Iron Deficiency Protects Against Severe *Plasmodium falciparum* Malaria and Death in Young Children

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Background. Iron supplementation may increase malaria morbidity and mortality, but the effect of naturally occurring variation in iron status on malaria risk is not well studied.
Methods. A total of 785 Tanzanian children living in an area of intense malaria transmission were enrolled at birth, and intensively monitored for parasitemia and illness including malaria for up to 3 years, with an average of 47 blood smears. We assayed plasma samples collected at routine healthy-child visits, and evaluated the impact of iron deficiency (ID) on future malaria outcomes and mortality.
Results. ID at routine, well-child visits significantly decreased the odds of subsequent parasitemia (23% decrease, P , .001) and subsequent severe malaria (38% decrease, P 5 .04). ID was also associated with 60% lower all-cause mortality (P 5 .04) and 66% lower malaria-associated mortality (P 5 .11). When sick visits as well as routine healthy-child visits are included in analyses (average of 3 iron status assays/child), ID reduced the prevalence of parasitemia (6.6-fold), hyperparasitemia (24.0-fold), and severe malaria (4.0-fold) at the time of sample collection (all P , .001).
Conclusions. Malaria risk is influenced by physiologic iron status, and therefore iron supplementation may have adverse effects even among children with ID. Future interventional studies should assess whether treatment for ID coupled with effective malaria control can mitigate the risks of iron supplementation for children in areas of malaria transmission.