Original Article

Thrombocytopenia—An Indicator for Severe Plasmodium Vivax Infection?

Thrombocytopenia with P.Vivax

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ABSTRACT

Objective: To see the effect of thrombocytopenia in plasmodium vivax infection

Study Design: Prospective study.

Place and Duration of Study: This study was conducted at Trauma and General Hospital, Karachi from June 2013 to October 2014.

Materials and Methods: Ninety seven patients were included in the study with low platelets and positive malarial parasite (MP) or immunochromatographic test (ICT) malaria. Patients that were presenting with other causes of thrombocytopenia were excluded from the study including plasmodium falciparum or dengue fever.

Result: Total 97 patients were included in the study. Among them 63 (64.9%) were males. Mean age was 33.15±8.513 years. In our study none of the patient develops bleeding or required platelet transfusion.

Conclusion: Thrombocytopenia is now commonly seen in plasmodium vivax infection, but usually do not lead to bleeding like dengue fever or plasmodium falciparum infections.

Key Words: Malaria, Thrombocytopenia, plasmodium vivax, malarial parasite(MP), immunochromatographic test for malaria (ICT MP), Platelets

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INTRODUCTION

Malaria is a disease of global importance. The WHO has reported a worldwide annual incidence of 247million cases and malarial mortality of one million per year.[1] Comparing the non falciparum species, plasmodium vivax has the greatest geographic range and burden of disease. Plasmodium vivax infections throughout the world ranges between 130 and 390 million, with 2.6 million individuals living at risk of infection.[2,3] Infection with plasmodium falciparum is mainly associated with thrombocytopenia, and other severe complications of malaria, though recently it has been seen with plasmodium vivax infection as well. With the help of advanced molecular diagnosis it became evident that major complications may also occur with plasmodium vivax mono infection and are encountered in endemic settings nearly as commonly as falciparum malaria.[4]

All the complications are almost equal in both falciparum and vivax malaria. A retrospective study of hospitalized individuals in Papua Indonesia suggested that plasmodium vivax is a major cause of morbidity in early infancy. Among 187 infants aged <3 months, admitted during a four year period with thrombocytopenia. Death rates among these patients were comparable between viax and falciparum infection.[5] A study from Venezuela reported thrombocytopenia in 58.9% children with vivax malaria, with 25.6% requiring platelets transfusion.[6] Another study done in pediatric population at Bikaner in North West India, showing thrombocytopenia in 61.5% of children and bleeding symptoms in 10.8% cases.[7]

Although many studies have been done among the pediatric population, but there is still a lack of studies assessing thrombocytopenia and its severity in relation to bleeding in adult population. Hence this study is conducted to see the effect of thrombocytopenia due to vivax malaria in adults and requirement of platelets among them.

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MATERIALS AND METHODS

It was a prospective, cohort study conducted at Trauma and General Hospital Karachi, during the period of July 2013 to October 2014. Prior permission for the study was taken from the patients and Hospital management. The statistical analysis was done on SPSS version 16.

Inclusion criteria: All patients with an age range of 15 to 55 years coming with high grade fever with positive vivax malaria either on peripheral smear or ICT malaria and low platelets were enrolled for the study. Thrombocytopenia was defined as platelet count <150,000.

Exclusion criteria: Patients that were co-infected with falciparum malaria, falciparum alone or with dengue fever were excluded from the study.

Patients with underlying conditions with low platelets like chronic liver disease, autoimmune illnesses, sepsis or DIC were also excluded from the study.

All patients were subjected to routine laboratory investigations like complete blood count with platelets, urea, creatinine, electrolytes, ALT, blood sugar, M.P, ICT MP. Patients with suspected chronic liver disease also had hepatitis B and C serology.

RESULTS

Ninety seven patients were included in the study. Among them 63 (64.9%) were male. Mean age was 33.15±8.513 years. The youngest patient was 18 years and eldest was 55 year old. All patients had low platelets ranging from 7000u/L to 147,000u/L (table 1). In 97 patients MP was positive in 25, while ICT MP in 72 patients with negative MP (Table 2). Total leucocyte count was low in 76 patients with a minimum of 1.5×10^3 /L, and maximum of 5.4×10^3 /L. Out of 97 patients 26 had increased ALT with a maximum of 146 IU. None of the patients included in the study had bleeding from any site or required platelet transfusion.

Table No.1: Different Pattern of platelet count n=97

Platelet count	Percentage
<5000 u/L	0%
5000-10,000 u/L	2.1%
10,001-20,000 u/L	18.6%
20,001-50,000 u/L	17.5%
50,000-100,000 u/L	38.1%
100.001-150,000 u/L	23.7

Table No.2: Total Positive MP and ICT MP n=97

	MP	ICT MP
Positive	**25**	**72**
Negative	**--**	**25**
Not done	**72**	**--**

DISCUSSION

Malaria is a major threat to many parts of Pakistan. Malaria is endemic in Pakistan, with 64% and 36% of malaria cases are due to plasmodium vivax and falciparum.[8] The clinical manifestations of malaria diversify with geography, epidemiology, immunity and age. In areas where malaria is endemic, children and pregnant women are at the highest risk of getting the infected. Malaria should be suspected in patients with febrile illness, if they have had exposure to a region where malaria is endemic. [9]The incubation period of vivax is usually two weeks, and relapses occur within three months. The symptomatology of malaria included fever, abdominal pain, cough, diarrhea or myalgias.[9] There are many hematological abnormalities including hemolysis, thrombocytopenia and leucopenia is present in falciparum malaria but recently during the last decade has been commonly seen in vivax malaria as well.[10] Many explanations have been given to these manifestations of decreased platelets, like; adherence of platelets stimulated by TNF to endothelium, [11] bridges formed by platelets between RBC'S and endothelial cells as in falciparum malaria [12] and stimulation of platelets by parasitized RBC'S triggering apoptosis in endothelial cells preheated with TNF in a pathway mediated by TGF β1.[13] Recently it has been seen in vivax malaria also and thus concluded to have same mechanism of low platelets as in falciparum. [14]Profound thrombocytopenia is a well known complication of falciparum malaria, but has been observed in vivax malaria too. In recent years its occurrence has increased, but most of the patients do not have major bleeding as in falciparum malaria or dengue fever. Most of the publications regarding relation of vivax infection with low platelets published in late 1990's, but regardless of being described as a complication by WHO, thrombocytopenia is not considered as a severity criteria,[15] due to inability to cause bleeding or death in any patient. Most of the studies have been done on pediatric population with severe thrombocytopenia, and none of them reported any major bleeding or complication, even on low platelets of<50,000/uL.[16,17] Most of the studies have also shown a negative co-relation between low platelets and parasitemia,[18,19] only one study done at Brazil shows direct co-relation.[16,17]

Thus there has been lack of studies on thrombocytopenia causing bleeding in adults. Our study included only adults with vivax malaria and excluded plasmodium falciparum, dengue fever and patients with sepsis as these are also common causes of thrombocytopenia. In our study none of the patients even on low platelets of 7000u/L had bleeding. Although there was a case reported from India in 2009, which had platelet count of 8000 u/L and had spontaneous bleeding from the gums.[20] Even though having low platelets of <10,000u/L among two patients in our study, platelets were not transfused and they had spontaneous recovery only with anti-malarial medication. The same observation is also noted in one study done in 2004, in whom 1.5% of the subjects had platelet count between 5000u/L to 20,000u/L, with no evident bleeding and none of them required platelets.[21]None of our patients were given folic acid or folinic acid as it is mostly given to patients with low platelets. Folate is essential for DNA synthesis and the survival and growth of the malaria parasite. There is a study done in 2007 which showed increased incidence of malaria in endemic areas if iron and folic acid are given together.[22] Another study done in 2007 which

showed failure rate of antimalarials if folic acid is given simultaneously.[23]

CONCLUSION

The trend of vivax malaria, has been changing. Similar incidence of complications including thrombocytopenia is seen in both faciparum and vivax malaria. Although the bleeding is not commonly seen in vivax, despite very low platelets. The level of parasitemia until now has no direct relationship with thrombocytopenia, but no studies have been done in adult population. It is recommended to do such study in adults which may help in treating such cases more easily and to make a guideline for management of plasmodium vivax infection with low platelets.

Conflict of Interest: This study has no conflict of interest to declare by any author.

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