Thrombocytopenia in Malaria - Correlation with Type and Severity of Malaria

UM Jadhav, VS Patkar, NN Kadam

Abstract

Aim of the Study: Malaria is a major health problem in the tropics with increased morbidity and mortality. Thrombocytopenia is a common finding in malaria. Although a reliable diagnostic marker, prognostic implications could vary in the two types of malaria. This study was undertaken to correlate the presence and severity of thrombocytopenia with the type of malaria.

Design: A total of 1565 subjects were included in the study and identified positive for malaria parasites on peripheral smear examination with conventional microscopy. Platelet count was done on a fully automated, quantitative, hematology Coulter analyser.

Results: Normal platelet count was noted in 21.6% cases. The mean platelet count in vivax malaria (n=973) was 1,15,390/µl (SD 64,580) with a range of 8000-5,73,000/µl, as against falciparum malaria (n=590) where the mean platelet count was 100,900/µl (SD 75,437) with a range of 2000-497,000/µl (Pearson coefficient 8.825, p < 0.0001). Platelet count < 20,000/µl was noted in only 1.5% cases in vivax malaria as against 8.5% cases of falciparum malaria, and none of the subjects with vivax malaria had a platelet count less than 5000/µl.

Conclusion: Although absence of thrombocytopenia is uncommon in malaria, its presence is not a distinguishing feature between the two types. Thrombocytopenia less than 20,000/µl 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 the relatively more benign course in P. vivax malaria.

INTRODUCTION

Malaria remains today one of the major health problems in the tropics with increased morbidity and mortality. Falciparum malaria presents with protean manifestations and is associated with a variety of complications and has a high mortality. Plasmodium falciparum, in contrast to the benign malarials, may progress to a life-threatening multi-system disease. The global case fatality rate of falciparum infection is around 2 million deaths per year. Thrombocytopenia is a common finding in malaria, but its correlation with the type of malaria and prognostic implications in context with severity of the low platelet count has not been evaluated in large studies. In view of paucity of data from Indian studies, we have attempted to correlate the low platelet count and type of malaria.

MATERIALS AND METHODS

A total of 1565 subjects, either hospitalized or treated on an outpatient basis over a period of three years were included in the study. All the study subjects were identified positive for malaria parasites on peripheral smear examination with conventional microscopy. Platelet count was done on a fully automated, quantitative Coulter AcT Diff Analyser. (Coulter Corporation. Beckman Coulter Company. Miami, Florida. USA). 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 whole blood. Coefficient of variation (CV) for the platelet count was ≤7%. 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. Subjects with a diagnosis of associated dengue fever and leptospirosis were excluded from the study, as both these conditions are known to significantly contribute to thrombocytopenia. P. falciparum antigen test (PFHrp antigen test- Paracheck) was
performed in subjects with *P. vivax* malaria on the peripheral smear with a platelet count less than 20,000 cells/µl for more emphatic exclusion of associated *P. falciparum* infestation. *P. falciparum* antigen test was also performed in subjects with high index of clinical suspicion or multi-organ involvement. *P. falciparum* malaria was treated with either chloroquine, quinine or artesunate depending upon the clinical severity. *P. vivax* malaria was treated with chloroquine followed by a two weeks course of primaquine. Data was entered on an Excel spreadsheet and statistical analysis was performed with SPSS Version 10. P values less than 0.05 were considered significant.

**RESULTS**

The mean age of patients was 37.4 ± 14.2 years. The study included 58.5% males (n=915) and 41.5% females (n=650). The commonest presenting manifestations were fever with chills and rigors, headache and backache. Nine hundred and seventy three subjects had *P. vivax* malaria, 590 subjects had *P. falciparum* malaria and two subjects had mixed parasitemia of *P. vivax* and *P. falciparum* malaria. Platelet count less than 1,50,000/µl was noted in 79.4% cases.

The mean platelet count in *P. vivax* malaria was 1,15,390/µl (SD 64,580) with a range of 8000-5,73,000/µl, as against *P. falciparum* malaria where the mean platelet count was 100,900/µl (SD 75,437) with a range of 2000-497,000/µl (p < 0.0001) as shown in Table 1. Figure 1 shows the graphic representation of the platelet count range in correlation with the type of malaria. Platelet count ranging from 50,000/µl to 150,000/µl was noted in 65% cases of *P. vivax* malaria as against 50% cases of *P. falciparum*. Platelet count < 20,000/µl was noted in only 1.5% cases of *P. vivax* malaria as against 8.5% cases of *P. falciparum* malaria. Platelet count < 5,000/µl was noted in 0.7% cases (n=11) and all of them had *P. falciparum* malaria. None of the subjects with *P. vivax* malaria had a platelet count less than 5000/µl as shown in Table 3. All subjects with *P. vivax* malaria with a platelet count less than 20,000/µl were negative for *P. falciparum* malaria on the PfHrp Antigen test. None of the subjects with *P. vivax* malaria and low platelet counts had clinical manifestations of thrombocytopenia or bleeding from any site. Mean hemoglobin concentration was 11.6gm/dl in subjects with

**Table 1: Baseline hematological profile of the subjects with malaria**

<table>
<thead>
<tr>
<th>N</th>
<th>Mean Value</th>
<th>Std. Deviation</th>
<th>Minimum Value</th>
<th>Maximum Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count</td>
<td>Vivax</td>
<td>973</td>
<td>6252</td>
<td>2247</td>
</tr>
<tr>
<td>Falciparum</td>
<td>590</td>
<td>6127</td>
<td>3922</td>
<td>1300</td>
</tr>
<tr>
<td>Total</td>
<td>1563</td>
<td>6206</td>
<td>2985</td>
<td>1300</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Vivax</td>
<td>973</td>
<td>12.5</td>
<td>6.7</td>
</tr>
<tr>
<td>Falciparum</td>
<td>590</td>
<td>11.6</td>
<td>7.5</td>
<td>2.1</td>
</tr>
<tr>
<td>Total</td>
<td>1563</td>
<td>12.2</td>
<td>7.1</td>
<td>2.1</td>
</tr>
<tr>
<td>Platelet count</td>
<td>Vivax</td>
<td>973</td>
<td>115389</td>
<td>6458</td>
</tr>
<tr>
<td>Falciparum</td>
<td>590</td>
<td>100900</td>
<td>7544</td>
<td>2000</td>
</tr>
<tr>
<td>Total</td>
<td>1563</td>
<td>109847</td>
<td>6920</td>
<td>2000</td>
</tr>
</tbody>
</table>

WBC count between groups: p = 0.42; Hemoglobin between groups: p = 0.01; Platelet count between groups: p < 0.0001

(Note: Two cases of mixed manifestations of *P. vivax + P. falciparum* malaria not included in the above analysis.)

**Table 2: Least significant difference test for the platelet count.**

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Type of Malaria</th>
<th>Variable</th>
<th>Mean Difference</th>
<th>S.E</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td>Vivax</td>
<td>Falciparum</td>
<td>14489</td>
<td>3.59&lt;</td>
<td>.0001</td>
</tr>
<tr>
<td></td>
<td>Vivax + Falciparum</td>
<td>6289</td>
<td>48.74</td>
<td>0.197</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Falciparum</td>
<td>Vivax</td>
<td>14489</td>
<td>3.59&lt;</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>Falciparum</td>
<td>Vivax + Falciparum</td>
<td>4840</td>
<td>48.77</td>
<td>0.321</td>
</tr>
</tbody>
</table>

**Table 3: Correlation of platelet count less than 5000 with the type of malaria**

<table>
<thead>
<tr>
<th>Platelet count (per µl)</th>
<th>Vivax</th>
<th>Falciparum</th>
<th>Vivax + Falciparum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5000</td>
<td>0%(n=0)</td>
<td>1.9%(n=11)</td>
<td>0%(n=0)</td>
<td>0%(n=0)</td>
</tr>
<tr>
<td>&gt; 5000</td>
<td>100.0%(n=973)</td>
<td>98.1%(n=579)</td>
<td>100.0%(n=2)</td>
<td>100.0%(n=2)</td>
</tr>
<tr>
<td>Total</td>
<td>100.0%(n=973)</td>
<td>100.0%(n=590)</td>
<td>100.0%(n=2)</td>
<td>100.0%(n=1565)</td>
</tr>
</tbody>
</table>

Pearson Chi-square = 18.307, p < 0.0001
Falciparum malaria and 12.5gm/dl in subjects with *P. vivax* malaria (p < 0.047) and the lowest hemoglobin concentration was 2.1gm/dl in *P. falciparum* infestation and 3.8gm/dl in *P. vivax* infestation. There was no statistically significant difference noted in the mean total white cell count in subjects with *P. falciparum* and *P. vivax* malaria (6127/cumm versus 6252/cumm, p = 0.685). On least significant difference test, statistical significant difference persisted between the platelet count (p<0.0001) of *P. falciparum* and *P. vivax* malaria as shown in Table 2.

**DISCUSSION**

Falciparum malaria presents with protean manifestations and is associated with a variety of complications and has a high mortality. Thrombocytopenia is a common feature of acute malaria and occurs in both *P. falciparum* and *P. vivax* infections regardless of the severity of infection. 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 also. Thrombocytopenia is rarely accompanied by clinical bleeding or biochemical evidence of DIC. Platelet counts can fall to below 25,000/µl but this is uncommon. Platelet counts rise rapidly with recovery.

The prevalence of thrombocytopenia was 78.4% of the cases studied in our series and highlights the fact that a persistent normal platelet count is unlikely in the laboratory findings of malaria. Thrombocytopenia was seen in 40-90 percent of patients infected with *P. falciparum* infection in India. Maximum thrombocytopenia occurred on the fifth or sixth day of infection, and gradually returned to normal within 5-7 days after parasitemia ceased. The mechanism of thrombocytopenia in malaria could be due to peripheral destruction and consumption by DIC. Platelet counts can fall to below 25,000/µl but this is uncommon. Platelet counts rise rapidly with recovery.

Thrombocytopenia may present rapidly with symptoms of profound thrombocytopenia. Center for Drug Evaluation and Research (CDER) CDER, USA continues to receive reports of thrombocytopenia in association with quinine in use for nocturnal leg cramps and should evoke interest in context with therapy of malaria and thrombocytopenia. We did not correlate the baseline thrombocytopenia with post-treatment thrombocytopenia, which could have been useful in this context. However, there are no literature reports of quinine-induced thrombocytopenia in malaria.

In conclusion, absence of thrombocytopenia is uncommon in the laboratory diagnosis of malaria. Presence of thrombocytopenia is not a distinguishing feature between the two types of malaria. Thrombocytopenia less than 20,000/µl can occur in *P. vivax* malaria although statistically more significant with *P. falciparum* malaria. The parachek should have been ideally done on all cases with *P. vivax* malaria and...
is considered in limitation of the study. The above findings can have therapeutic implications in context of avoiding unnecessary platelet infusions with the relatively more benign course in *P. vivax* malaria.

**REFERENCES**


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**Announcement**

**Diamond APICON - 2005 - Medical Quiz**

A Medical Quiz has been organized at Diamond APICON-2005 to be held at Hotel Renaissance, Mumbai on 24th January, 2005. There will be four teams of three participants each. Team entries consisting of three participants will be preferred. However, if four team entries are not received, then single entries will be entertained and lots will form teams. If the entries are more, then selection of team will be done by a Screening test/Lots. Decision of formation of teams will rest with the undersigned. There are attractive prizes for winners.

Those who want to participate are requested to send their entries to the undersigned by 31st October, 2004. The Medical Quiz is only for the Registered Delegates of Diamond APICON-2005.

**Dr. SB Gupta**, President Elect and Chairman Scientific Committee, Diamond APICON-2005. 18, Greylands, Railway Officers' Flats, New Marine Lines, Mumbai 400 020.

Tel.: 022-22624556; Fax: 022-22651044; Cell: 09821364565/09821638617; E-mail: sbgupta@vsnl.net; Website: www.apiindia.org

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**Announcement**

**Third National Workshop on "Simple Diagnostic Methods in Infectious Diseases"** will be held from 7th - 11th December, 2004 at Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry.

The number of participants will be restricted to 20.

The last date of receipt of applications is **30th September, 2004**

For details please contact: **Dr. Subhash Chandra Parija**, Course Coordinator, Professor and Head, Department of Microbiology, JIPMER, Pondicherry 605 006.

Tel.: Off.: 0413-2272380-90; Extn. 3200; Residence: 0413-2253016; Mobile 0413 3114418

Telegram: JIPMER, Fax: 0413-2272067; e-mail: idworkshop@rediffmail.com

For further details about the workshop log on to the website www.jipmer.edu