

A STUDY OF THROMBOCYTOPENIA IN PATIENTS WITH P. VIVAX MALARIA.

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ABSTRACT: BACKGROUND: Malaria is commonly associated with various degrees of haematological complications most frequently with anaemia and thrombocytopenia. However there are contrasting reports about frequency of thrombocytopenia in P. vivax infection. **MATERIAL AND METHODS:** A total of 140 patients were included in the study. The details of the patients history along with their clinical features, laboratory reports were recorded in a standard proforma. Sample of venous blood were collected for haematological examination like Haemoglobin, total and differential count and platelet count, which was done under automated cell counter. **RESULTS:** Out of 140, there were 119(85%) patients who had thrombocytopenia, of them 75(54%) patients had mild, 38(27%) patients had moderate and 6(4%) patients had severe thrombocytopenia., 30(21%) out of 140 patients had leucopenia. Significant inverse association was seen between degree of parasitemia and platelet count. **CONCLUSION:** Various theories have been postulated for the cause of thrombocytopenia in P. Vivax infection but none of them is conclusive. Frequency or severity of thrombocytopenia doesn't appear to be any particular strain of plasmodium infection.

KEY WORDS: Malaria, P.vivax, Parasitemia, Thrombocytopenia.

INTRODUCTION: Malaria is a mosquito born disease caused by eukaryocytic protest of genus plasmodium. It remains today one of the major health problems in the tropics with increased morbidity and mortality. 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 In contrast most of the P. vivax infections are relatively milder and run a benign course.³ Malaria is commonly associated with various degree of haematological complications most frequently with anaemia and thrombocytopenia.⁴ However there are contrasting reports about frequency of thrombocytopenia in P. vivax infection. Its occurrence was reported to be infrequent.^{5,6,7} On the contrary it was reported by 2/3 rd of the patients in another study.⁸ In present study, we have tried to find the frequency of occurrence of thrombocytopenia in P. vivax malaria and tried to correlate it's severity with the degree of parasitemia.

MATERIAL AND METHODS: This was a cross sectional study, carried out in the Department of Medicine, Surat Municipal Institute of Medical Education & Research, Surat from June 2009 to August 2010. Patients fitting in the case definition of malaria with positive peripheral smear for P. vivax were included.^{9,10} Total number of patients in our study was 140. The details of the patients history along with their clinical features, laboratory reports were recorded in a standard proforma. Informed consent was taken from the patients. Patients with mixed infection with P. falciparum, or having co-morbidity like diabetes mellitus, hypertension and pulmonary tuberculosis were excluded. Patients already on antimalarials were also excluded. Both thick and thin slides were

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made. Thick smears were screened for the presence of *P. vivax*, if found positive further confirmation done on thin smear examination under oil emersion lens. The parasitemia was quantified using the '+' sign as follows:¹¹

- + 1-10 parasites/ 100 thick films
- ++ > 10 parasites/ 100 thick films
- +++ 1-10 parasites / thick film
- ++++ > 10 parasites / thick film.

Sample of venous blood were collected for haematological examination like Haemoglobin, total and differential count and platelet count, which was done on the day of admission under automated cell counter. If indicated Bleeding and Clotting time were done. Platelet count was repeated during the treatment and before discharging the patients. A standard proforma was used for recording all the data observed in the study. Other investigations were done if the patients fit the category of severe and complicated malaria as per WHO criteria.^{12,13}

RESULTS: Out of 140, 46(32%) patients had Hb >12gm%, 42(30%) patients had Hb between 10-12gm%, 33(24%) patients had Hb between 8-10gm%, 14(10%) patients had Hb between 5-8 gm% and 5(4%) patients had Hb < 5%. In complicate malaria, out of 83, 26(31%) patients had Hb > 12gm% 23(28%) had Hb between 10-12gm%, 20(24%) patients had Hb between 8-10 gm%, 9(11%) patients had Hb between 5-8 gm% and 5(6%) patients had Hb < 5gm% (Table no. 1).

Out of 140, there were 119(85%) patients who had thrombocytopenia, of them 75(54%) patients had mild, 38(27%) patients had moderate and 6(4%) patients had severe thrombocytopenia. 21(15%) patients had normal platelet count. In uncomplicated malaria out of 57, there 44(77%) patients who had mild thrombocytopenia and 13(23%) patients had normal platelet count. In complicated malaria out of 83, there were 75 patients (90%) who had thrombocytopenia, of them 31(37%) patients had mild, 38(46%) patients had moderate and 6(7%) patients had severe thrombocytopenia. 8(10%) patients had normal thrombocyte count (Table no. 2).

Out of 140, 30(21%) patients had leucopenia, 15(11%) patients had leucocytosis and 95 (68%) had normal total count (Table no. 3). In our study there was significant association between degree of parasitemia and platelet count. As the degree of parasitemia increased the platelet count decreased (Table no. 4).

DISCUSSION: Malaria is a common infection in most parts of India and association with thrombocytopenia during the clinical course of the disease has been reported.¹⁴ Thrombocytopenia in *P. Falciparum* infection has been consistently reported in various studies.^{4, 15, 16} However Martelo in 1969 reported thrombocytopenia in *P. vivax* infection only in 15% of their patients, OH MD et al reported the incidence in 29.6% cases.^{17, 18} Recently marked association in incidence of thrombocytopenia in *P. vivax* infection is being observed, 65% by Alfaso J et al and 73.92% of their cases by Joshi.^{19, 20}

In our study mean haemoglobin was 10.7±2.5 gm% as compared to 13.9±4 gm% reported in Colombian study, platelet count was 87128±53996 as compared to 269000±85000 in Colombian study.²¹ In our study thrombocytopenia was observed in 85% of patients same was observed by Ali Hussain et al.²² In an unpublished data Spinello Antinori reported the incidence of thrombocytopenia in 96% of their patients.²³ In other Indian studies Joshi et al reported mean platelet count (MPC) as 116250 cells/mm³ while Jadhav et.al. study the MPC was 115390 and thrombocytopenia was

observed in 73.92% and 65% cases respectively.^{20,24} In our study platelet count of less than 20,000 was observed in 4% of patients same as Ali Hassan et. Al.²² Joshi reported platelet count of <20000 in 2.17% of patients while Jadhav reported this phenomenon in 1.5% of their patients.^{20,24} Severe thrombocytopenia with platelet count of 5000 cells/mm³ in *P. vivax* malaria was observed by Kakar et al.²⁵

In our study 119 patients who had thrombocytopenia, 75(54%) had mild, 38(27%) had moderate and 6(4%) had severe form. In another study out of 83.3% of patients with thrombocytopenia 53.6% had mild 29.5% had moderate and 1.3% had severe variety.²⁶ In another study done by U. Patel et al.²⁷ reported 1 with severe 13 with moderate and 7 with mild thrombocytopenia(n=21).

In our study, 7 patients had bleeding tendencies, 1 patient with platelet count of 12000 had petechiae, slight haematemesis and some vaginal bleeding. Other 6 patients whose platelet counts was between 17000 – 39000, out of them 5 had haematuria, 2 had epistaxis and 1 had petechiae. All of them recovered with standard antimalarial treatment and none of them required platelet transfusion. In another study, 33 out of 75 *P. vivax* malaria patients with thrombocytopenia were given platelet transfusion²⁶ but the indication for transfusion is not mentioned expect all having platelet count <60,000 cells/mm³. In Kocher et. al. study, 3 of the 143 patients with *P. vivax* infection developed epistaxis requiring platelet transfusion, but they reported severe thrombocytopenia in 18.18% of their patients.²⁸

We found significant inverse relation in our study between degree of parasitemia and platelet counts in *P. vivax* patients. Kochar et.al. and Coelho HCC didn't find any relationship in severity of thrombocytopenia and parasitemia while another study found a significant inverse relationship.^{28, 29, 30} Gonzalez B. et.al. and Saravu K. did find a negative correlation between parasitemia and thrombocytopenia.^{31, 32}

Cytokine released during an acute inflammatory response could contribute to the pathogenesis of thrombocytopenia in *P. vivax* infection. Raised TNF- α levels are suggested as the possible cause of thrombocytopenia. In a study *P. vivax* were observed in platelets on electron microscopy and their direct lytic effect was suggested as the cause of thrombocytopenia.³³ Recombinant macrophage colony stimulating factor (M-CSF) causing reversible dose dependent thrombocytopenia was demonstrated. Increased M-CSF levels in malaria causing increased macrophage activity may indicate platelet destruction.³⁴ Sequestration in spleen, dyspoietic process in bone marrow with decreased platelet production and immune mediated lysis are other theories postulated for thrombocytopenia in *P. vivax* infection.

CONCLUSION: Although thrombocytopenia in *P. Falciparum* infection was reported quite frequently it's occurrence in *P. vivax* infection was supposed to be infrequent. In our study we found a very high percentage of patients having thrombocytopenia with *P. vivax* infection, Anaemia was also a frequent association. In majority of patients thrombocytopenia was of mild form but few demonstrated bleeding tendencies with severe thrombocytopenia. None of these patients required platelet transfusion and no mortality occurred during the study. We also found a significant correlation between parasitemia and thrombocytopenia. Various theories have been postulated for the cause of thrombocytopenia in *P. Vivax* infection but none of them is conclusive. Frequency or severity of thrombocytopenia doesn't appear to be any particular strain of plasmodium infection.

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Haemoglobin (gm%)	Type of malaria		Total (n=140)
	Uncomplicated (n=57)	Complicated (n=83)	
<5	00(00%)	05(06%)	05(04%)
5-8	05(09%)	09(11%)	14(10%)
8-10	13(23%)	20(24%)	33(24%)
10-12	19(33%)	23(28%)	42(30%)
>12	20(35%)	26(31%)	46(32%)
Mean±SD	11±2.3	10.6±2.7	10.7±2.5

Table no. 1: Haemoglobin levels in complicated and uncomplicated malaria.

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Severity of Thrombocytopenia (PC/cumm)	Type of malaria		Total (n=140)
	Uncomplicated (n=57)	Complicated (n=83)	
Severe(<20000)	00(00%)	06(07%)	06(04%)
Moderate(20000-50000)	00(00%)	38(46%)	38(27%)
Mild(50000-150000)	44(77%)	31(37%)	75(54%)
Normal(>150000)	13(23%)	08(10%)	21(15%)
Mean±SD	112017±49119	70036±50678	87128±53996

Table no. 2: Platelet counts in complicated and uncomplicated malaria.

Total count /cumm	Type of malaria		Total (n=140)
	Uncomplicated (n=57)	Complicated (n=83)	
<4000(leucopenia)	08(14%)	22(27%)	30(21%)
4000-10000	46(81%)	49(59%)	95(68%)
>10000(leucocytosis)	03(05%)	12(14%)	15(11%)
Mean±SD	6168±2044	6385±3151	6297±2748

Table no. 3: Total count in complicated and uncomplicated malaria.

Degree of Parasitemia (PSMP)	Mean Platelet count/cumm	Total
+	84630±49980	55
+2	80916±51346	36
+3	70740±57650	31
+4	68940±40413	18

Table no. 4: correlation between degrees of parasitemia with platelet count.

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