659

Biomarkers of Environmental Enteric Dysfunction in Pregnancy and Adverse Birth Outcomes: An Observational Study Among Women Living With HIV in Tanzania

676

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Objectives: Environmental enteric dysfunction (EED), a subclinical state of intestinal inflammation, may contribute to poor fetal growth in low-resource settings. Pregnant women living with HIV may be particularly susceptible to effects of EED, given their increased risk of infections and adverse birth outcomes. We sought to explore the associations of biomarkers of EED, inflammation and growth hormones with birth outcomes in pregnant women living with HIV in Dar es Salaam, Tanzania.

Methods: We performed a sub-study of 706 HIV-infected pregnant women participating in a randomized, double-blind, placebo-controlled trial assessing the effect of vitamin D_3 supplementation. Maternal serum samples collected at 32 weeks gestation were analyzed for anti-flagellin and anti-LPS IgA and IgG via ELISA as well as using an 11-plex Micronutrient and EED Assessment Tool, which includes markers of EED [intestinal fatty acid-binding protein (I-FABP) and soluble CD14], systemic inflammation [C-reactive protein and α1-acid glycoprotein (AGP)], insulin-like growth factor 1 (IGF-1) and fibroblast growth factor 21 (FGF21). Biomarkers were categorized as quartiles. Associations with birth outcomes were assessed using linear regression analyses.

Results: Pregnant women in the highest quartile of I-FABP had more than twice the risk of stillbirth compared to those in the lowest quartile (RR 2.43, 95% CI 0.98–6.03, $p_{trend} = 0.02$). Compared to women in the lowest quartile of AGP, those in the highest quartile gave birth to infants weighing 176g less (95% CI -280 to -71g, $p_{trend} = 0.005$). Maternal AGP was associated with increased risk of small-for-gestational age births; those in the highest quartile had a 70% greater risk compared to the lowest (RR 1.70, 95% CI 1.08–2.69, $p_{trend} = 0.03$). IGF1 was positively associated with birthweight and birthweight-for-age z-score; FGF21 was negatively associated with gestation duration and risk of preterm birth.

Conclusions: Maternal biomarkers of EED, systemic inflammation, and the growth hormone axis were associated with birth outcomes. Further studies are needed to confirm these results and study the biologic mechanisms involved.