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Thrombocytopenia in Plasmodium vivax Malaria

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Abstract:

Introduction: Malaria is a disease that affects almost all blood components. Thrombocytopenia is frequently noticed with P. falciparum malaria but is less reported and studied with P. vivax malaria.

Materials and Methods: *The study was conducted in Infectious Disease & Beliaghata General Hospital, Kolkata -10; West Bengal, India. We included patients who were diagnosed with vivax malaria. The data regarding their clinical and hematological profile was collected and analysed.*

Result: *A total of 60 patients were included. 44 (73.33%) had platelet count <100000/mm3. Mean platelet count was 85,800/cmm, range being 40,000/mm3–2, 10,000/mm3.*

Conclusion: *Thrombocytopenia is now being seen more commonly with vivax malaria. Patients with platelet count <1 lac/cumm have more severe disease.*

Keywords: ***Vivax malaria; Thrombocytopenia; Hematological profile; unusual manifestation of P.V.***

Introduction:

Malaria is caused by Plasmodium parasites. It is spread through the bites of infected female Anopheles mosquitoes. Out of 5 species, P. falciparum and P. vivax are the greatest threat. Plasmodium vivax is the dominant malaria parasite in most countries outside of sub-Saharan Africa.(1) There were 212 million new cases of malaria worldwide in 2015 (range 148–304 million). The African Region accounted for most global cases of malaria (90%), followed by the South-East Asia Region (7%) and the Eastern Mediterranean Region (2%).(2) In 2015, there were an estimated 429 000 malaria deaths (range 235 000–639 000) worldwide. Most of these deaths occurred in the African Region (92%), followed by the South-East Asia Region (6%) and the Eastern Mediterranean Region (2%).(2)

Infection with Plasmodium falciparum (P. falciparum) is known to cause thrombocytopenia and severe malaria but same has been reported in P. vivax malaria for the last decade. With implementation of molecular diagnosis, it became evident that P. vivax monoinfection could also be involved in multiple organ dysfunction and severe life-threatening disease as seen in P. falciparum infection.(3,4) Causes of thrombocytopenia is still poorly understood. Initial hypothesis was decrease bone marrow production but now it is ruled out. Many explanations have also been proposed for severe manifestations in vivax malaria like-

a) Adherence of platelets stimulated by tumor necrosis factor (TNF) to endothelium.
b) Bridges formed by platelets between RBCs and endothelial cells as in falciparum malaria
c) Stimulation of platelets by parasitised RBCs triggering apoptosis in endothelial cells pretreated with TNF in a pathway mediated by tumor growth factor- (TGF-) β1.

Recent evidence showing P. vivax infected RBCs adhering to lung endothelial cells and to the placental tissue ex vivo indicates that, in vivax malaria, mechanisms similar to those associated with falciparum malaria severity may be involved.(5) All the complications seen in falciparum malaria are now reported with vivax also.(6,7,8) A study on pediatric population from Bikaner in northwest India reported a high proportion (63.1%) of severe malaria contributed by P. vivax monoinfection. They reported all severe manifestations in vivax malaria in children including severe anemia, thrombocytopenia, cerebral malaria, acute respiratory distress syndrome (ARDS), hepatic dysfunction, renal dysfunction, and abnormal bleeding. They reported thrombocytopenia in 61.5% children and bleeding symptoms in 10.8% cases.(7) A study from Venezuela reported thrombocytopenia in 58.9% children with P. vivax malaria, with 25.6% requiring platelet transfusions.(9) Thus, although many studies regarding thrombocytopenia in P. vivax malaria are available, most of them were done on pediatric population or included children also. There is lack of studies assessing thrombocytopenia and severity in P. vivax exclusively in adults. Hence, we carried out this study to find out the status of thrombocytopenia in P. vivax in

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adult population and find if it has any association with severity.

Methodology:

The study was conducted in a tertiary care centre for infection "Infectious Disease & Beliaghata General Hospital, Kolkata -10; West Bengal, India". It was an obserbational study. All patients, who are 18yr. or above, diagnosed with malaria on peripheral smear were enrolled for the study. Study was conducted on July, 2016 to December, 2016. Total number of population was 60.The patients with falciparum infection either alone or in combination with vivax or who did not give written informed consent were excluded. The patients with underlying disease which may cause similar complications like dengue and sepsis were also excluded. Thrombocytopenia was defined as platelet count <1 lac/cumm. Platelate count was done at "Automatic cell counter, part-4" and corroborated with slide count from peripheral smear. The plasmodium vivax was diagnosed by "Rapid kit test-"followed by thik &thin smear of peripheral blood. The plasmodium falciparum was excluded by rapid kit test, followed by thik &thin smear of peripheral blood. Others most common causes of thrombocytopenia was dengue was excluded by NS1Ag, and dengue IgM. Others causes of thrombocytopenia were aplastic anemia, severe sepsis, leukemia were excluded by CBC & Peripheral smear. Chicken pox, measle, diphtheria were excluded clinically. Second round of MP & platelate were done after 72hours.

Result:

A total of 76 patients diagnosed on peripheral smear with malaria were enrolled for the study. 16 were excluded for various reasons (P. falciparum monoinfection or mixed P. vivax and P. falciparum infection or coinfection with dengue or associated sepsis). 60 patients had P. vivax monoinfection as diagnosed on peripheral blood smear. Hence, total 60 patients with P. vivax monoinfection were included in the study. The age of included patients ranged from 18 to 70 years. Number of patient had low platelet count <1 lac/cumm was 44 (73.33%). Average platelet count amongst them was 85,800/cumm and mean hemoglobin was 9.2 gm%. One patient was presented with cerebral malaria with platelate count was 40,000/cmm. Two patient shown feature of acute renal failure and one patient had jaundice. None of them had ARDS, Circulatory failure. None of them had any bleeding disorder. No age or sex prediction was observed.

Discussion:

Malaria is a disease that affects almost all blood components. The essential pathological feature of severe falciparum malaria is sequestration of erythrocytes in the deep vascular beds of vital organs leading to cerebral malaria, renal failure, hepatic dysfunction, or ARDS. Hemolysis, reduced cell deformity of parasitized and nonparasitized erythrocytes, increased splenic clearance are the causes of anemia. Reduced platelet production and survival, and increased splenic uptake of platelets are causes of severe thrombocytopenia leading to bleeding diathesis. Initially thrombocytopenia was thought to be a feature of P. falciparum. Since the beginning of the 1970s, reports of similar degree of thrombocytopenia in P. vivax and P. falciparum infections started coming in.[10] Most of the major publications related to frequency of thrombocytopenia in P. vivax malaria were published in the late 1990s, probably due to availability of automated machines. Around the same time, reports of severe, complicated malaria with P. vivax infection also started being published. But by WHO, thrombocytopenia is not considered to be a severity criterion by itself due to the inability to cause death per se.[11]

Many studies have shown a wide range of thrombocytopenia and severity in P. vivax malaria but they included only pediatric patients. In other study percentage of thrombocytopenia was 24% to 94% but in this study it is 73.33%. No study has reported any major bleeding or complication or mortality resulting from even severe thrombocytopenia. Only few studies have so far reported mortality from P. vivax infection; some have reported multiple complications, but none of these studied in adult population exclusively.[12,13,14,15] Kochar et al. in 2009 studied adult patients and reported all complications in patients with Plasmodium vivax malaria.[16] Thus, there has been a lack of studies on thrombocytopenia in P. vivax malaria in adults. Most have included both adult and pediatric populations and have not excluded the other causes of thrombocytopenia. Also, there is no study which has assessed the association of thrombocytopenia with severity in P. vivax malaria in adults. Our study included only adult population. We excluded P. falciparum, dengue positive as well as sepsis patients as these are the major causes of thrombocytopenia in our region. We also assessed the association of thrombocytopenia with severity in adult P. vivax patients. Thus, this study highlights that all complications of P. falciparum can be seen with P. vivax. Thrombocytopenia may be used as a severity marker of severe malaria. It should be included in the WHO definition of severe malaria. But only platelate count is not a independed predictor of severity of malaria.

Conclusion:

The clinical scenario of P. vivax malaria is changing. P. Vivax is no more a benign malaria. Similar incidence of thrombocytopenia is now seen in vivax and falciparum

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malaria patients. All complications seen in falciparum positive cases are being seen in vivax positive cases also. Thrombocytopenia may not be a cause of mortality by itself, but it can be as severity marker of malaria. P. vivax malaria need futher study especially in the light of thrombocytopenia. We also recommend separate guidelines for management of P. vivax with platelet count <1 lac/cumm.

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Consent: Informed consent is taken from each patient

Conflict of Interests: The authors declare that there is no conflict of interests regarding the publication of this paper.

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