ORIGINAL ARTICLE
RESPONSE OF PLASMODIUM VIVAX MALARIA INDUCED THROMBOCYTOPENIA TO ANTIMALARIAL TREATMENT

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Background: Thrombocytopenia is often seen in the patients of malaria infected with Plasmodium vivax. We studied patients admitted in hospital having coexisting thrombocytopenia and malaria, and recorded the response to anti-malarial therapy. Methods: In this cross-sectional descriptive study, a total of 120 patients admitted in medical ward with Plasmodium vivax malaria and co-existing thrombocytopenia were studied. Results: Out of total 120 slide positive Malaria patients who had low platelet count (<150×10^9/L), platelet count increased to ≥150×10^9/L in 73 (60.8%) patients after five days of anti-malarial therapy while in 47 (39.2%) patients thrombocytopenia persisted. After ten days of anti-malarial therapy, platelet count in all the patients recovered to ≥150×10^9/L. None of the patients required platelet transfusion. Conclusion: In majority of the patients of Plasmodium vivax malaria having thrombocytopenia, platelet count returns to normal within five to ten days of start of anti-malarial treatment and platelet transfusion is not required.

Keywords: Malaria, thrombocytopenia, Plasmodium vivax, Chloroquine

INTRODUCTION
Despite recent advancements in diagnostic and treatment modalities, malaria is still one of the most prevalent human problems with high mortality and morbidity. About 300–500 million cases occur per year with over one million deaths annually. The incidence of malaria in Pakistan is one case per thousand population. According to WHO estimates, over 40% of the world population is living in malaria endemic areas including Africa, India, Pakistan, Bangladesh and areas of Middle East.

Acute malaria is usually associated with mild to moderate thrombocytopenia and it is a sensitive indicator of malarial parasite infection. Although low platelets play an important role in the pathogenesis of severe disease, nevertheless, most of the studies suggest that thrombocytopenia is not associated with an adverse outcome or death. The exact cause of thrombocytopenia in malaria is poorly understood. Increased platelet destruction and decrease in platelet life span are implicated in the pathogenesis of thrombocytopenia. Malaria due to Plasmodium falciparum (malignant tertian malaria) is associated with severe complications and sometimes death. However, malaria due to Plasmodium vivax (benign tertian malaria) is usually mild and still responds well with chloroquine therapy. There are few local and international studies showing the response of anti-malarial drugs to thrombocytopenia. Therefore, we conducted this study to see that how much time (in days) it takes for the thrombocytopenia to return to normal values in response to anti-malarial treatment and whether platelet transfusion is required in Plasmodium vivax malaria.

MATERIAL AND METHODS
This descriptive cross-sectional study was conducted in indoor patients at the Department of Medicine, Combined Military Hospital, Sialkot from April 2010 through September 2010. All consecutive adult patients with age more than 18 years and fever of less than five days without any localizing signs having positive Plasmodium vivax parasite on peripheral blood film and having thrombocytopenia (Platelet count <150×10^9/L) were included in the study. Patients with coexisting Plasmodium falciparum infections were excluded from the study. Patients with bleeding disorders, with localizing signs, and those who were already on anti-malarial drugs were excluded from the study. Informed consent was taken from every patient included in the study.

Venous blood samples were taken by venepuncture. The samples were placed in Blood CP bottles containing tri-potassium ethylene diamine tetra acetic acid (K_2EDTA) as the anticoagulant, in a final concentration of 2 mg/ml. These samples were immediately transported to the Pathology Department. Thick and thin blood films were stained with Leishman’s stain and examined by Pathologist. In those patients with negative peripheral film for malarial parasite, repeat smear was examined after twelve hours. Complete blood counts were generated by Sysmex KX-21 automated haematology analyser. Standard 18 parameters along with histograms were generated. Those specimens with reduced platelet...
count were counter checked by manual method. Patients with reduced platelet count were divided into three groups.

1. Group-I: platelet count less than 150×10^9 /L but more than 100×10^9 /L.
2. Group-II: platelet count less than 100×10^9 /L but more than 50×10^9 /L.
3. Group-III: platelet count less than 50×10^9 /L.

Patients were initially treated with Chloroquine in standard doses. Those patients who did not have a satisfactory initial response to Chloroquine were treated with Quinine sulphate in standard doses. Blood sample for platelet count was repeated on fifth day and tenth day from start of anti-malarial therapy to check the recovery of platelet counts. The findings were recorded on a pro forma and data was analysed using the SPSS-11.

RESULTS

During the study period we had a total of 120 patients with positive Plasmodium vivax infection and low platelet counts. Out of total 120 patients, 78 (65%) were males and 42 (35%) were females. Age range of the patients was 18–57 years with mean 32.3±2.1 years. Maximum numbers of the patients were in the fourth decade of life as shown in figure-1. Out of total 120 patients with thrombocytopenia before anti-malarial therapy, 34 (28.3%) patients were in group-I. Only five (4.2%) patients were in group-III. Out of 120 treated patients, 116 (96.7%) patients responded to chloroquine therapy while for the remaining 4 patients (3.3%) quinine sulphate had to be started. Out of 120 patients who had low platelet count (<150×10^9 /L), platelet count increased to ≥150×10^9 /L in 73 (60.8%) patients after five days from start of treatment while in 47 (39.2%) patients it was still decreased, i.e., (<150×10^9 /L). However, on ten days from start of treatment all the patients had recovery of platelet count to normal reference values, i.e., (≥150×10^9 /L) (Table-1). None of our patients developed complications such as bleeding and no one was given platelet transfusion.

![Figure-1: No of patients in different age groups (n=120)](image)

**Table 1: Response of thrombocytopenia to anti-malarial treatment**

<table>
<thead>
<tr>
<th>No of patients having recovery of Platelet count to ≥150×10^9 /L</th>
<th>After 5 days of start of anti-malarial therapy</th>
<th>After 10 days of start of anti-malarial therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>73 (60.8%)</td>
<td>120 (100%)</td>
<td></td>
</tr>
<tr>
<td>47 (39.2%)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Thrombocytopenia is common in malaria. Some studies suggest that thrombocytopenia is associated with increased concentrations of IL-10, rather IL-10 causes decrease in platelet production. Furthermore, in our study 5 (4%) of patients had platelet count below 50×10^9 /L, as compared to 15.8% of malaria patients as reported by a study from Peshawar.

In our study, the response to conventional anti-malarial drugs that is chloroquine was very good. Out of total 120 patients, only 4 (3.3%) patients did not respond to chloroquine therapy. This correlates well with >90% susceptibility to chloroquine therapy to Plasmodium vivax infection in Pakistan. These patients responded to quinine sulphate.

We had no case associated with fatal disease in Plasmodium vivax mono-infection. However recent studies from Thailand, Indonesia, India and Papua New Guinea have shown that 21–27% of patients with severe malaria have Plasmodium vivax mono-infection.

The clinical range of these cases is extensive with an overall mortality of 0.8–1.6%. The lowest platelet count recorded in our study was 45×10^9 /L and it took nine days to return to normal values, i.e., ≤150×10^9 /L. This compares well with a study reported from Venezuela in which platelet counts improved within one week’s time. In our study there was not a single case with platelet counts less than 20×10^9 /L. This is expected as there are isolated case reports of this level of thrombocytopenia in Plasmodium vivax malaria till recent past. However a couple of recent studies have reported severe thrombocytopenia with Plasmodium vivax malaria.

CONCLUSION

In majority of the patients of Plasmodium vivax malaria having thrombocytopenia, platelet count returns to normal within five to ten days of start of anti-malarial treatment and platelet transfusion is not required.
REFERENCES

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