Hepcidin levels are high and iron absorption is limited in acute malaria. The mechanism(s) that regulate hepcidin secretion remain undefined. We have measured hepcidin concentration and cytokines in 100 Kenyan children with acute falciparum malaria and different degrees of anemia. Hepcidin was increased on admission and fell significantly one week and one month after treatment. The association of hepcidin with hemoglobin was not linear and hepcidin was very low in severe malarial anemia. Parasite density, IL-10 and IL-6 were significantly associated with hepcidin concentration. Hepcidin response to acute malaria supports the notion of iron sequestration during acute malaria infection and suggests that iron administration during acute malaria is futile. These data suggest iron supplementation policies should take into account the high hepcidin levels and probable poor utilization of iron for up to one week after treatment for the majority of patients with acute malaria.