Research Article

Study on thrombocytopenia occurring in *P vivax* malaria at a tertiary centre in Southern India

Sanju Daniel John*, Peter George**

*Resident, **Professor, Department of Medicine, Father Muller Medical College, Father Muller Road, Mangalore -575002, Karnataka, INDIA.
Email: drsanjujohn1986@gmail.com

Abstract

Background: Malaria caused by *P vivax* is endemic to most of the tropical nations and are associated with various hematological abnormalities. Complications were more common among *P falciparum infections as compared to P vivax infections.* Recent literature suggests more severe forms of P vivax infections including cases with severe thrombocytopenia. Objectives: To study the occurrence of thrombocytopenia in *P vivax* malaria at a tertiary centre in Southern India. **Materials and Methods:** This retrospective cohort study was done among in-patients with P vivax malaria at a tertiary care center in Southern India over a period of 18 months from October 2012. A total of 200 patients with positive peripheral smear for P vivax malaria and negative for HRP-2 test were included in the study. The thrombocytopenia was graded as per the protocol and results were analyzed by frequency, percentage, mean, standard deviation and chi-square tests. **Results:** among the 200 patients males (74.5%) were affected than females. Mean platelet count at admission was 85,277.78 /cmm. We observed grades of thrombocytopenia were grade -1 in 16.5%, grade -2 in 28.5%, grade -3 in 36.5% and grade -4 in 16.5% of these patients. Complications like ARDS (1%) and acute renal failure (1%) were seen in patients with severe thrombocytopenia. **Conclusions:** In this study, we found severe thrombocytopenia to occur in *P vivax* mono-infection. We felt *P vivax* should no longer be considered benign and thrombocytopenia could be an early feature of *P vivax* mono-infection.

Key Words: Malaria, *P vivax*, severe thrombocytopenia, Southern India.

***Address for Correspondence**
Dr. Sanju Danniel John, Resident, Department of Medicine, Father Muller Medical College, Father Muller Road, Mangalore -575002, Karnataka, South INDIA.
Email: drsanjujohn1986@gmail.com
Received Date: 29/04/2014 Accepted Date: 27/05/2014

Access this article online	
Quick Response Code:	Website: www.statperson.com
	DOI: 03 June 2014

INTRODUCTION

Malaria poses a great socioeconomic burden on the general population. According to World Malaria Report 2011, in the South East Asian (SEA) region, both the highest number of confirmed cases (1,495,817) and the highest number of deaths (1023) were reported from India[1]. In endemic areas, malaria has been considered as the major cause of thrombocytopenia and thereby, it is used as an indicator in patients presenting with fever. Platelet counts of less than 150,000/mm^3 increases the likelihood of malaria by 12-15 times [2, 3]. Both non-immunological and immunological destruction of platelets have been implicated for the cause of thrombocytopenia. The mechanisms include coagulation disturbances, sequestration in spleen, antibody mediated platelet destruction and oxidative stress. Abnormalities in platelet structure and function can be seen in malaria as the parasites invade the platelets [4]. A typical attack of malaria is characterized by paroxysms of fever alternating with periods of fatigue, associated with chills, rigors, sweats, headache, myalgia, back pain, abdominal pain, nausea, vomiting, diarrhoea, pallor and jaundice [5]. Infections due to Plasmodium vivax were earlier thought to follow a benign course. Haematological abnormalities are very common in malaria, but severe thrombocytopenias were rarely associated with Plasmodium vivax. In the last decade, there are increasing reports of changing trends in the presentation of the disease caused by Plasmodium vivax. Increasing reports

How to site this article: Sanju Daniel John, Peter George. Study on thrombocytopenia occurring in P vivax malaria at a tertiary centre in Southern India. *International Journal of Recent Trends in Science and Technology* June 2014; 11(2): 155-158. http://www.statperson.com (accessed 03 June 2014).

of fatal complications such as adult respiratory distress syndrome, severe anaemia, acute renal failure and cerebral malaria in Plasmodium vivax mono-infections makes it a global concern [6].

OBJECTIVE OF THE STUDY

To study the occurrence of thrombocytopenia in *P* vivax malaria infected patients at a tertiary centre in South India.

MATERIALS AND METHODS

Source of Data: The data was collected from patients admitted to a tertiary care center in Southern India with P vivax mono-infection who were positive for Plasmodium vivax by peripheral smear and negative for Histidine rich protein-2 (HRP-2) test.

Study design: This is a retrospective study done over a period of 18 months from October 2012. A total of 200 in-patients with positive peripheral smear for P vivax and negative for HRP-2 test were selected using purposive sampling techniques. They were followed from admission till recovery, discharge or death whichever was earlier.

The following investigations were done in all cases:

1. Haemoglobin estimation, total blood count, differential leucocyte count and platelet count
2. Peripheral smear for malarial parasite-both thick and thin smears stained with JSB stain and seen under oil immersion
3. Histidine rich protein-2 test to rule out P. falciparum
4. Liver and renal function tests.

Inclusion criteria:

1. Those admitted with positive peripheral smear for P vivax malaria and negative for HRP-2 test.
2. Age more than 18 years.

Exclusion criteria:

1. Patients with P falciparum infection.
2. Those with chronic kidney disease, chronic liver disease, haemato logical malignancies, undergoing chemotherapy and radiotherapy.

Data Analysis: Data collected was analyzed by frequency, percentage, mean, standard deviation and chi-square test. Grading of thrombocytopenia was carried according to NCI Common Terminology - Criteria for Adverse Events Version 3.0 [7]. Based on these patients with thrombocytopenia have been divided into following five grades:

- Grade 0: Within normal limit, platelet count 1,50,000 or above
- Grade 1: Platelet count between 75,000 and 1,50,000
- Grade 2: Platelet count between 50,000 and 75,000
- Grade 3: Platelet count between 25,000 and 50,000
- Grade 4: Platelet count less than 25,000.

RESULTS

In the present study, 200 patients positive for P vivax fulfilling the selection criteria were included. Out of 200 patients, 149 (74.5 %) were males and 51 (22.5 %) were females. Ratio of male to female = 2.9:1. Patients included were aged between 17 - 82 years and maximum incidence was seen in the age group of 21-40 yrs with the mean age in this study being37.32 years. The mean haemoglobin in the study population was 12.46 ± 1.9 g% and mean white blood cell count was 5777.5± 4452.6 (ranging between 1000 - 6200). Mean platelet count was 85277.8± 49207.3 (ranging between 7000 - 2, 73, 0000). As depicted in table -1; fever was the presenting complaint in all the patients (100 %) followed by headache (68.0%), vomiting (27.5% %), jaundice (28.5%), pain abdomen (9.0%), body pain (17.5%) and bleeding tendencies (2.0%).

Table 1: Spectrum of clinical symptoms among the subjects

Symptoms	Number of Patients	Percentage (%)
Fever	200	100
Headache	136	68
Jaundice	59	28.5
Vomiting	55	27.5
Nausea	52	26
Body pain	35	17.5
Pain abdomen	18	9
Diarrhoea	13	6.5
Bleeding manifestations	4	2
Oliguria	1	0.5

Most common sign was anaemia (29.5%), followed by hepatomegaly (18%), splenomegaly (16.5%) and jaundice (13%) as seen in table 2.

Table 2: Analysis of the signs

Sign	No. of Patients	Percentage
Hepatomegaly	37	18.5%
Splenomegaly	32	16.0%
Icterus	26	13.0%
Signs of dehydration	21	11.0%
Pallor	17	8.5%
CNS manifestations	15	7.5%
Respiratory signs	2	1.0%

Among the study group, 195 (93.5%) subjects had thrombocytopenia; with Grade 1 in 16.5%, grade -2 in 28.5%, grade - 3 in 36.5% and grade 4 in 16.5% of these subjects (table -3).

Table 3: Grading of thrombocytopenia

Grade	Platelet count	Number	Percentage
0	>150,000/mm^3	5	2.5%
1	75,000-150,000/mm^3	33	16.5%
2	50,000-75,000 /mm^3	57	28.5%
3	25,000-50,000/mm^3	72	36%
4	<25,000/mm^3	33	33%

Leucocytosis was observed among the patients in our study, of which most of the patients had neutrophilia(68.1%), lymphopenia in 23.9%, monocytosis in 3% and eosinphilia in 5% of the study population. A complication such as hepatic dysfunction (5%), ARDS (1%) and acute renal failure (1%) was seen in patients with severe thrombocytopenia.

DISCUSSION

Malaria caused by P vivax is prevalent in most parts of India. Malaria can produce a variety of haematological variation, especially the thrombocytes and can mimic any haematological disorder. Anaemia and thrombocytopenia are important complications seen frequently in *P vivax* malaria. In endemic areas, malaria has been considered as the most important cause for febrile thrombocytopenia. In endemic areas there is 12-15 times chance of identifying malaria in a febrile patient with less than 1, 50,000/mm^3 of platelets [2,3,8]. In current study, 93.5% patients had thrombocytopenia. Colonel *et al* [9] reported thrombocytopenia in 72% of the patients having malaria. Jamal *et al* [10] in their study on paediatric population reported 72% of patients to have platelets less than 150000 mm^3. While certain studies reported slightly lower incidence of thrombocytopenia [11, 12]. The mechanism of thrombocytopenia in malaria is uncertain and various theories have been postulated. Immune mediated lysis of platelets, bone marrow suppression and splenic sequestration are considered to be the cause for thrombocytopenia in malaria [14, 15]. There can also be abnormalities in the platelet structure and function due to immune response or from invasion of the platelets by the parasite [15]. In acute malarial infection platelets are found to be hypersensitive and there is increased concentrations of platelet-specific proteins such as beta thromboglobulin (ß-TG), platelet factor - 4 (PF-4), thromboxane - A2 and prostacyclin [15]. The activated platelet has reduced sialic acid in their membrane resulting in its intravascular lysis and thus thrombocytopenia. During malarial infection, two major changes in the platelet function were demonstrated: platelet hyperactivity followed by platelet hypoactivity. The hyperactive platelets induce hemostatic responses which possibly prevent bleeding episodes, a rarity in malaria [15, 16]. Thrombopoeitin is required for platelet production and hence is elevated when there are low platelet counts [17]. Metanat M [18] observed that patients with malaria had low levels of platelet superoxide dismutase and glutathione peroxidase activity from oxidative damage of platelets, resulting in severe thrombocytopenia. In this study, we found significant thrombocytopenia. Metanat M and Sharifi-Mood from Iran demonstrated a new genotype of *P* vivax as a cause for severe thrombocytopenia [18]. Recent studies done by George P in South India [19] and Gonzalez B *et al* [20] in Venezuela have shown thrombocytopenia is more common among P vivax mono-infection in contrast to past observations in P falciparum.

CONCLUSION

In current study, we found severe thrombocytopenia in P vivax malaria patients. Severe complicated P vivax malaria cases are increasingly seen world over and no longer considered to be benign. Thrombocytopenia could be an early feature of P vivax mono-infection. Early suspicion, recognition and prompt treatment of the disease can reduce associated morbidity and mortality.

REFERENCES

1. World Health Organization, Regional office of South East Region (Internet). Health Topics: Malaria: World malaria Report 2011. Available at:http://www.who.int.
2. Maina R.N. *et al*. Impact of Plasmodium falciparum infection on haematological parameters in children living in Western Kenya. Malar J 2010:9:S4.
3. Adedapo AD, Falade CO, Kotila RT, Ademowo GO. Age as a risk factor for thrombocytopenia and anaemia in children treated for acute uncomplicated falciparum malaria. J Vector Borne Dis 2007:44:266-71.
4. Faseela TS, Roche, Anita KB,Malli CS, Rai Y. Diagnostic value of platelet count in malaria. J Clin Diagn Res 2011; 5:464-6.
5. Oh MD, Shin H, Shin D, Kim U, Lee S, Kim N, *et al*. Clinical features of vivax malaria. Am J Trop Med Hyg 2001; 65(2):143–6.
6. White NJ, Breman JG. Malaria. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, and Jameson JL. (eds.) Harrison's Principles of Internal Medicine. 17th ed. 2008; p. 203:1280-1293
7. National Cancer Institute Criteria for Adverse Events Version 3. Bethesda: U S. Department of Health and Human Services; 2006. p. 4.
8. Lathia TB, Joshi R. Can hematological parameters discriminate malaria from nonmalarious acute febrile illness in the tropics? Indian J Med Sci 2004:58:239-44.
9. Colonel KM, Bhika RD, Khalid S, Khalique ur-Rehman S, Syes ZA. Severe thrombocytopenia and prolonged bleeding time in patients with malaria (a clinical study of 162 malaria cases). World Appl Sci J 2010; 9: 484-8.
10. Jamal A, Memon IA, Latif F. The association of Plasmodium vivax malaria with thrombocytopenia infebrile children. Pak Paediatr J 2007; 31: 85-9.
11. 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.
12. Zaki SA, Shanbag P. Atypical manifestations of malaria. Res Rep Trop Med 2011; 2: 9-22.
13. Wickremasinghe SN, Abdalla SH: Blood and bone marrow changes in malaria. Baielleires Best Pract Res Clin Haematol 2000, 13: 277-99.
14. Makkar RP, Mukhopadhyay S, Monga A, Monga A, Gupta AK :Plasmodium vivax malaria presenting with

severe thrombocytopenia. Braz J Infect Dis 2002; 6: 263-5.
15. Mohanty S., Marwaha K., Ghosh S. *et al*. Functional and ultrastructural changes of platelets in malaria infection. J Clin Invest 1988; 71: 832-6.
16. Khan SJ, Khan FR, Usman M, Zahid S. Malaria can lead to thrombocytopenia. Rawal Med J 2008; 33: 183-5.
17. Kreil A, Wenisch C, Looareesuwan S. Thrombopoetin in Plasmodium falciparum malaria. Br J Hematology 2000; 109: 534-6.
18. Metanat M, Sharifi-Mood B. Malaria vivax and Severe Thrombocytopenia in Iran. Iranian J Parasitol 2010; 5: 69-70.
19. George P, Alexander LM. A study on the clinical profile of complicated Plasmodium vivax monoinfections. Aaian Pac J Trop Med 2010; 3: 560-2.
20. Gonzalez B, Rodulfo H, De Donato M, Berribeitia M, Gomez C, Gonzalez L. Hematologic variations in patient with malaria caused by Plasmodium vivax before, during and after treatment. Invest Clin 2009; 50: 187-201.

Source of Support: None Declared
Conflict of Interest: None Declared