

SHORT REPORT

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

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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. Within each subgroup, there was no clinical difference, especially in terms of splenomegaly, between children with or without thrombocytopenia.

Paris

The study population consisted of 68 traveller children living in France (60 African, eight French; 30 males; mean age 7.6 years, range 8 months to 15 years) and hospitalised with acute *P falciparum* malaria. No patient had severity criteria according to WHO guidelines.¹ Thrombocytopenia $<50\,000/\text{mm}^3$ was found in 8.8% and $<150\,000/\text{mm}^3$ in 45.6%. Half of the patients received chemoprophylaxis during their travels. All patients with thrombocytopenia had a normal platelet count after 3–28 days.

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 $60\,000/\text{mm}^3$ and the two initial blood smears and thin films were negative. After three days, this patient was still febrile with $30\,000/\text{mm}^3$ 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

Table 1 Platelet counts and haemoglobin levels in children with *P falciparum* malaria in the three areas

	Platelet count (/mm ³)			Haemoglobin (g/l)
	Mean (range)	<50000	<150000	Mean (range)
<i>Paris (acute malaria)</i>				
Non-chemoprophylaxis	161000 (46000–353000)	3/34 (8.8%)	15/34 (44.1%)	97 (75–134)
Chemoprophylaxis	159000 (31000–470000)	3/34 (8.8%)	16/34 (47%)	104 (70–136)
<i>Dakar</i>				
Acute	121000 (30000–309000)	4/16 (25%)	6/16 (37.5%)	88 (52–133)
Severe	174000 (8000–524000)	4/44 (9%)	20/44 (45.5%)	64 (18–132)
Cerebral malaria	160000 (34000–420000)	4/25 (16%)	11/25 (44%)	77 (35–103)
<i>Libreville</i>				
Acute	142000 (20000–565000)	6/38 (15.8%)	19/38 (50%)	89 (63–125)
Severe	161000 (21000–426000)	6/35 (17.1%)	25/35 (71.4%)	78 (21–128)
Cerebral malaria	180000 (63000–346000)	0/8	3/8 (37%)	81 (31–131)

criteria, 16 patients had acute malaria and were not hospitalised, 44 had severe malaria, and 25 had cerebral malaria and were hospitalised. A thrombocytopenia $<50\,000/\text{mm}^3$ was found in 14.1% of the children and $<150\,000/\text{mm}^3$ 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 $<50\,000/\text{mm}^3$ was found in 14.8% of children and $<150\,000/\text{mm}^3$ 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 $<150\,000/\text{mm}^3$ was found in 43–58% of children, and profound thrombocytopenia $<50\,000/\text{mm}^3$ 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 $<150\,000/\text{mm}^3$. When thrombocytopenia is associated with low number of parasites,⁵ 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.¹ In severe forms, platelet and erythrocyte sequestrations are frequent,⁶ and thrombocytopenia is present.^{1–3, 6}

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.³ Activation of the coagulation cascade occurs even in mild malaria, but is probably proportional to disease severity.¹ 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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