A Multi-country Association Analysis of Maternal Selenium (Se) Levels and Infant Birth Outcomes: Findings From the Women First Study

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Objectives: Selenium (Se) soil content varies worldwide impacting population levels. Maternal Se deficiency may be related to preterm birth, small for gestational age (SGA), and low birth weight (LBW, < 2,500g) possibly through its roles in antioxidant and thyroid hormone function particularly during the first trimester. We examined associations of Se levels and birth outcomes in a multi-country nutritional intervention trial of pregnant women.

Methods: This is a secondary analysis of the Women First trial (NCT01883193), a randomized controlled study investigating timing of maternal multiple micronutrient (with 130 mcg Se) and protein-energy supplementation (MNS) on fetal growth. MNS was started 3 months prior to conception (Arm 1), at ~12 wk of gestation (Arm 2), or not at all (Arm 3) in women in India, Guatemala, and Pakistan. Gestational age was determined by first trimester ultrasound. At 12 and 34 wk gestation, maternal serum Se was measured by ICP-MS (n = 143–325 per timepoint per site). TSH was measured by 1-step sandwich (Guatemala and Pakistan) or chemiluminescence immunoassay (India). We used t-test or ANOVA to test group differences and linear models to test association of Se with infant outcomes and TSH, adjusting for treatment arm and study site.

Results: Se levels were highest in Guatemalan women (mean ± SD, 12 wk: 102.1 ug/L ± 12.6; 34 wk: 103.9 ± 14.2) and lowest in Pakistani women (12 wk: 85.7 ± 14.5; 34 wk: 77.9 ± 14.8) at both timepoints ($P < 0.0001$). MNS supplementation before or during gestation increased serum Se levels at 34 wk in Guatemalan women only ($p = 0.038$). In Pakistan a negative association between maternal Se at 34 wk and LBW was seen in female ($n = 153$; $p = 0.041$) but not male ($n = 143$; $p = 0.97$) infants. Se levels were not associated with preterm birth or SGA status at any site. TSH levels did not differ by study arm but were lower in Pakistan at 12 and 34 wk compared to other sites. There was no association between TSH and Se levels at any timepoint at any site.

Conclusions: Maternal Se levels may impact fetal birth weight in vulnerable populations in a sexually dimorphic manner. Preconception Se supplementation as part of a comprehensive MNS did not increase Se levels in Pakistan where soil Se content is low. Although Se did not correlate with TSH levels in this study, future work will incorporate co-influence of iodine.

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