

METABOLIC PHENOTYPES IN MATERNAL OBESITY THAT CONTRIBUTE TO HIGHER BIRTHWEIGHT

Stacey M. Horwitz¹, Jerad Dumolt², Anita Kramer², Kathryn Erikson², Theresa L. Powell^{2,3}

¹MD candidate in the University of Colorado School of Medicine, ²Department of Obstetrics and Gynecology and ³Department of Pediatrics, University of Colorado, Anschutz Medical Campus

Context

Mothers that give birth to large for gestational age (LGA) babies have significant birth-related traumas. These LGA neonates also have a greater long-term risk for developing metabolic and neurological diseases. Most obese mothers give birth to appropriate for gestational age (AGA) babies, while 10-15% give birth to LGA infants. Currently, the mechanisms that drive fetal overgrowth in some obese mothers are unknown.

Objective

This study examines maternal, placental, and fetal factors that have associations with neonatal overgrowth in obese pregnant women.

Methods

Maternal and umbilical cord plasma and placentas were collected from obese women that delivered AGA (n=21) or LGA (n=30) infants. Using ELISA, concentrations of insulin, leptin and adiponectin were determined in maternal venous and umbilical cord plasma. A colorimetric assay measured total maternal triglycerides. Multiplex sandwich assay was used to test additional markers, including glucagon-like peptide-1 (GLP-1). GLP-1R protein expression was examined in syncytiotrophoblast microvillous membrane (MVM) and basal membrane (BM).

Results

There were no significant differences between cohorts for maternal insulin, leptin, adiponectin, C-peptide, interleukin-6, tumor necrosis factor α , and glucose. Maternal plasma triglyceride levels were higher in LGA males than AGA males. Insulin and C-peptide levels in umbilical cord plasma were higher in LGA infants. Maternal adiponectin levels trended higher in LGA, while leptin trended lower for LGA males (versus AGA males). GLP-1 levels are significantly higher in both maternal and cord plasma in pregnancies with LGA babies compared to AGA. GLP-1 levels also demonstrated a positive correlation with birthweight. GLP-1R was identified in the syncytiotrophoblast microvillous membrane (MVM) by immunoblot and by immunohistochemistry.

Conclusion

This study identified increased maternal and fetal GLP-1 as a strong correlate for excessive fetal growth in pregnancies complicated by maternal obesity. The GLP-1R has been localized on the syncytiotrophoblast MVM. This data suggests that maternal GLP-1 modulates placenta function to increase fetal growth. Higher fetal insulin in the LGA cord plasma leads us to speculate that high fetal GLP-1 contributes to insulin resistance, however, the mechanism is still unknown.