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Thrombocytopenia as a Hematological Parameter of Diagnosis and Prognosis of Malaria in Children

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Abstract

Malaria remains a global health problem with an estimated three to five hundred million new cases occurring each year. Although infection due to Plasmodium falciparum is responsible for the greatest overall morbidity and mortality, P. vivax contributes seventy to eighty million new cases to the annual worldwide burden of disease, especially in temperate regions [1].Worldwide, there are more than 250 million cases of malaria every year, killing between 1-3 million people.(Gursharan and Neha, 2011; Colonel et al., 2010), 88% of them occurred in subsahran African children below five years.

Even though Africa accounts for 90% of the mortality burden for malaria, south-east Asia still suffers considerable mortality and morbidity. India contributes 75%-77% of the total malaria in south East Asia and about 95% of the population of moderate to high risk of malaria in Southeast Asia region is living in India [2].In India about 27% population lives in malaria high transmission area (more than 1 case per 1000 population) and 58% in low transmission area. [3]

Malaria is a vector born disease caused by the bite of the female Anopheles mosquito inoculating the sporozoites in the human blood stream leading to clinical manifestations. [4]Active malarial transmission happens throughout the year, while aggressive out bursts of disease are seen mainly during and after the 'monsoon' season (June to November).

Hematological abnormalities have been observed in patients with malaria, with anemia and thrombocytopenia being the most common [5, 6]. Although thrombocytopenia is often reported, the occurrence of bleeding is rare in these patients [7].

A number of observational studies have confirmed the association of thrombocytopenia to malaria but till date the cause of thrombocytopenia is poorly understood. The speculated mechanism leading to thrombocytopenia are coagulation disturbances, splenomegaly, bone marrow alteration, antibody mediated platelet destruction, oxidative stress, and the role of platelets as cofactors in triggering severe malaria [8, 9, 10].

But before taking thrombocytopenia as a hematological parameter of the malaria significant correlation between malaria and the presence of thrombo cytopenia is mandatory asthrombo cytopenia is seen in some other acute febrile illnesses too. The correlation of thrombocytopenia with different types of malaria and its prognostic implications in context with severity of the low platelet count has not been evaluated in large studies particularly in children [11]. In view of paucity of data in

children from Indian studies, we conducted this study to find out occurrence and severity of thrombocytopenia in children with malaria and to correlate the low platelet count and type of malaria.

Materials and Methods

The study was conducted at Dr. B.C. Roy PGIPS, Kolkata, which is a tertiary referral center. This was a retrospective study of medical records of children, admitted in the hospital with the diagnosis of malaria. The study period was between January 2017 to December 2018. The inclusion criterion was children up to 12 years with a diagnosis of malaria.

Exclusion criteria

Patients with acute febrile illness and negative for MP on peripheral blood film or malaria dual antigen test in three consecutive samples at intervals of twelve hours were excluded. Similarly Patients with history or clinical features suggesting chronic liver disease and those with history of bleeding disorder, hematological malignancy, diagnosed cases of Idiopathic thrombocytopenic purpura were also exclude from the study.

Patients were divided into three subgroups based on platelet count. Thrombocytopenia was defined as platelet count of less than 150000 / cmm. Thrombocytopenia was considered severe if platelet count was <50,000 / cmm, moderate if 50,000-100,000 / cmm, and mild if 100,000-150,000 / cmm.

Data were analyzed by Chi- Square test using the SPSS version. P value of < 0.05 was taken as significant.

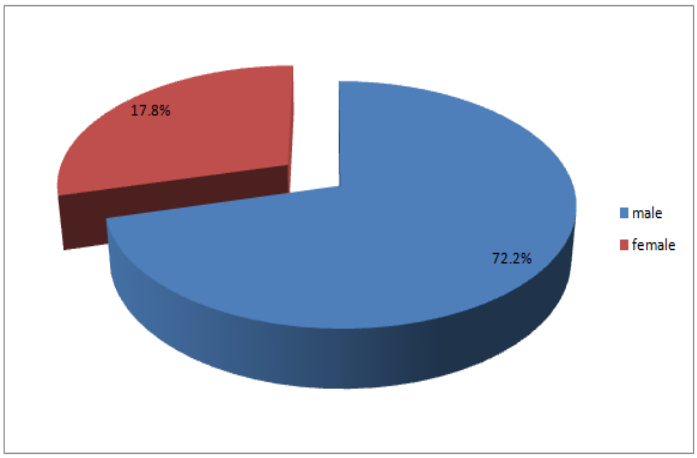
Results

In our study 90 patients with malarial positive was investigated with platelet count. Out of 90 patients 65(72.2%) patients were males and 25(17.8%) patients were females. Majority of the patients were between 4- 9 years (43.33% patients).[Table 1] The sex distribution of the cases are shown in (Fig.1)

Table 1.age and sex distribution of children with malaria

Age group (yrs.)	No. of cases	Male	Female	Percentage
1-4	20	14	6	22.2%
>4-9	32	25	7	35.6%
>9-12	38	26	12	42.2%
Total	90	65	25	100%

Figure 1.Sex distribution



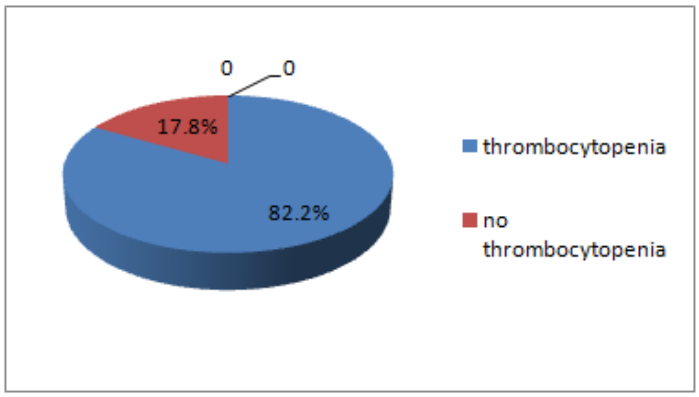
In the study group of 90 patients; 14 (15.6%) patients had mixed malaria, 56 (62.2%) were positive for plasmodium vivax and isolated P. falciparum was detected in 20 (22.2%) children [Table2].

Table 2: Platelet counts in patients with different type of malaria

Category	>1,50,000/ cmm	1,50,000-1,00,000/ cmm	1,00,000-50,000/cmm	<50,000/ cmm	total
P.vivax	3	17	26	10	56
P. falciparum	10	1	4	5	20
Mixed	4	2	5	3	14
total	17	20	35	18	90

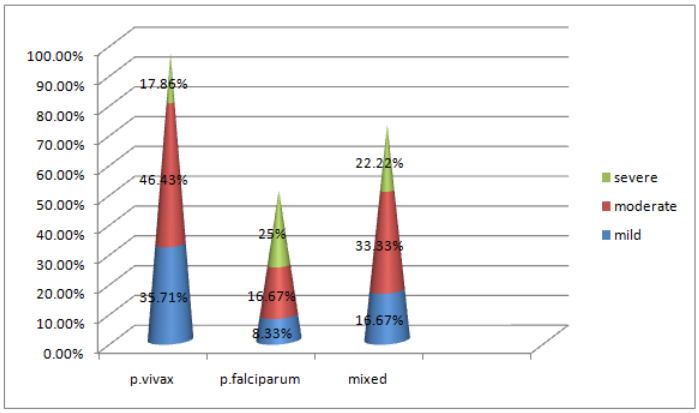
Thrombocytopenia was observed in 74 cases out of total 90 children (82.2%) having malaria (Fig.2)

Fig.2: Distribution of cases of malaria regarding association with thrombocytopenia



Out of 56 cases detected with vivax malaria 53 (94.6%) cases had platelet count less than 150000/cmm. , out of which 26 patient(46.43%) had a platelet count less than 100000 but more than50000/cmm. and only 10 patients(17.86%) had severe thrombocytopenia. Out of 20 patients detected with falciparum malaria 10patients (50%) had platelet counts less than 150000/ commute of which 5(25%) patients had platelet count less than 50000/cmm. It was noted that severe thrombocytopenia was more common with plasmodium falciparum than vivax infection. The children diagnosed as case of mixed infection also showed mostly moderate thrombocytopenia (33.33%)(Fig.3).

Figure 3. The distribution of children according to species and severity of thrombocytopenia



Discussion

Malaria is a major health issue for people residing in tropical countries like ours. Malaria is endemic in many parts of India and unfortunately Kolkata still comes under high risk zone of malaria. In endemic areas, malaria has been reported as the major cause of low platelet count and is a sensitive but non-specific indicator of infection with malaria parasite. [12]

Thrombocytopenia and anemia are the most frequently malaria associated hematological complication of malaria. Platelet counts of less than 150000/cmm. Increases the likelihood of malaria by 12-15 times [13,14]. It has been found in many studies that sensitivity of platelet count for diagnosing malaria was 100%, and the specificity was 70% and thus presence of thrombocytopenia in a child with fever in an endemic area should make one suspect malaria and tests for the same should be done.[15]

Finding of thrombocytopenia with anemia is an important clue to the diagnosis of malaria in patients with acute febrile illness are comparable to studies done by other investigators as 71% by Robinson, Jenney, Tachado, Yung, Manitta, Taylor et al. [16] and 58.97% by Rodriguez-Morales, Sanchez, Vargas, Piccolo, Colina, Arria [17]. Hence patients with acute febrile illness without localizing signs and having combination of anemia and thrombocytopenia should alert the treating physician about the possibility of malaria infection which can be confirmed with specific tests. In our study thrombocytopenia was found in 83.33% of patients of which 75% are infected with P. vivax alone, 12% are P. falciparummono infection and rest are of mixed or both type. The prevalence of thrombocytopenia in malaria was reported as 85% (falciparum) and 72% (vivax) in the study by Horstmann et al [18].

In our study thrombocytopenia was observed in 94.6% of patients with vivax malaria, in that 17.86% had severe thrombocytopenia. The least platelet count documented in our study was 8000/cmm, and it was seen in vivax infection. Also in other studies severe thrombocytopenia is commonly reported to be associated with Plasmodium falciparum infection and has been reported to occur in

patients co infected with both Plasmodium falciparum and Plasmodium vivax, its occurrence has been rarely reported in cases of Plasmodium vivax malaria [19]. In our study, 25% of the patients with P. Falciparum had severe thrombocytopenia.

The pathogenesis of thrombocytopenia in malaria is unclear, although increased platelet destruction rather than decreased production appears to be responsible. Bone marrow studies have revealed adequate or increased numbers of megakaryocytic and analyses of plasma thrombopoietin levels have ruled out reduction of this cytokine as the cause of thrombocytopenia.[20] Platelet consumption by disseminated intravascular coagulation (DIC) has also been suggested; DIC, however, is seldom seen in even the most severe cases of malaria.[21]

The spleen has been implicated as a site of excess sequestration. Splenomegaly alone, however, cannot be the mechanism as most patients who develop thrombocytopenia do so early in the course of the infection before splenic enlargement has developed. An immune mechanism that would lead to opsonization of platelets with phagocytosis by fixed macrophages has been proposed. [22,23] Studies showing the inverse relationship between titers of serum platelet-associated IgG and the platelet count in P. vivax infections support that hypothesis.[24] Studies in experimental animals suggest an activation of caspases and subsequent apoptosis may be involved in the development of malaria-associated thrombocytopenia. [20]

Oxidative stress damage of thrombocytes has also been implicated in the etiopathogenesis based on the finding of low levels of platelet superoxide-dismutase and glutathione peroxides activity and high platelet lipid per oxidation levels in malaria patients, when compared to hose with healthy subjects [22]

Thrombocytopenia in malaria can partly be attributed to pseudo thrombocytopenia due to clumping of platelets [25]. There is no matched control group. This is one of the limitations of this study.

Conclusion

Mild to moderate thrombocytopenia was observed in hospitalized children suffering from both Plasmodium vivax and falciparum types of malaria. Severe thrombocytopenia is not frequent. The presence of thrombocytopenia is not a distinguishing feature between the two types. Severe thrombocytopenia doesn't necessarily indicate the severity of malaria. It is rare to have bleeding with thrombocytopenia caused by malaria. We can propose that the platelet count can serve as an important initial screening tool in this setting. This may be used in addition to the clinical and microscopic parameters to heighten the suspicion of this disease and prompt initiation of the treatment. Usually thrombocytopenia responds very well to anti-malarial treatment and necessitates no platelets transfusion. The above findings can have therapeutic implications in context of avoiding unnecessary platelet infusions with the relatively more benign course in Plasmodiumvivax malaria.

References

1. Mendis K, Sina BJ, Marchensini P, et al: The neglectedburden of Plasmodium vivax malaria. Am J Trop Med Hyg 2001; 64S: 97-106.
2. Dhanpat KK, Gajanand ST, Poonam CK, Sanjay KK, Ghanshyam SS, et al. Clinical features of children hospitalised with malaria-A study from Bikaner, North West India. Am J Trop Med Hyg 2010;83(5):981-989.
3. WHO World Malaria Report. Geneva Switzerland: WHO Press; 2008.
4. Tieveny LM, McPhee SJ, Papadakis MA, editors. Current medical diagnosis and treatment. 46th ed. New York: *McGraw Hill*; 2007

5. http://www.brown.edu/Research/EnvStudies
6. Khan SJ, Khan FR, Usman M, Zahid S. Malaria can lead to Thrombocytopenia. Rawal Med J 2008; 33: 183-185.
7. Lacerda MVG, Mourão MPG, Alexandre MAA, Siqueira AM, Magalhães BML, Martinez-Espinosa FE, Filho FSS, Brasil P, Ventura AMRS, Tada MS, Couto VSCD, Silva AR, Silva RSU, Alecrim MGC: Understanding the clinical spectrum of complicated ***Plasmodium vivax*** malaria: a systematic review on the contributions of the Brazilian literature. ***Malar J*** 2012,**11:**12.
8. S.S. Jamal Khan, F.R. Khan, M. Usman and S. Zahid. ''Malaria can lead to thrombocytopenia'' Rawal medical Journal, vol.33,no 2,pp183-185.2008.
9. T.S. Faseela, R.A.Ronald, K.B. Anita, C.S. Malli and Y. Rai. Diagnostic value of platelet count in malaria''Journal of clinical and diagnostic research, vol.5,no. 3,pp 464-466, 2011.
10. A. Rasheed, S. Saeed and S.A.Khan. ''platelet count in malaria'' Pakistan journal of pathophysiology, vol.19,no.3,pp.86-88,2008.
11. Jadhav UM, Patkar VS, Kadam NN. Thrombocytopenia in malaria – correlation with type and severity of malaria. J Assoc Physicians India 2004; 52:615–618.
12. Ref 5
13. Maina RN, Walsh D, Gaddy C, Hongo C, Waithumbi J et al. Impact of Plasmodium falciparum infection on hematological parameter in children living in Western Kenya. Malar journal 2010;9(suppl.3):S4.
14. Lathia TB, Joshi R. Can hematological parameters differentiate malaria from non malarial acute febrile illness in the tropics? Indian Journal Med Science 2004;58(6):239-244.
15. Patel U, Gandhi G, Friedman S, Niranjan S. Thrombocytopenia in malaria. *Natl Med Assoc*2004; *96:* 1212–4.
16. Robinson P, Jenney AW, Tachado M, Yung A, ManittaJ, Taylor K et al. Imported malaria treated in Melbourn Austrlia: Epidemiology and clinical features in 246 patients. JTravel Med 2001; 8:76–81.
17. Morales AJ, Sanchez E, Vargas M, Piccolo C, ColinaR, Arria M. Anemia and Thrombocytopenia in children with Plasmodium vivax malaria. J Trop Pediatr. 2005; 10: 1093-1097.
18. Horstmann R.D., M.Dietrich, U.Bienzle and H. Rasche,2005. Malaria induced thrombocytopenia. Annals of Hematol;42(3):157-64.
19. Thapa R, Biswas B, Mallick D, Sardar S, Modak S. Childhood plasmodium vivax malaria with severe thrombocytopenia and bleeding manifestations. J Pediatric Hematoloncol 2009; 31:758-759.
20. Piguet PF, Kan CD, Vesin C: Thrombocytopenia in an animal model of malaria is associated with an increased caspase-mediated death of thrombocytes. Apoptosis 2002; 7:91-98.
21. Kakar A, Bhoi S, Prakash V, et al: Profound thrombocytopenia in Plasmodium vivax malaria. DiagnMicrobiol Infect Dis 1999; 35:243-244.
22. Makkar RPS, Monga SMA, Gupta AK: Plasmodium vivax malaria presenting with severe thrombocytopenia. Braz J Infect Dis 2002; 6:263-265.
23. Lee SH, Looareesuwan S, Chan J, et al: Plasma macrophage colony-stimulating factor and P-selectin levels in malaria-associated thrombocytopenia. ThrombHaemost 1997; 77:289-93.
24. Kelton JG, Deystone J, Moore J, et al: Immune-mediated thrombocytopenia of malaria. J Clin Invest 1983; 71:832-836.

25. Scott CS, Van Zyl D, Ho E, Ruivo L, Mendelow B, Coetzer TL. Thrombocytopenia in patients with malaria, automated analysis of optical platelet count and platelet clumps with Cell Dyn CD4000 analyses. Clin Lab Haematol2002; 24: 295–302.