

## Thrombocytopenia In P. Vivax Malaria

Dr. Himanshu A. Joshi\*, Dr. Seema S. Shah\*\*

\*Associate Prof. In Pediatrics, \*\* Assistant Prof. In Pediatrics, GMERS Medical College, Gandhinagar.

**Abstracts:** Background: Plasmodium Falciparum and P. Vivax are endemic infections in India and commonly associated with Hematological Abnormalities. Severe thrombocytopenia is frequently noticed with P. Falciparum Malaria, but its occurrence is less reported and studied with P. Vivax Malaria. In present study we have tried to evaluate severity & prognostic implications of thrombocytopenia in cases of P Vivax Malaria. The study was conducted in Department of Pediatrics, GMERS Medical College, Gandhinagar. Method: The study group consisted of 92 Pediatric Patients diagnosed on thick & thin blood smear examination having thrombocytopenia. The platelet counts were done by Abacus Junior B Blood Cell Counter. Result: Platelet Count  $<150000$  Cell/mm<sup>3</sup> (thrombocytopenia) was observed in 73.92% patients of P. Vivax Malaria. The mean platelet count 1,16,520 is significantly low and the range being 18000 cell/mm<sup>3</sup> to 5,10,000 cells/mm<sup>3</sup>. Anaemia with mean Hemoglobin level 8.8 gm/dl. was reported in the patients with P. Vivax Malaria with thrombocytopenia. Discussion: In our view, this statistically low platelet count in P.Vivax Malaria is having significance & should be kept as differential diagnosis in Acute Febrile conditions. Unnecessary Platelet transfusions can be prevented as noticed in the study. Platelet transfusion was not required in the patients having severe thrombocytopenia (platelet count  $<20000$  cells/mm<sup>3</sup>) as bleeding tendencies and systemic complications were not observed as compared to Falciparum Malaria. Platelet count and clinical recovery were immediate on 2<sup>nd</sup> day after initiation of treatment and complete recovery within 7 day without any complications and mortality suggest a good prognosis. Conclusion: Anaemia with severe thrombocytopenia in P. Vivax Malaria required further study to differentiate other febrile conditions with low platelet count and unaltered hemoglobin levels. [ Joshi H et al NJIRM 2012; 3(2) : 125-128]

**Key words:** Plasmodium Vivax Malaria, Thrombocytopenia

**Author for correspondence:** Dr. Himanshu A. Joshi, Associate Prof. In Pediatrics, GMERS Medical College, Gandhinagar. e- mail : drhimanshu.joshi60@gmail.com

**Introduction:** Plasmodium Vivax malaria is endemic in India. Thrombocytopenia is commonly associated with<sup>1</sup> Plasmodium Falciparum Malaria and rarely with Plasmodium Vivax Malaria<sup>2</sup> In the present series we have tried to study the thrombocytopenia in Plasmodium Vivax Malaria. Fortunately many cases were associated with severe thrombocytopenia but not required platelet transfusion.

**Material And Methods :** From April 2011 to November 2011, a total number of 92 patients with P. Vivax Malaria, in Paediatric Department at GMERS Medical College, Gandhinagar were taken for study in this series. The commonest manifestation of the patients were fever with rigours, bodyache, headache and febrile convulsions. The diagnosis was based on thick and thin blood smear examination with external quality control. Special precautions were taken to exclude P. Falciparum Malaria & mixed infection. The

platelet count were done by Abacus Junior – B Blood Cell Counter. After receipt of treatment with Chloroquine and supportive care, all patients were successfully discharged from hospital. No deaths or further complications were observed.

**Result:** Age: There was no difference in the rate of thrombocytopenia among different age groups. No significant difference in Platelet counts were observed between male and female patients.

Platelet Count	<20,000 Cells /mm <sup>3</sup>	20,000 to 50,000 Cells /mm <sup>3</sup>	50,000 to 1,50,000 Cells /mm <sup>3</sup>	>1,50,000 Cells /mm <sup>3</sup>
No. of Patients	2	25	41	24
%	2.17	27.17	44.56	26.08
Hb%	8.87 gm / dl			11.8 gm/dl
%	73.92%			26.08

Platelet count less than 1,50,000 cells/mm<sup>3</sup> was noted in 73.92% patients. The mean platelet count in P. Vivax malaria was 1,16,520 cells/mm<sup>3</sup> ± 90334 and with a range of 18,000 cell/mm<sup>3</sup> to 5,10,000 cells/mm<sup>3</sup>. Platelet count less than 20000 cell/mm<sup>3</sup> was observed in only 2.17% patients. Platelet count ranging from 20,000 cells/mm<sup>3</sup> to 50000 cell/mm<sup>3</sup> was observed in 27.17% patients. Platelet count ranging from 50,000 to 1,50,000 cells/mm<sup>3</sup> was noted in 44.56% patients. Normal Platelet count was noted in 26.08% patients.

None of the subjects with P. Vivax Malaria and low platelet count had clinical manifestation of thrombocytopenia or bleeding from any site and platelet transfusion was not required.

The hemoglobin level also altered in the P Vivax Malarial infection. Mean Hemoglobin level with the subjects of P.Vivax Malaria and thrombocytopenia was 8.87 gm/dl. while the mean hemoglobin level was 11.8 gm/dl in patients with normal platelet count. Lowest Hemoglobin level 3 gm/dl was observed.

Platelet count less than 18000 cell/mm<sup>3</sup> was not reported in any case of P.Vivax Malaria. The minimum count in this series is 18000 cells/mm<sup>3</sup>. After starting the treatment with chloroquin & primaquin, the recovery in thrombocytopenia was quick on 2<sup>nd</sup> day & total cure was within 5 to 6 days. No deaths & complication were recorded.

**Discussion:** Malaria is a common infection in most parts of India and is commonly associated with mild thrombocytopenia<sup>3</sup> OF 173 cases of Malaria in U.S. Soldiers reported by Martelo et al<sup>4</sup> in 1969, 93 % had P. Vivax but only 15 % had thrombocytopenia with no documentation of the lowest platelet count. In Horstman's series<sup>5</sup> the lowest platelet count in 39 cases of P. Vivax Malaria was 44000 cells/mm<sup>3</sup>. Recently a case of Vivax Malaria associated with an initial Platelet count of 5000 cells/mm<sup>3</sup> was reported from India.<sup>6</sup> We have attempted correlation of thrombocytopenia in P. Vivax Malaria with severity of disease, platelet transfusion & complications.

The absence of the normal quantity of platelets on a peripheral smear in a case of fever is often a clue

to the presence of malaria as seen in this study. The mean platelet count was 1, 16, 520 cell/mm<sup>3</sup> in P.Vivax Malaria in 73.92% cases is definitely a striking feature. Similar thrombocytopenia was observed by V.M.Jadhav & V.S. Patkar in their study.<sup>7</sup>

Platelet count can fall below 20,000 cells/mm<sup>3</sup> in P.Vivax Malaria 2.17% (2 patients) but it is more common with Falciparum Malaria.<sup>8</sup> Risk of bleeding is significantly high with such condition.

Profound thrombocytopenia with Platelet count as low as 5000 cells/mm<sup>3</sup> has been reported in Indian literature in a female patient with Vivax Malaria.<sup>6</sup> None of the subject suffering from Vivax Malaria in our series had platelet count less than 18000 cells/mm<sup>3</sup>. 2 patients has platelet count <20000 cells/mm<sup>3</sup>, without any evident bleeding. This must be considered in the context that very low platelet count can be transient in the course of vivax malarial illness and may not necessarily have prognostic implications or merit platelet infusion.

In our study severe Vivax Malaria patients had thrombocytopenia, (73%) however, Platelet concentrate transfusion is indicated only in the patients with systemic bleeding. Platelet transfusion was not required in any patient. Thrombocytopenia, per se, cannot be a distinguishing feature in a particular case of malaria, although there is a statistical significant difference in the prevalence and severity of thrombocytopenia between the two types of malaria. The mean platelet count in Falciparum Malaria was 100,900. Cell/mm<sup>3</sup>. (SD ± 75437) was reported in a study.

Hemoglobin levels in the subjects with thrombocytopenia with Vivax Malaria are affected with mean 8.87 gm/dl that is significantly lower than the patients with normal platelet count. (11.89 gm/dl). This clue can be helpful in distinguishing other fevers with thrombocytopenia with unaltered hemoglobin levels and conditions like Dengue fever in which Hemoglobin level paradoxically rise. Similar finding were observed in the study of Alfonso. J. Rodrigues Morales in which 94.87% patients with P. Vivax malaria had anaemia on para clinical examination.

The exact mechanism for thrombocytopenia is unknown, but various theories are postulated as under :-

Fazardo and Talent in 1974 demonstrated P. Vivax within Platelets by electron microscopy and suggested a direct lytic effect of the parasite on the Platelet.<sup>9</sup> Both nonimmunologic destruction as well as immune mechanism<sup>10</sup> involving specific Platelet associated IgG antibodies that bind directly to Malarial Antigen in Platelets have been recently reported to play a role in the lysis of Platelets and the development of thrombocytopenia.<sup>11</sup>

In clinical trials, Recombinant Macrophage colony stimulating factor (M-CSF) has been known to cause a reversible dose dependant thrombocytopenia. Elevated M-CSF levels in Malaria by increasing macrophage activity may indicate Platelet destruction in such cases.<sup>12</sup>

Oxidative stress damage of thrombocytes has also been implicated in the etiopathogenesis based on the findings of low levels of Platelet superoxide dismutase and glutathione peroxidase activity and high Platelet lipid level in P. Vivax Malaria patients when compared to those healthy subjects.<sup>13</sup>

Thrombopoietin (TPO) is the key growth factor for Platelet production and is elevated in states of Platelet depletion. TPO serum levels have been showed to be significantly higher in subjects with severe Vivax malaria normalizing within 14-21 days.

Dyspoietic process in the marrow with diminished Platelet production have all been postulated is the cause for thrombocytopenia in P Vivax Malaria.

**Conclusion:** Isolated reported cases of thrombocytopenia in patients with P. Vivax infections from Brazil and India are found in literature.<sup>15</sup> Thrombocytopenia is a frequently observed feature with P. Vivax Malaria. Occasionally it may be severe thrombocytopenia.(Platelet count <20,000 cells/mm<sup>3</sup>). Thrombocytopenia <20000 cells/mm<sup>3</sup> can occur in P. Vivax Malaria, although statistically more common with P. Falciparum Malaria. The above findings can have therapeutic implications in context of avoiding unnecessary

platelet infusions with relatively more benign course of P. Vivax Malaria.

This study therefore highlights the fact that in patients with acute febrile, illness with marked thrombocytopenia, P. Vivax malaria should also be kept as a differential diagnosis and treated according to the local drug resistance pattern prevalent in the area. The recovery is immediate with initiation of treatment (2<sup>nd</sup> day) and complete within seven days without any complications and mortality. Only one study from South America with a series of patients of P. Vivax malaria with thrombocytopenia is reported (Alfanzo J. Rodriguez) to have thrombocytopenia in 65% patients with mean platelet count 1,38,523/- cells/mm<sup>3</sup>.

Anaemia was observed in patients with thrombocytopenia with P. Vivax Malaria significant low levels of hemoglobin 8.8 gm/dl was noticed in patients with severe thrombocytopenia, this clue can be helpful in differentiating other febrile conditions with unaltered hemoglobin levels. Additional research on the Immunological mechanisms associated with thrombocytopenia in P. Vivax infection as well as relation to parasite level in this population is necessary.

Dengue fever now a days emerging as one of the cause of thrombocytopenia. It is a challenge to differentiate Vivax Malaria, Falciparum malaria and Dengue fever. Long studies reflecting the and severity of thrombocytopenia in such cases of fever may be of great help to clinicians in diagnosing the disease.

**Acknowledgement:** To all my patients and relatives who supported me throughout my study.

#### References:

1. Perrinl. H, Mackey LJ. The Hematology of Malaria in Man. Semin Hematol. 1982, 19: 70-82.
2. Yamaguchi S, Kubola T., Yamagishi T. et al. Severe thrombocytopenia suggesting immunological mechanism in two cases of Vivax Malaria. Am. J. Hematology 1997; 56; 183-6.
3. Looarecsuwan S., Davis I.G., Allen D.L etal. Thrombocytopenia in Malaria, southeast Asian J. Trop. Med. Public Health 1992; 23:44.

4. Martelo O.J. Smoller M. Saladin T.A. Malaria in American Soldiers. Arch. Int. Medi. 1969; 123:383-7.
5. Horstmann R.D., Dietrich M. Rasche H., Malaria induced thrombocytopenia, Blood 1991;42:157-64.
6. Kakar A, Bhois, Prakash V, Kakar S, Profound thrombocytopenia in plasmodium Vivax Malaria. Diagn. Microbiol, Infect Dis.1999, 35:243-4.
7. V.M.Jadhav, V.S. Palkav. JAPI Vol.52 Aug. 2004.
8. Fajardo L.F., Tallent C. Malarial Parasites within Human Platelets Jama 1974, 229:1205.
9. Loouresuwan S, Davis I.g., Allen D.L. et al, Thrombocytopenia in Malaria southeast Asian J.A. tropical Med. Public health 1992;23(1) 44-50.
10. Yamaguchi S, Kobuta T et al. Severe thrombocytopenia suggesting immunological mechanism in two cases of Vivax Malaria. Am. J. Hematology 1997; 56(3):183-6.
11. Lee S.H. Looaresuman S., Chan j. et al. Plasma macrophage colony stimulating factor and P. Solection levels in Malaria associated Thrombocytopenia thrombhaemost. 1997, 77 (2) 289-93.
12. Evel O, Vural H., Akosyn N et al. Oxidative stress of Platelets and Thrombocytopenia in patients with Vivax malaria. Clini Biochem 2001; 34(4), 341-4. Alfonso J. Rodrigues-Morales.
13. Alfonso J. Rodrigues – Morales Anaemia and thrombocytopenia in children with plasmodium Vivax Malaria – Oxford Journal.
14. Makkar R.P., Mukhopadhyay S. Plasmodium Vivax Malaria presenting with severe thrombocytopenia Braz. J. Intectious Dis 2002, 6 263-5.
15. Lacerda MV, Alexandrema. Ideopathic thrombocytopenia purpura due to Vivax Malaria in the Brazilian Amazon. Act Prop. 2004-90, 187-90.