# Fresh isolates from children with severe Plasmodium falciparum malaria bind to multiple receptors.

Heddini, A; Pettersson, F; Kai, O; Shafi, J; Obiero, J; Chen, Q; Barragan, A; Wahlgren, M; Marsh, K.

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## Abstract

The sequestration of Plasmodium falciparum-infected erythrocytes (pRBC) away from the peripheral circulation is a property of all field isolates. Here we have examined the pRBC of 111 fresh clinical isolates from children with malaria for a number of adhesive features in order to study their possible coexpression and association with severity of disease. A large number of adhesion assays were performed studying rosetting, giant rosetting, and binding to CD36, intercellular adhesion molecule 1, platelet endothelial cell adhesion molecule 1, thrombospondin, heparin, blood group A, and immunoglobulins. Suspension assays were performed at the actual parasitemia of the isolate, while all the static adhesion assays were carried out at an equal adjusted parasitemia. The ability to bind to multiple receptors, as well as the ability to form rosettes and giant rosettes, was found to be more frequent among isolates from children with severe versus mild malaria ($P = 0.0015$). Rosettes and giant rosettes were more frequent for children with severe malaria, and the cell aggregates were larger and tighter, than for those with mild disease ($P = 0.0023$). Binding of immunoglobulins (97% of isolates) and of heparin (81% of isolates) to infected erythrocytes was common, and binding to heparin and blood group A was associated with severity of disease ($P = 0.011$ and $P = 0.031$, respectively). These results support the idea that isolates that bind to multiple receptors are involved in the causation of severe malaria and that several receptor-ligand interactions work synergistically in bringing about severe disease.