Thrombocytopenia and *Plasmodium falciparum* malaria in children with different exposures

F Moulin, F Lesage, A-H Legros, C Maroga, A Moussavou, P Guyon, E Marc, D Gendrel

We studied thrombocytopenia during acute *Plasmodium falciparum* malaria in 64 traveller children from Paris (France), 85 children from Dakar (Senegal) with an intermittent exposure (69 with severe attack or cerebral malaria), and 81 children from Libreville (Gabon) with a perennial exposure (43 with severe attack or cerebral malaria). Initial thrombocytopenia was present in 43–58% of children with *P falciparum* malaria but was not more frequent in severe outcome or cerebral malaria. Low parasitaemia may lead to the misdiagnosis of malaria and delayed treatment when there is associated thrombocytopenia.

Thrombocytopenia is frequent in patients with acute malaria and is sometimes profound in cases of severe disease.1–3 However, a comparison of the frequency of thrombocytopenia in children living in areas in which malaria is endemic, and in traveller children, has not been reported.

### METHODS

A prospective study was performed in three populations examined in 1999 and 2000:

- Traveller children living in France and hospitalised in Paris with acute *P falciparum* malaria contracted while travelling through Africa.
- Children with intermittent exposure examined or hospitalised with acute *P falciparum* malaria in Hopital Principal, Dakar, Senegal, where the transmission of malaria is seasonal.4
- Children with perennial exposure examined or hospitalised in Libreville (Gabon), where malaria is transmitted throughout the whole year.5

Initial blood cell and platelet counts were determined by an automatic method; diagnosis of *P falciparum* malaria was made after thin film microscopic examination.

### RESULTS

Table 1 presents the results. None of the patients had bleeding or clinical symptoms of disseminated intravascular coagulation, but fibrin degradation products were not measured.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Platelet counts and haemoglobin levels in children with <em>P falciparum</em> malaria in the three areas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Platelet count (/mm$^3$)</td>
</tr>
<tr>
<td></td>
<td>Mean (range)</td>
</tr>
<tr>
<td>Paris (acute malaria)</td>
<td></td>
</tr>
<tr>
<td>Non-chemophrophylaxis</td>
<td>161000 (46000–353000)</td>
</tr>
<tr>
<td>Chemophrophylaxis</td>
<td>159000 (31000–470000)</td>
</tr>
<tr>
<td>Dakar</td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>121000 (30000–309000)</td>
</tr>
<tr>
<td>Severe</td>
<td>174000 (8000–524000)</td>
</tr>
<tr>
<td>Cerebral malaria</td>
<td>160000 (34000–420000)</td>
</tr>
<tr>
<td>Libreville</td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>142000 (20000–565000)</td>
</tr>
<tr>
<td>Severe</td>
<td>161000 (21000–426000)</td>
</tr>
<tr>
<td>Cerebral malaria</td>
<td>180000 (63000–346000)</td>
</tr>
</tbody>
</table>

In three patients with platelets count <100 000, no blood parasites were found in the initial thin film, routinely examined at time of hospital admission. In two of these patients, a subsequent examination by the University Department of Parasitology laboratory revealed a low number of parasites (<0.01% parasitised red cells). The third patient’s initial platelet count was 60 000/mm$^3$ and the two initial blood smears and thin films were negative. After three days, this patient was still febrile with 30 000/mm$^3$ platelets, and a third blood film revealed only two red cells containing a mature *P falciparum* trophozoite.

### Dakar

The study population consisted of 85 patients (42 males; mean age 6.5 years, range 6 months to 14 years); according to WHO guidelines, there were no clinical differences, especially in terms of splenomegaly, between children with or without thrombocytopenia.
criteria, 16 patients had acute malaria and were not hospitalised, 44 had severe malaria, and 25 had cerebral malaria and were hospitalised. A thrombocytopenia < 50 000/mm$^3$ was found in 14.1% of the children and < 150 000/mm$^3$ in 43.6%. There was no difference between the three severity groups. Three of the 85 patients died. Their platelet counts were respectively 77 000, 164 000, and 186 000/mm$^3$. In all patients with thrombocytopenia, platelet count returned to normal in 2–5 days.

Libreville
The study population consisted of 81 hospitalised patients (40 males; mean age 6.1 years, range 7 months to 15 years); 38 had acute malaria (non-hospitalised), 35 severe malaria, and eight cerebral malaria (hospitalised). A thrombocytopenia < 50 000/mm$^3$ was found in 14.8% of children and < 150 000/mm$^3$ in 58%; there was no correlation with severity. One child with cerebral malaria died. His platelet count was 170 000/mm$^3$.

DISCUSSION
This study shows that thrombocytopenia is a common feature of Plasmodium falciparum malaria and is independent of importance of parasite exposure. In the three different populations studied, a platelet count < 150 000/mm$^3$ was found in 43–58% of children, and profound thrombocytopenia < 50 000/mm$^3$ was not more frequent in cerebral malaria or severe forms than in acute attacks. In Paris where no severe malaria was diagnosed, the rate of thrombocytopenia is the same as in Dakar or Libreville. In the present study, four children died, but only one had thrombocytopenia < 150 000/mm$^3$. When thrombocytopenia is associated with low number of parasites, thrombocytopenic purpura is often diagnosed, which delays antimalarial treatment and increases the risk of complications.

The mechanism of thrombocytopenia in malaria is probably the consequence of several factors. Experimental data and clinical studies have successively emphasised the role of immune factors and the destruction or sequestration of platelets. In severe forms, platelet and erythrocyte sequestration are frequent, and thrombocytopenia is present. However, no studies have shown that thrombocytopenia at the initial stage of acute malaria could be a marker of severity. Patients with P vivax malaria, a mild infection without severe forms, also frequently have thrombocytopenia. Activation of the coagulation cascade occurs even in mild malaria, but is probably proportional to disease severity. Fibrin degradation products and plasma antithrombin III activity were not measured in our patients, but no bleeding or other clinical symptoms of disseminated intravascular coagulation were found, and thrombocytopenia was also detected in ambulatory children with common acute malaria. In this study, thrombocytopenia appeared to be frequent in acute P falciparum malaria. Thrombocytopenia might be a useful indicator of malaria in children, but not a marker of severity.

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