Hepcidin Levels in Pregnant Women With Schistosomiasis Differ By Anemia Type and May Help Identify Risk of Low Iron Endowment Among Infants

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Background

Hepcidin, a peptide hormone made in the liver, plays a crucial role in iron homeostasis. Hepcidin is upregulated during infections such as schistosomiasis, which contributes to anemia of inflammation (AI). Few studies have addressed the role of AI in human pregnancy, including its impact on newborn iron endowment. We hypothesize that hepcidin levels are elevated in pregnant women with Schistosoma japonicum infection with AI compared to iron deficiency anemia or no anemia and that treatment with praziquantel will improve newborn iron endowment in pregnant women with AI.

Methods

As part of a randomized controlled trial, 358 pregnant women with S. japonicum infection in Leyte, the Philippines were enrolled at 12 to 16 weeks gestation and received praziquantel or placebo at enrollment. All study participants received iron supplementation starting at enrollment. Markers of iron status and inflammation, including hemoglobin, sTfR, ferritin, and hepcidin, along with socioeconomic data were collected at 12 weeks and 32 weeks for the women. These markers were also captured in cord blood at 6 months and 12 months of age for the infants. Among the pregnant women, iron deficiency anemia (IDA) was defined as anemia with ferritin < 30 ng/ml, and non-iron deficiency anemia (NIDA) of ferritin ≥ 30 ng/ml. NIDA was largely due to AI in this study. To assess iron status we used sTfR:log(ferritin) ratio, with a higher ratio level indicating more iron depletion.

Results

Of the 358 pregnant women, 38.0% (n=136) had IDA and 8.9% (n=32) had NIDA at 32 weeks gestation. Women with NIDA had significantly higher hepcidin levels ($p<0.001$) and CRP levels ($p<0.05$) than women with IDA or no anemia. At 32 weeks gestation, hepcidin was a significantly better predictor of NIDA in pregnant women than serum transferrin receptor, at an optimal cutoff level of >6.2 ng/ml. Infants born to women with the highest hepcidin tertile had significantly higher sTfR:log(ferritin) ratio levels in cord blood, compared to the middle and lowest tertiles. Newborns with hepcidin levels in the lowest tertiles at birth had higher sTfR:log(ferritin) through 12 months. Maternal anemia type from 12 to 32 weeks gestation, as well as infant hemoglobin and ferritin, did not differ by pregnant women's treatment status.

Conclusion

Among this population of schistosomiasis-infected pregnant women, we demonstrate a significant burden of both IDA and NIDA. NIDA was associated with higher levels of hepcidin. Hepcidin was a better predictor of NIDA than sTFR. The positive relationship between maternal hepcidin and infant sTfR:log(ferritin) suggests that elevated hepcidin may be associated with either poor utilization of iron supplementation during pregnancy or reduced availability of iron transfer to the fetus in utero. However, maternal anemia type was not associated with newborn iron endowment, and infant anemia risk was not modified by treatment of schistomiasis during pregnancy.