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Frequency of Thrombocytopenia in *Plasmodium vivax* Malaria

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ABSTRACT

Background: *Plasmodium vivax* is the most widely distributed human malarial parasite**.** Mild thrombocytopenia is a common feature of acute malaria caused by *P. vivax* regardless of the severity of infection which may progress to severe thrombocytopenia. The aim of our study was to find the frequency of thrombocytopenia in *Plasmodium vivax*. **Materials and Methods:** This descriptive cross sectional study was carried out at Peadiatrics unit, Shaikh Zayed Hospital, Lahore from July, 2013 to November, 2014 comprising of 56 children of both gender age 14 years and below who presented with fever of more than 101ºF and *Plasmodium vivax* rings, trophozoites or schizonts on peripheral blood smear (thick and thin smear). Full blood counts and platelet counts were done along with other routine as well specific investigations where required. The data was entered in standardized proforma and analyzed on SPSS 17. **Results:** There were 40 (71.43%) males and 16 (28.57%) females with the mean ages of 6.3±4.4 and 9.4±3.3 of males and females respectively with an overall mean age of 7.6±4.2. The frequency of thrombocytopenia was noted in 46 patients (82.14%). Mild thrombocytopenia was in 15 patients (26.79%) with mean of 119,000.89±8,000.76SD, moderate in 23 (41.07%) with mean of 89,210.56±5637.23 and severe thrombocytopenia was in 8 patients (14.29%) with mean of 29,678.98±2389.54. **Conclusion:** Thrombocytopenia is common in *P. vivax* malaria in our set up and all patients with such malaria must be screened for thrombocytopenia.

Key words: Thrombocytopenia, *Plasmodium vivax,* Fever.

INTRODUCTION

Malaria is an acute and chronic parasitic infection caused by intracellular *Plasmodium protozoa*, including *Pasmodium falciparum, malariae, ovale* and *vivax*. It has played major role in human history and has done more harm to more people than any infectious disease with an estimated 300-500 million cases and more than 01- million deaths each year.[1,2] *Plasmodium falciparum* malaria is one of the commonest potentially fatal infection in the world with high incidence in India, Nepal, Bangladesh and Pakistan. It is important public health problem in Pakistan causing at least 5,00000 cases of malaria annually.[3]

Plasmodium vivax is the most widely distributed human malaria parasite with an at risk population of 2.5 billion persons, causing approximately 100–300 million clinical cases each year[4]. It is commonly associated with heamatological abnormalities[5] including progressively decreasing haemoglobin, thrombocytopaenia, leucocytosis, leucopaenia, reticulocytosis and disseminated intravascular coagulation[6-9]. Leucopenia, leucocytosis, neutopenia, neutrophilia, eosinophilia and monocytosis also have been reported[10,11].

Thrombocytopenia is a classic feature of malaria. However, severe thrombocytopenia is less well described in humans[12] with vivax malaria. Human cases of immune-mediated vivax thrombocytopenia have been reported[13-15] and low platelet counts have been found in more *P. vivax* cases (74.7%) than *P. falciparum* cases (59.9%) in non-immune humans[16].

The exact cause of thrombocytopenis is not

known, however proposed causes for severe thrombocytopenia are, immune complex mediated destruction, spleenomegaly and spleenic sequestration of platelets, cytokine mediated destruction, decreased secretion of thrombopoitin associated with malarial hepatopathy, bleeding with evidence of DIC and ineffective thrombopoeisis[17]. Various studies have reported different frequencies of thrombocytopenia and other hematological abnormalities; the objective of our study was to find the frequency of thrombocytopenia in *P. vivax.*

MATERIAL AND METHODS

This descriptive cross sectional study was carried out at Peadiatrics Unit, Shaikh Zayed hospital, Lahore including 56 patients with positive *P. vivax* infection during the period of July, 2013 to November, 2014. Children of both gender of any age (14 years and below) with fever more than 101°F and *P. vivax* rings, trophozoites or schizonts on peripheral blood smear were included in the study. Patients with history of bleeding disorder, cerebral malaria, acute renal failure and drug intake such as Quinine, sulfadoxine-pyrimethamin, thiazides, co-trimoxazole, and other haemolytic agents were excluded from the study. Those patients having co-infection with malarial parasites other than vivax especially the dengue fever, were also excluded from the study.

Informed written consent was taken from parents / guardians. Detail history and physical examination were performed. All patients were subject to the routine laboratory investigations like hematological profile (complete blood count with platelet count), urine routine microscopy, renal function test, serum electrolytes, liver function test, blood sugar levels, and chest X-ray. Viral markers were done in patients with icterus to rule out viral hepatitis. Thrombocytopenia was defined as platelet count less than 150,000/mm^3. Patients with thrombocytopenia were divided in three categories; mild thrombocytopenia (less than 150,000/mm^3 but more than 50,000/mm^3) moderate thrombocytopenia (less than 50,000/mm^3 but more or equal to 20,000/ mm^3) and severe thrombocytopenia (less than 20,000/ mm^3). The diagnosis of malaria was confirmed by thick blood films stained with GIEMSA stain for malaria parasite. All malaria positive smears were studied for confirmation, identification of species and review of peripheral blood smears for platelets count and other hematological changes. The type of treatment of patients were according to their needs and non harmful. Exclusion and inclusion criteria were strictly followed to controlled confounder and bias in the study results. All the data was analyzed in SPSS version 17. All the results are presented in tables and graphs.

RESULTS

The total number of patients presenting with *Plasmodium vivax* malaria were 56 comprising of 40 (71.43%) males and 16 (28.57%) females. The mean ages of males and females were 6.3years ± 4.4SD and 9.4±3.3 respectively with an overall mean age of year 7.6±4.2.

The frequency of thrombocytopenia was noted in 46 (82.14%). Mild thrombocytopenia was in 15 (26.79%) with mean of 119,000.89±8,000.76, moderate in 23 (41.07%) with mean of 89,210.56±5637.23 and severe thrombocytopenia was noted in 8 (14.29%) with mean of 29,678.98±2389.54 (Table 1)

Distribution of thrombocytopenia according to age groups and gender is shown in Table 2.

Table 1: Distribution of thrombocytopenia.

Severity	Frequency	Mean±SD
Mild	15 (26.79%)	119,000.89 ± 8,000.76
Moderate	23 (41.07%)	89,210.56 ± 5637.23
Severe	8 (14.29%)	29,678.98 ± 2389.54

Table 2: Age and gender distribution of thrombocytopenia in *P. vivax* malaria.

	Mild	Moderate	Severe
Age groups			
6 Mon. to 5 yrs	11 (23.91%)	15 (32.61%)	1 (2.17%)
6 to 10 yrs	2 (4.35%)	5 (10.87%)	3 (6.52%)
11 to 14 yrs	2 (4.35%)	3 (6.52%)	4 (8.69%)
Gender			
Male	11 (23.91%)	12 (26.09%)	2 (4.35%)
Female	4 (8.69%)	11 (23.91%)	6 (13.04%)

DISCUSSION

Malaria is an parasitic infection affecting almost all blood components. Hemolysis, reduced cell deformity of parasitized and nonparasitized erythrocytes, increased splenic clearance, reduced platelet production and survival, and increased splenic uptake of platelets cause severe anemia and thrombocytopenia which can lead to bleeding diathesis. Initially thrombocytopenia was thought to be a feature of *P. falciparum* but reports of similar degree of thrombocytopenia in *P. vivax* and *P. falciparum* infections were documented since 1970s[18]. Most of the major publications related to frequency of thrombocytopenia in *P. vivax* malaria were published in the late 1990s, probably it was due to the availability of automated machines[19].

In our study, thrombocytopenia was noted in 82.14% patients with *P. vivax* malaria. Mild thrombocytopenia was 26.79%, moderate was 41.07% and severe thrombocytopenia was observed in 14.29%. Many local studies have supported our finding. Jamal A, et al, in their study on paediatrics patients from Karachi, have reported low platelet counts in 72% of their patients who were suffering from *Plasmodium vivax* infection[20] but other two studies from Karachi have reported thrombocytopenia 50% [21] and 61.7% [22]. Similarly, a study done by Saleem Ahmed Khan et al from Lahore reported thrombocytopenia in 82.5% patients with *P.vivax* infection. In our study, no patient presented clinically with bleeding and did not require platelets transfusion.

In other malaria endemic countries, similar frequencies of thrombocytopenia in accordance to our results are also present. These are 79.6% by Dhungat MP et al,[24] 81.57% by Jojera1 AS[25] and 73.92% by Joshi HA, et al[26].

The pathogenesis of thrombocytopenia in vivax malaria has not been clearly understood.[27,28] Fajardo and Tallent in 1974 by electron microscopy demonstrated P. vivax within platelets and they suggested a direct lytic effect of the parasite on the platelets[29]. Oxidative stress damage of thrombocytes has also been implicated by Erel O, et al[30] in the etiopathogenesis. By comparing to those of healthy subjects, they found low levels of platelet superoxide-dismutase and glutathione peroxidase activity and high platelet lipid peroxidation levels in malaria patients[29]. Nonimmunological destruction has been proposed by Looaresuwan S, et al.[31] while immune mechanisms has been show by Yamaguchi S, et al,[32] involving specific platelet associated IgG antibodies that bind directly to the malarial antigen in the platelets have been recently reported to play a role in the lysis of platelets and the development of thrombocytopenia recombinant – macro-phage colony stimulating factor (M-CSF) has been known to cause a reversible dose dependent thrombocytopenia. According to some clinical trials, elevated MCSF levels in malaria, by increasing macrophage activity may mediate platelet destruction in such cases.[33]

Limitation of our study was its small sample size. Also we did not follow our patients for a longer duration and the effect of anti malarial treatment on platelets count. We recommend that further extended studies should be performed to elaborate the role of *plasmodium vivax* infection on platelets count and also the effect of other plasmodium species causing malaria. The other hematological abnormalities must also be studied for better management of patients with malaria.

CONCLUSION

Thrombocytopenia is a common finding in malaria caused by *P*. vivax. It has some diagnostic significance; this may be used in addition to the clinical assessment, to heighten the suspicion of malaria. In an endemic area, we recommend that the platelets count has to be checked in all patients who present with acute febrile illness. This will help in predicting the presence of malarial infestation even in the early stages of the disease.

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