OCCURRENCE OF THROMBOCYTOPENIA IN VIVAX MALARIA

Pranjal Pankaj¹, K. Chandran², Shrawan Kumar³, Manish Kumar Singh⁴

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ABSTRACT: INTRODUCTION: Plasmodium Vivax malaria is endemic in the northern and eastern part of India. Although Plasmodium falciparum has been commonly implicated as the cause of complicated malaria but now the trend is changing and vivax is increasingly presenting with severe complications. **AIMS AND OBJECTIVES:** To study the occurrence and severity of thrombocytopenia in patients of vivax malaria. **MATERIAL AND METHODS:** A total of 100 patients were included in the study and identified positive for malaria parasites on peripheral smear examination with conventional microscopy. Platelet count was done on a fully automated, quantitative, hematology Counter at the time of presentation of patient. **INCLUSION CRITERIA:** freshly diagnosed cases of vivax malaria. **EXCLUSION CRITERIA:** Patients with associated falciparum, dengue, leptospirosis or any other known cause of thrombocytopenia. **RESULTS:** Platelet count was found to be normal in 32 patients. The mean platelet count in vivax malaria was 1,15,390/ μ l (SD 64,580) with a range of 8000-5,73,000/ μ l, Mild thrombocytopenia (50000 to 150000) was found in 36 patients. Moderate thrombocytopenia(20000 to 50000) was found in 20 patients. Severe thrombocytopenia (<20000) was found in 12 patients. Platelet transfusion was given in 9 patients and bleeding manifestations were noted in 4 patients. Thrombocytopenia was found to be more common among males (80.59%) and more common in younger age groups. **CONCLUSION:** Presence of thrombocytopenia is not a distinguishing feature between Vivax and Falciparum types. Thrombocytopenia less than 20,000/ μ l can occur in P. vivax malaria. The mechanism of occurrence of complications in vivax malaria is still poorly understood but this study can have therapeutic implications regarding more aggressive treatment of plasmodium vivax which was once considered purely benign and uncomplicated.

KEY WORDS: Malaria; vivax; thrombocytopenia.

INTRODUCTION: Malaria is a mosquito borne disease caused by a eukaryotic protest of the genus plasmodium. Plasmodium vivax is the most frequent and widely distributed cause of recurring (tertian) malaria worldwide. Each year there are more than 250 million cases of malaria, killing between 1 and 3 million people [1]. Most deaths occur because of P. falciparum infection, [2] which causes life-threatening cerebral, respiratory, renal, hepatic, hemodynamic, and hematologic dysfunction in 1% of cases [3]. In contrast, most P. vivax infections are relatively milder and run a benign course [4]. But in recent times there have been several reports of thrombocytopenia and other complications in the patients of plasmodium vivax malaria. In view of paucity of Indian data we have tried to correlate occurrence of thrombocytopenia in vivax including severe cases requiring platelet transfusion.

AIMS AND OBJECTIVES:

1. To study the occurrence and severity of thrombocytopenia in patients of vivax malaria.

2. To evaluate the requirement of platelet transfusions in severe thrombocytopenia in cases of vivax malaria.

MATERIALS AND METHODS: A total of 100 subjects, either hospitalized or treated on an outpatient basis over a period of three years were included in the study. All the study subjects were identified positive for malaria parasites on peripheral smear examination with conventional microscopy. Platelet count was done on a fully automated, quantitative hematology cell counter. Platelet count was the number of thrombocytes derived from directly measured platelet pulses, multiplied by a calibration constant and expressed in thousands of thrombocytes per microliter of whole blood. Baseline platelet counts were done on the day of presentation. Repeat platelet counts were done in subjects with marked thrombocytopenia until normal or near-normal values were reached. Subjects with a diagnosis of associated dengue fever and leptospirosis were excluded from the study, as both these conditions are known to significantly contribute to thrombocytopenia. P. falciparum antigen test (PfHrp antigen test- Paracheck) was performed in subjects with P. vivax malaria on the peripheral smear with a platelet count less than 20,000 cells/ μ l for more emphatic exclusion of associated P. falciparum infestation. P. falciparum antigen test was also performed in subjects with high index of clinical suspicion or multi-organ involvement. Data was entered on a excel spreadsheet and statistical analysis was performed with Microsoft excel.

INCLUSION CRITERIA:

1. Freshly diagnosed cases of plasmodium vivax malaria.

EXCLUSION CRITERIA:

1. Patients with associated plasmodium falciparum infection.
2. Patients with associated diagnosis of dengue fever or leptospirosis.
3. Patients with other known causes of thrombocytopenia.

OBSERVATIONS: The mean age of patients was 37.4 ± 14.2 years

TABLE 1: Age distribution of total number of cases

AGE GROUPS	NUMBER OF PATIENTS (out of 100)
20 – 29	35
30 – 39	28
40 – 49	20
50 – 59	17

TABLE 2: Sex distribution of total number of cases

SEX	No. of patients
MALES	67
FEMALES	33

ORIGINAL ARTICLE

Graphic representation of sex distribution

TABLE 3: Percentage of patients developing thrombocytopenia in vivax malaria

	N
Normal platelets	32%
Thrombocytopenia	68%

TABLE 4: Sex distribution of patients who developed thrombocytopenia

SEX	PERCENTAGE OF PATIENTS DEVELOPING THROMBOCYTOPENIA (OUT OF TOTAL CASES OF THROMBOCYTOPENIA i.e. 68)
MALE	54 (79.4%)
FEMALE	14(20.6%)

TABLE 5: Occurrence of thrombocytopenia among males

	PERCENTAGE OF MALES (OUT OF TOTAL MALES i.e. 67)
THROMBOCYTOPENIA PRESENT	54(80.59%)
THROMBOCYTOPENIA ABSENT	13(19.40%)

ORIGINAL ARTICLE

TABLE 6: Occurrence of thrombocytopenia among females

	PERCENTAGE OF FEMALES (OUT OF TOTAL FEMALES i.e. 33)
THROMBOCYTOPENIA PRESENT	14(42.42%)
THROMBOCYTOPENIA ABSENT	19(57.58%)

TABLE 7: Age distribution of patients developing thrombocytopenia

AGE GROUPS	NUMBER OF PATIENTS(OUT OF 68)
20 – 29	29
30 – 39	18
40 – 49	12
50 - 59	9

TABLE 8: Percentage of patients developing thrombocytopenia among their age groups

AGE GROUPS	PERCENTAGE OF PATIENTS DEVELOPING THROMBOCYTOPENIA AMONG THEIR GROUP
20 – 29	82.86%
30 – 39	64.28%
40 -49	60.00%
50 – 59	52.94%

TABLE 9: Severity of thrombocytopenia

Severity of thrombocytopenia	No. of patients
Normal platelet count	32
Mild thrombocytopenia (50000 – 150000)	36
Moderate thrombocytopenia (20000 – 50000)	20
Severe thrombocytopenia (< 20000)	12

Graphic representation of occurrence and severity of thrombocytopenia

TABLE 10: Patients of thrombocytopenia requiring platelet transfusion

	N
Platelets transfused	9
not transfused	59

TABLE 11: Patients of thrombocytopenia having bleeding manifestations

Bleeding manifestations present	4
No bleeding manifestation	64

RESULTS: The mean age of patients was 37.4 ± 14.2 years. Platelet count was found to be normal in 32 patients. The mean platelet count in vivax malaria was 1,15,390/ μ l (SD 64,580) with a range of 8000-5,73,000/ μ l, Mild thrombocytopenia(50000 to 150000) was found in 36 patients. Moderate thrombocytopenia(20000 to 50000) was found in 20 patients. Severe thrombocytopenia (<20000) was found in 12 patients. Out of 12 patients having severe thrombocytopenia, bleeding manifestations(epistaxis, gum bleeding and Hematuria) were noted in 4 patients. 9 patients required platelet transfusion either because of bleeding manifestations or persistently low platelet count despite treatment. 80.59% of males had thrombocytopenia at presentation compared to 42.4% of females. The highest incidence of thrombocytopenia was found in youngest age group(20 – 29 yrs) i.e.82.86%.

DISCUSSION: Severe and complicated malaria is usually caused by *P. falciparum* but it has been increasingly observed that *P. vivax* malaria, which was otherwise considered to be benign malaria, with a low case-fatality ratio, can also occasionally result in severe disease as with *P. falciparum*

malaria[8-12]. 68% of patients with vivax malaria in our study had thrombocytopenia out of which 32% had moderate to severe thrombocytopenia.

The mechanism of thrombocytopenia in malaria is uncertain. Immune-mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have all been postulated. Abnormalities in platelet structure and function have been described as a consequence of malaria, and in rare instances platelets can be invaded by malarial parasites themselves. Thrombopoietin (TPO) is the key growth factor for platelet production and is elevated in states of platelet depletion. TPO serum levels have been shown to be significantly higher in subjects with severe malaria, normalizing within 14-21 days of therapy.[5] Immune-mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have all been postulated in the cause for thrombocytopenia. Abnormalities in platelet structure and function have been described as a consequence of malaria, and in rare instances platelets can be invaded by malarial parasites themselves. Two types of changes in platelet dysfunction are seen in malaria. Initially there is platelet hyperactivity, this is followed by platelet hypoactivity. Platelet hyperactivity results from various aggregating agents like immune complexes, surface contact of platelet membrane to malarial red cells and damage to endothelial cells. The injured platelets undergo lysis intravascularly. The release of platelet contents can activate the coagulation cascade and contributes to DIC. Transient platelet hypoactivity is seen following this phase and returns to normal in 1 to 2 weeks.[6,7] In many studies undertaken, the significance of haemostatic abnormalities as a consequence of malaria has been difficult to assess as a result of the presence of various associated complications such as liver dysfunction, uraemia and treatment with low molecular weight dextran, dexamethasone and heparin. Still there are various national and international studies suggesting that vivax malaria can have fatal complications.[13-20]

CONCLUSION: Thrombocytopenia is a common complication of malaria but it is no longer a distinguishing feature between vivax and falciparum. Even vivax malaria can present with life threatening thrombocytopenia having bleeding manifestations and requiring platelet transfusions. The mechanism of occurrence of complications in vivax malaria is still poorly understood but this study can have therapeutic implications regarding more aggressive treatment of plasmodium vivax which was once considered purely benign and uncomplicated.

REFERENCES:

1. Kahl U. Malaria kills over 1 million people every year. Genomic mapping of malaria parasite and mosquito raise hope for a vaccine as well as more effective drugs. *Lakartidningen* 2003; 100 (12): 1042-1047.
2. Greenwood BM, Bojang K, Whitty CJ, et al. Malaria. *Lancet*. 2005; 365: 1487.
3. Warrell DA, Molyneux ME, Beales PF. Severe and complicated malaria (2nd ed). *Trans R Soc Trop Med Hyg*. 1990; 84 (suppl 2): 1-64.
4. Wickramasinghe M. Multi-system failure in Plasmodium vivax malaria: report of a case. *Ceylon Med J*. 1981; 26: 107-115
5. Kreil A, Wenisch C, Brittenham G, Looareesuwan S, Peck- Radosavljevic M. Thrombopoietin in Plasmodium falciparum malaria. *Br J Haematol* 2000; 109:534-6.

6. Srichaikul T, Pulket C, Sirisatepisan T, Prayoonwiwat W. Platelet dysfunction in malaria. *Southeast Asian J Trop Med Pub Health* 1988; 19:225-33.
7. Mohanty S, Marwaha K, Ghosh S, et al. Functional and ultrastructural changes of platelets in malaria infection. *Trans R Soc Trop Med Hyg* 82:369-75, *J Clin Invest* 1988; 71:832-6.
8. Genton B, D'Acremont V, Rare L, Baea K, Reeder JC, et al. *Plasmodium vivax* and mixed infections are associated with severe malaria in children: A prospective cohort study from Papua New Guinea. *PLoS Med* 2008; 5: e127. doi:10.1371/journal.pmed.0050128
9. Tjitra E, Anstey NM, Sugiarto P, Warikar N, Kenangalem E, et al. (2008) Multidrug-resistant *plasmodium vivax* associated with severe and fatal malaria. A prospective study in Papua, Indonesia. *PLoS Med* 5: e128. doi:10.1371/journal.pmed.0050128
10. Maitland K, Williams TN, Newbold CI. *Plasmodium vivax* and *P. falciparum*: Biological interactions and the possibility of cross-species immunity. *Parasitol Today* 1997; 13: 227–231.
11. Gunawardena DM, Carter R, Mendis KN. Patterns of acquired anti-malarial immunity in Sri Lanka. *Mem Inst Oswaldo Cruz* 1994; 89: 61-63.
12. Horstmann RD, Dietrich M, Bienzle U, Rasche H. Malaria induced thrombocytopenia. *Blood* 1991; 42: 157-64.
13. Crabbe G, Van Paucke M, Cantinseaux B, artefactually normal automated platelet counts due to Malaria infected RBC. *Clin Lab Haematol* 2002; 24:179-82. <http://www.ncbi.nlm.nih.gov/pubmed/12067284>
14. Jadhau UM, Patkarvs, Kadam NN. Thrombocytopenia in Malaria. *J Assoc PhysiciansIndia* 2004; 52:615-8 <http://www.ncbi.nlm.nih.gov/pubmed/15847353>
15. Robinson P, Jenney AW, Tachadu M, Yung A, Manitta J, Tuylork et al. Biggs BA. Imported Malaria treated in Melbourne, Austrtali. *J Travel Med* 2001; 8 (2):76-81. <http://www.ncbi.nlm.nih.gov/pubmed/11285166>
16. Rodriguez – Morales AJ, Sanchez E, Vargas M, Piccolo C, Colina R, Arria M, Anemia and Thrombocytopenia in Children with *Plasmodium Vivax* malaria – *J Trop Pediatr.* 2005; 10:1093. <http://www.ncbi.nlm.nih.gov/pubmed/15980019>
17. Bashwari LA, Mandil AM, Bahnassy AA, Alshamsi MA, Bukhari HA – Epidemiological Profile of Malaria in a University Hospital in the Eastern Region of Saudi Arabia. *Saudi Med.J* 2001; 22(2):133-8.
18. Patel U, Ghandi G, Friedman S, Niranjana S. Thrombocytopenia in Malaria. *J. Natl Med Asso* 2004; 96(9):1212-4.
19. Lathia TB, JoshiR. Can Haematological Parameter Discriminate Malaria from Non malarious Acute Febrile Illness in the Tropics? *Indian J. Med Sci* 2004; 58(6):239-44. <http://www.ncbi.nlm.nih.gov/pubmed/15226575>
20. A.R. Memon, S.Afsar. Thrombocytopenia in Hospitalized Malaria Patients. *Pakistan J. Med Sci* 2006; 22(2):141-143.

ORIGINAL ARTICLE

AUTHORS:

1. Pranjali Pankaj
2. K. Chandran
3. Shrawan Kumar
4. Manish Kumar Singh

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Medicine, Rama Medical College Hospital & Research Centre, Mandhana, Kannur, Uttar Pradesh.
2. Professor, Department of Medicine, Rama Medical College Hospital & Research Centre, Mandhana, Kannur, Uttar Pradesh.
3. Associate Professor, Department of Medicine, Rama Medical College Hospital & Research Centre, Mandhana, Kannur, Uttar Pradesh.

4. Assistant Professor, Department of Medicine, Rama Medical College Hospital & Research Centre, Mandhana, Kannur, Uttar Pradesh.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Pranjali Pankaj,
House No. 201, Staff Quarter – 2,
Rama Medical College, Mandhana,
Kanpur, Uttar Pradesh – 209217.
Email- drpranjali@rediffmail.com

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