munir SM. 2009. Thrombocytopenia in malaria. *J Coll Physicians Surg Pak.*, 19(11):708-10.

Siddig M, Kadaru Y. and Mustafa MS. 2004. Screening blood donors for malaria parasite in Sudan. *Ethiop.J.Health Dev.*, 18(2):70-3.

Thapa R, Biswas B, Mallick D, Sardar S, Modak S. 2009. Childhood plasmodium vivax malaria with severe thrombocytopenia and bleeding manifestations. *J Pediatr Hematol Oncol.*, 31(10):758-9.

UKM Uttra, Devrajani BR, Shaikh K, Shaikh KR, Shah SZA. 2010. Severity of thrombocytopenia and prolonged bleeding time (A Clinical Study of 162 Malaria Cases). *World Appl. Scie. J.*, 9(5):484-88.

WHO Factsheet 94: Malaria, updated Jan 2009

Yasinzai, M.I. and J.K. Kakarsulemankhel, 2008. Incidence of Human Malaria Infection in Desert Area of Pakistan: District Kharan. *J. Agric. & Social Sci.*, 4(1): 39-41.
