Changing Spectrum Of Complications In Plasmodium Vivax Malaria

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Abstracts: Aims: To study the incidence and outcome of complications in Plasmodium vivax. Material and methods: An analysis of smear positive Plasmodium vivax patients admitted to Civil Hospital, Ahmedabad from July 2007 to September 2007 was done. Results: There were 118 cases of malaria: Plasmodium vivax only in 23 cases (19.4%), 1 was mixed infection and 94 were Plasmodium falciparum only. Out of the 23 vivax cases, thrombocytopenia was seen in 22 cases (95.6%), hepatitis and jaundice seen in 7 cases (30.4%), and acute renal failure in 5 (21.7%). Death occurred in 2 (8.6%) and 20 (86.9%) patients recovered. The study included 19 adult patients and 4 pediatric cases. Conclusions: Plasmodium vivax can cause thrombocytopenia, jaundice, acute renal failure all of which occurs more commonly in Plasmodium falciparum. The study intends to highlight that Plasmodium vivax can also cause grave systemic complications but prognosis is favorable if early referral and timely supportive treatment is given. [Patel A et al NJIRM 2012; 3(5) :114-117]  

Key words: Plasmodium vivax, complications, thrombocytopenia, renal failure.

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Introduction: Inspite of intensive worldwide efforts to reduce its transmission, malaria still remains a major cause of morbidity and mortality in tropical and subtropical areas. Malaria is a serious endemic disease in the world. It affects nearly 5% of the world population. The incidence of malaria worldwide is estimated to be 300 – 500 million cases each year. Malaria is thought to kill between 1.1 to 2.7 million people worldwide each year of whom about 1 million are children under the age of 5 years in these areas. Ninety percent of these occurring in the sub-Saharan Africa and mostly caused by Plasmodium falciparum. The predominant causal organisms in the south east Asia region (SEAR) are Plasmodium vivax followed by Plasmodium falciparum. Malaria is a parasitic disease with predominant hematological manifestations, the main clinical features being fever, anemia and splenomegaly. It can also cause hematological abnormalities from asymptomatic thrombocytopenia to fulminant disseminated intravascular coagulation. Early investigators suggested that the major coagulation abnormality was DIC, but in recent years it has been observed that thrombocytopenia is much more common than DIC. A mild to moderate thrombocytopenia is often found in patients with vivax malaria while severe thrombocytopenia is rarely seen. Plasmodium falciparum can cause a wide spectrum of renal and renal related disorders ranging between urinary abnormalities, proteinuria (>1g/m/24 hr) to acute renal failure. ARF occurs more frequently in falciparum malaria. Reported incidence of ARF in falciparum malaria is highly variable between 1-4%. However, ARF in association with P. vivax malaria is rarely reported. In 2006, the period between July to September, there was an epidemic of malaria in the state of Gujarat. It was noticed that P. vivax malaria was also presenting with complications which were considered very rare previously. Is vivax malaria changing its face? So we decided to study the cases coming with vivax malaria in 2007 in the same period from July to September. This is the rainy season and malaria epidemics occur most during this time in Gujarat. Present study was conducted to study the incidence and outcome of complications in P. vivax infected patients and to highlight some of the grave systemic complications which can be life threatening.

Material and Methods.: The present study was conducted in the Department of Pathology at BJMC, Ahmedabad, Gujarat, India over a period of 3 months between July 2007 to September 2007.
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During this period, 118 patients were admitted to Civil Hospital, Ahmedabad with malaria. Blood samples were collected in EDTA vaccuette from patients who were clinically suspected of malaria. Cases were screened by thick smears, thin smears and QBC technique and Panmalaria card test and Optimal card test. Thick smears were prepared and stained by Giemsa stain after dehemoglobinisation. Search was made in atleast 100 oil immersion fields. Thin smears were stained by Leishman technique. Atleast 300 oil immersion fields were scrutinized.

Hematological changes in malaria positive cases were studied using automated hematology cell counters and Leishman stained peripheral blood smears. Pan malaria card test were carried out in patients who showed negative blood films for malarial parasite. Optimal card test was done to rule out falciparum infection.

Cases with mixed infection and falciparum infection were excluded. Hemoglobin, total count, Differential count, Biochemical assay (BU, S.Cr, S.Na+, S.K+, S.Prot, S.Bil, SGOT, SGPT, S.Uric acid,) and platelet counts were studied by standard methods. Coagulation profile was done as and when required. Complications of vivax malaria were recorded in individual patients during the course of hospitalization.

A complete physical examination was performed in all the cases. Past history of malaria, thrombocytopenia, history of drug intake or any other hematological condition was recorded. DIC was ruled out by peripheral smear examination and when necessary coagulation profile was done. Platelet count was done by standard method. A count of 1 lakh – 1.5 lakh was mild, 20,000 -1 lakh moderate and less than 20,000 considered severe thrombocytopenia.

Blood culture was taken at the time of admission in all cases to rule out septicemia as a cause of fever and thrombocytopenia. Dengue serology (IgM and IgG) was also done in all cases followed.

Results: During the study period 118 cases were admitted to Civil Hospital, Ahmedabad with malaria. Out of these, 23 cases were diagnosed as having plasmodium vivax only; 1 mixed infection and 94 were Plasmodium falciparum positive. A total of 23 vivax positive patients were included in this study done in the period from July 2007 to September 2007. Cases with falciparum malaria and mixed infection were excluded. There was male predominance (15 males and 8 females). The study included 19 adult patients and 4 pediatric patients. Rapid malaria test was positive in all the cases and correlated with the vivax species identified on the peripheral smear.

The presenting complaints were fever with chills, decreased urine output, headache, nausea, myalgia. There was no past history of malaria, drug intake, or any other hematological condition that could have led to thrombocytopenia or jaundice.

On peripheral blood smear examination, five cases showed normocytic normochromic anemia, none had macrocytic and eighteen had microcytic hypochromic anemia. Total leucocyte count was normal in 20 cases, 1 case had leucocytosis and 2 had leucopenia. Atypical lymphocytes were observed in 5 cases and monocyctosis in 5 cases and none had eosinophilia.

Out of the 23 vivax cases, thrombocytopenia was seen in 22 cases. FDP levels were not raised in any of our cases. The platelet count reverted to normal following treatment with disappearance of parasite from peripheral blood. Out of the 22 cases with thrombocytopenia, 3 had mild, 16 had moderate and 3 and severe thrombocytopenia (Table 1).

<table>
<thead>
<tr>
<th>Mild (1 lakh – 1.5 lakh/mm³)</th>
<th>Moderate (20,000 – 1 lakh/mm³)</th>
<th>Severe (&lt;20,000/mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>16</td>
<td>3</td>
</tr>
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The lowest count reported was 7000/mm³. The platelet counts reverted to normal at the time of discharge in most of the cases. One case died due
to severe bleeding (Table 2). Out of the 23 cases, hepatitis seen in 7 cases (30.4%). SGPT was raised. Out of 23 cases, acute renal failure was seen in 5 (21.7%) cases. The clinical presentations of these patients were fever, encephalopathy, hypotension, jaundice, intravascular hemolysis reflecting majority had severe malarial infection.

Table 2. Complications in P. vivax malaria

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Liver impairment</td>
<td>7</td>
<td>30.4</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>5</td>
<td>21.7</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>22</td>
<td>95.6</td>
</tr>
</tbody>
</table>

Discussion: Anemia is an important complication and cause of high morbidity and mortality in acute falciparum malaria. Our study has shown predominantly microcytic hypochromic anemia. Iron deficiency is prevalent in the Indian population and our sample belongs to the lower strata. This explains the finding of microcytic anemia predominantly.

Mild to moderate thrombocytopenia, is a common hematological finding in malaria which returns to normal following treatment. Two cases of vivax malaria with severe thrombocytopenia were reported from India. In 173 cases of malaria in US soldiers reported by Martelo et al in 1969, 93% had P. vivax, out of which 15% had thrombocytopenia. Hartman reported 72% patients with vivax malaria having thrombocytopenia, the lowest platelet count in their study being 44 ×10^9/L. U.M. Jadhav et al had observed platelet count ranging from 50,000 to 150,000/μl in 65% cases. Platelet count <20,000/μl was noted in only 1.5% cases. They didn’t find any case with platelet count <5000/μl. Meenal Jain and Mannohan Kaur also found thrombocytopenia in P. vivax patients. Aarti Kumar and Shashirekh found 24 out of 27 (88.7%) cases had thrombocytopenia. The lowest count in their study was 22 ×10^9/L. In our study 22 out 23 patients had thrombocytopenia. Several mechanisms suggested as the cause of thrombocytopenia in malaria include DIC, immune mechanisms, hypersplenism, and oxidative stress. DIC is no longer considered a cause for thrombocytopenia as most patients with malaria do not have DIC. In our study, no cases of DIC were observed though septicemia has been observed.

Immune complexes that are present in the circulation of malaria-infected patients may play a role in the peripheral destruction of platelets. Hill GJ et al in their study of 9 volunteers with thrombocytopenia in acute malaria found splenomegaly in only 5 of them. 12 had splenomegaly in our study. Moreover all cases of splenomegaly with infection irrespective of etiology do not show thrombocytopenia.

Erel O et al found that Platelet count, platelet superoxide dismutase and glutathione peroxidase activities of patients with vivax malaria were lower and platelet lipid peroxidation levels were higher, thus suggesting oxidative stress as a cause for thrombocytopenia. Changes in platelet function including raised concentration of platelet specific proteins such β thromboglobulin(BTG), platelet factor 4(PF4) have been found in acute malaria. In present study, one patient had severe bleeding and BT CT were abnormal in that case. Thus among the variety of mechanisms postulated as the cause of thrombocytopenia in malaria, none have been unequivocally proved. It is possible that several of these factors acting in concert are responsible.

Hyperbiliruinemia was observed in 7 cases (30.4%). 3 had hyperbilirubinemia with normal SGPT. Cases with normal SGPT indicates a hemolytic component which has been reported by several workers. SGPT was raised in 7 cases (30.4%) suggestive of hepatopathy in vivax malaria. Although, jaundice is commonly seen with falciparum infection, it is also reported with P. vivax infection and the incidence ranges from 0-9%; however, hepatic involvement has not been described with it.

Acute renal failure is commonly reported in falciparum malaria although its rare occurrence
has been reported in P. vivax malaria. Prakash et al. found acute renal in 3.2%. He found that most cases are oliguric, hypercatabolic and associated with other malarial complications, probably depending on the relative impact of different pathogenetic mechanisms. Ahmad et al. reported acute renal impairment in children due to P. vivax in 33% cases. In our study 5 (21.7%) cases had ARF. Only 1 was pediatric.

Atypical manifestations of P. vivax malaria have been reported previously. Mohapatra et al. reported jaundice (7.2%), cerebral involvement (0.9%), severe anemia (7.2%), and thrombocytopenia (3.6%). Reemerging Vivax malaria is being noticed. It is now presenting with more complications and not merely due to drug resistance. We decided to present our study because this is a very strange trend vivax malaria is appearing to take. Is this change similarly occurring in other areas of the world where malaria is endemic? Awareness is of course the first step to a cure of the disease. The prognosis of P. vivax associated with complications is favourable and antimalarials drugs remain the cornerstone in the treatment.

Conclusion: Plasmodium vivax malaria is increasingly presenting with various complications. It is presenting with grave systemic complications which may be life threatening but have favorable prognosis if early referral and and timely supportive is given. Further studies need to be done to find out if this change is occurring in other endemic areas as well. Plasmodium vivax must be kept as differential diagnosis in all cases of fever with thrombocytopenia. Awareness that it can also lead to complications is essential while following up these patients. Most importantly even complicated vivax malaria responds favorably to treatment.

References:
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