ABSTRACT

Importance  Anemia affects most pregnant African women and is predominantly due to iron deficiency, but antenatal iron supplementation has uncertain health benefits and can increase the malaria burden.

Objective  To measure the effect of antenatal iron supplementation on maternal *Plasmodium* infection risk, maternal iron status, and neonatal outcomes.

Design, Setting, and Participants  Randomized placebo-controlled trial conducted October 2011 through April 2013 in a malaria endemic area among 470 rural Kenyan women aged 15 to 45 years with singleton pregnancies, gestational age of 13 to 23 weeks, and hemoglobin concentration of 9 g/dL or greater. All women received 5.7 mg iron/day through flour fortification during intervention, and usual intermittent preventive treatment against malaria was given.

Interventions  Supervised daily supplementation with 60 mg of elemental iron (as ferrous fumarate, n = 237 women) or placebo (n = 233) from randomization until 1 month postpartum.

Main Outcomes and Measures  Primary outcome was maternal *Plasmodium* infection at birth. Predefined secondary outcomes were birth weight and gestational age at delivery, intrauterine growth, and maternal and infant iron status at 1 month after birth.

Results  Among the 470 participating women, 40 women (22 iron, 18 placebo) were lost to follow-up or excluded at birth; 12 mothers were lost to follow-up postpartum (5 iron, 7 placebo). At baseline, 190 of 318 women (59.7%) were iron-deficient. In intention-to-treat analysis, comparison of women who received iron vs placebo, respectively, yielded the following results at birth: *Plasmodium* infection risk: 50.9% vs 52.1% (crude difference, −1.2%, 95% CI, −11.8% to 9.5%; *P* = .83); birth weight: 3202 g vs 3053 g (crude difference, 150 g, 95% CI, 56 to 244; *P* = .002); birth-weight-for-gestational-age z score: 0.52 vs 0.31 (crude difference, 0.21, 95% CI, −0.11 to 0.52; *P* = .20); and at 1 month after birth: maternal hemoglobin concentration: 12.89 g/dL vs 11.99 g/dL (crude difference, 0.90 g/dL, 95% CI, 0.61 to 1.19; *P* < .001); geometric mean maternal plasma ferritin concentration: 32.1 µg/L vs 14.4 µg/L (crude difference, 123.4%, 95% CI, 85.5% to 169.1%; *P* < .001); geometric mean neonatal plasma ferritin concentration: 163.0 µg/L vs 138.7 µg/L (crude difference, 17.5%, 95% CI, 2.4% to 34.8%; *P* = .02). Serious adverse events were reported for 9 and 12 women who received iron and placebo, respectively. There was no evidence that intervention effects on *Plasmodium* infection risk were modified by intermittent preventive treatment use.

Conclusions and Relevance  Among rural Kenyan women with singleton pregnancies, administration of daily iron supplementation, compared with administration of placebo, resulted in no significant differences in overall maternal *Plasmodium* infection risk. Iron supplementation led to increased birth weight.

Trial Registration  clinicaltrials.gov Identifier: NCT01308112