Assessing Environmental Enteric Dysfunction via Multiplex Assay and its Relation to Infant Growth Among HIV-Exposed Infants in Dar es Salaam, Tanzania

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Objectives: Environmental enteric dysfunction (EED), a subclinical state of intestinal inflammation, may contribute to poor growth in children in low-resource settings, but validated biomarkers are lacking. Multiplex assays, such as the 11-plex Micronutrient and EED Assessment Tool (MEEDAT), hold promise due to their ability to capture multiple domains of EED; however, MEEDAT's ability to predict poor growth has not been well established. We sought to examine the relationship between markers of EED and growth among HIV-exposed infants in Dar es Salaam, Tanzania.

Methods: We performed a sub-study of 467 infants of HIV-infected mothers who participated in a randomized, double-blind, placebo-controlled trial assessing the effect of vitamin D3 supplementation during pregnancy. Infant serum samples collected at 6 weeks and 6 months were analyzed for anti-flagellin and anti-LPS IgA and IgG via ELISA as well as MEEDAT, which incorporates two markers of EED [fatty acid-binding protein (I-FABP) and soluble CD14 (sCD14)]. Biomarkers were categorized into quartiles for primary analyses and as continuous exposures for exploratory analyses. Associations with subsequent growth outcomes [length-for-age Z-score (LAZ), weight-for-length Z-score (WLZ), and weight-for-age Z-score (WAZ)] at 12 months of age were assessed using linear regression.

Results: At 12 months, nearly half ($\sim$46%) of infants were stunted (LAZ <-2), and $\sim$3% were wasted (WLZ <-2). Higher concentrations of anti-LPS IgG at 6 months were significantly associated with lower LAZ at 12 months ($p_{trend} = 0.034$). In continuous analyses, higher concentrations of anti-flagellin IgA at 6 weeks were significantly associated with lower LAZ at 12 months (β: -0.46, 95% CI: -0.82, -0.11) as were anti-LPS IgA (β: -0.28, 95% CI: -0.53, -0.03) and anti-LPS IgG (β: -0.24, 95% CI: -0.48, -0.01) at 6 months. Higher concentrations of anti-flagellin IgA and anti-LPS IgA at 6 months were significantly associated with lower WAZ at 12 months (β: -0.34, 95% CI: -0.61, -0.07; β: -0.24, 95% CI: -0.44, -0.04). No significant associations were observed between I-FABP or sCD14 and infant growth at 12 months.

Conclusions: Unlike anti-flagellin and anti-LPS Igs, MEEDAT's biomarkers of EED, I-FABP and sCD14, were not associated with subsequent growth among HIV-exposed infants in Tanzania.