ORIGINAL ARTICLE

SEVERITY OF THROMBOCYTOPENIA IN PATIENTS WITH *PLASMODIUM VIVAX* MALARIA; A SINGLE CENTER STUDY

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Background: Thrombocytopenia has been frequently observed in *plasmodium vivax* malaria in different studies. Finding out the severity of thrombocytopenia is perhaps equally important, as it has practical as well as prognostic implications. The objective of the study was to assess the severity of thrombocytopenia in patients suffering from malaria caused by *plasmodium vivax*. **Methods**: This cross-sectional study was carried out at Combined Military Hospital (CMH) Malir, Karachi, which is a tertiary care Hospital for all military personnel & their families in the province of Sindh. All patients of smear positive Vivax malaria during the study period were included, and those having thrombocytopenia from any other reason were excluded. They were treated with anti-malarial drugs and their platelet counts were monitored till they normalized and discharged from the hospital. Thrombocytopenia was defined as platelets count of <150,000/cu mm. Results were analysed by SPSS 11. **Results:** Out of 150 cases, 133 (88%) had thrombocytopenia. Their ages ranged from 15 to 55; mean age was 35 with SD±20. Low platelet count observed was between 11000 and 146000/cu mm with SD±27404. Mean value was 79 832/cu mm. None of the patient had any bleeding episode requiring a blood transfusion. **Conclusion:** *Plasmodium vivax* associated thrombocytopenia has a benign outcome irrespective of severity of the platelet counts.

Keywords: Malaria, Thrombocytopenia, *Plasmodium*, Parasite, Protozoan

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INTRODUCTION

Like falciparum malaria, thrombocytopenia has been frequently observed in *Plasmodium vivax* malaria in different studies.[1] Finding out the severity of thrombocytopenia is perhaps equally important, as it has practical as well as prognostic implications. Severe thrombocytopenia can lead to spontaneous bleed(s) that could have a fatal outcome. Most studies have been carried out in India but very few in this zone particularly focusing on *Plasmodium vivax* malaria exclusively. In this study the correlation of *Plasmodium vivax* malaria with thrombocytopenia has been elucidated. Previous studies were carried out in *Plasmodium falciparum* and *vivax* co-infection(s) having thrombocytopenia. Correlation of severity of thrombocytopenia in different types of malaria has been elaborated in an Indian study in which they found it to be more common with *Plasmodium falciparum* malaria.[2] Therefore we argue that It is equally important to assess the severity of thrombocytopenia in *Plasmodium vivax* malaria for management purpose.

MATERIAL AND METHODS

A total of 150 patients hospitalized over a period of eight months were included in this cross sectional study. Consent was taken from the patients before enrolling them in study. Study was approved by the ethical committee of the hospital. All the patients included were enrolled on the basis of being positively having *Plasmodium vivax* parasites on peripheral smear(s) examination with conventional microscopy. Platelet count was measured on a fully automated hem-analyser (Quantitative Coulter). Platelet count was the number of thrombocytes derived from directly measured platelet pulses, multiplied by a calibration constant and expressed in thousands of thrombocytes per microliter of the whole blood. Baseline platelet counts were done on the day of presentation. Repeat platelet counts were done in subjects with marked thrombocytopenia until normal or near-normal values were reached. Patients with a diagnosis of *falciparum* malaria, dengue fever and *leptospirosis* or any other identifiable/known reason for thrombocytopenia, were excluded from the study. *Plasmodium vivax* malaria was treated with Chloroquine and Quinine Sulphate whereas in patients with a severe thrombocytopenia a combination of Artemether & Lumafantrine was used. In both cases treatment regimen included a two weeks follow up course of Primaquine.

RESULTS

Out of 150, one hundred and thirty three patients of *plasmodium vivax* malaria (88%) had thrombocytopenia. Their ages were 15–55 years with mean age was 35±20 years. Low platelet observed was between 11000 and 146000/cu mm with SD±27 404. Mean value was 79 832/cu mm. Their main

presentation was fever with rigors and chills along with body-aches and pains. To assess the severity of thrombocytopenia they were divided into four groups, Group 1; had platelet counts ranging from 75 000 to 150 000: Group 2; had counts between 50,000 to 75,000: Group 3; had counts between 25 000 to 50 000 whereas the last Group, i.e., Group 4; had counts below 25 000 /cu mm. Severe thrombocytopenia was observed in only two cases 1.5%, moderate thrombocytopenia in 30.5% (n=40) cases and mild thrombocytopenia in rest of the patients 68% (n=89). Bleeding was not observed in any case even in with severe thrombocytopenia as shown in Figure-1. Hemoglobin observed less than 7 g/dl in 2.30% (n=3) patients Table-1. Total leukocyte count below 4 000/cu mm was encountered in 11% cases, whereas above 11000 in 6% and rest fell with in normal ranges, i.e., 4 000–11000/cu mm Figure 2. The lowest count observed was 2 100 /cu mm and max 15000/cu mm with SD±3364.

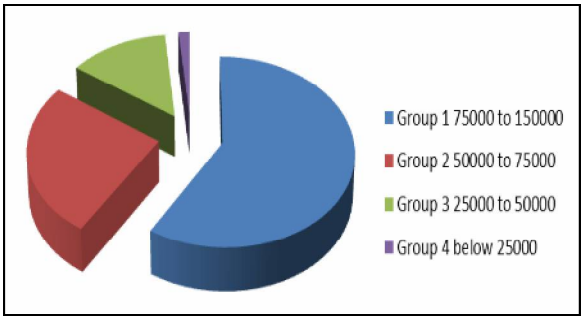

Figure-1: Frequency of thrombocytopenia with respect to severity

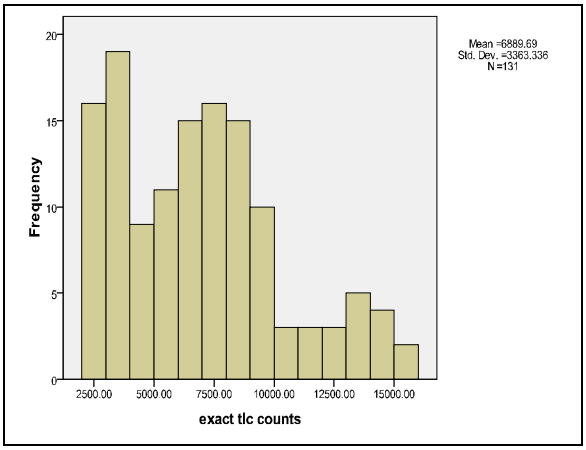

Figure-2: Histogram of Total Leucocyte Counts

Table-1: Haemoglobin in different cases

Haemoglobin Level (g/dl)	Number of Cases	Percentage
Below 7.0	3	2.3%
7.1–10.0	13	9.9%
10.1–13.0	85	64.9%
Above 13.0	30	22.9%

DISCUSSION

Malaria has been the point of discussion since ancient times because of its complications. Beside the haemolytic anaemia, in malaria that is more profound in disease caused by the *Plasmodium falciparum*, thrombocytopenia is also encountered. Likewise anaemia coupled with thrombocytopenia is more marked in the *Plasmodium falciparum* malaria. Most studies conducted in the past have focused on plasmodium *falciparum* as well as *vivax* malaria co-infection(s) and its effects of platelet counts. A study carried out in India exclusively studied the *Plasmodium vivax* group to find out the severity of thrombocytopenia. Similarly we endeavoured to confirm the findings in our population. Our study subjects were mostly young men working in different areas of the province of Sind, Pakistan. As believed, platelet counts can drop in febrile illnesses and reach critically low levels even in *Plasmodium vivax* malaria; levels as low as 5000/cu mm have been reported in a case report of *Plasmodium vivax* malaria[3] and likewise a count of 11000/cu mm was encountered in one patient in our study. Counts less than 25000 /cu mm was found in 1.5% that is almost same percentage that has been observed in Indian studies, we further confirm that this fall is a short term change/deficit that recovers once the patient gets better.[2–4]

The prevalence of thrombocytopenia in our study was 88% that was higher than the previous studies.[1,2] None of the patients had any bleed episode(s), despite having severe thrombocytopenia (as low as 11000/cu mm). This strongly supports the argument that *Plasmodium vivax* malaria is a benign natured disease, as also shown in previous study done by Joshi and Seema in paediatric patients 2012.[5]

Different mechanisms of thrombocytopenia have been suggested by Fazardo and Talent in 1974 with the help of an electron microscope, who reported a direct lytic effect of the parasite(s) on the human platelets.[6] Both immunological and non-immunological mechanism(s) with specific IgG antibodies that bind to malarial antigen in platelets have come to light & been explained recently[7] which include an Immune-mediated lysis, Sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production.

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.[8] Serum thrombopoietin levels increase in response to low platelet counts, this increase normalizes platelet counts in 2–3 weeks.[9] Malarial patients being treated with Quinine Sulphate can have profound thrombocytopenia because of the drug itself.[10] Therefore, a drug induced thrombocytopenia should also be kept in mind while relating thrombocytopenia with malaria. In another study from India, thrombocytopenia in malarial patients was frequently encountered in patients with high parasitemia and those with complications like acute renal failure.[11]

The discussion and/or elaboration of such factors as mentioned above, requires further large scale studies especially when studying questions like thrombocytopenia in *Plasmodium vivax* malaria with complications.

CONCLUSION

Plasmodium vivax malaria can cause a significant thrombocytopenia, but it is rarely life threatening. Knowing from experience that it has a benign course, unnecessary transfusion(s) can be avoided. Why *Plasmodium vivax* malaria has a benign outcome requires further research.

Meticulous monitoring is still recommended in patients with a critically low platelet count because of the ever present risk of spontaneous bleed(s).

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