Metabolic Phenotypes in Maternal Obesity that Contribute to Higher Birthweight

Stacee Horwitz,1 Jerad Dumolt,2 Anita Kramer,2 Kathryn Erikson,2 Theresa L. Powell 2,3

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

BACKGROUND

Pregnancies complicated by maternal obesity result in 10-15% babies to be born large for gestational age (LGA) 1. These infants have significant birth related traumas, and a higher long-term risk for developing metabolic and neurological diseases2. However, most obese mothers give birth to appropriate for gestational age babies (AGA). Currently, the mechanisms that lead to accelerated fetal growth remain unclear1.

In the obese pregnant population, it has been reported that levels of insulin, leptin and inflammatory cytokines are increased, and adiponectin is decreased, compared to normal body mass index (BMI) population1. These factors influence maternal metabolism, but their role in modulating the growth of the fetus in obese mothers is not clear.

We hypothesize that metabolic hormones and inflammatory cytokines contribute to accelerated fetal growth in obese mothers resulting in LGA neonates.

RESULTS

Maternal Plasma:

• Triglyceride levels were higher in LGA males than AGA males (Figure 1).
• Maternal GLP-1 levels were higher in LGA pregnancies compared to AGA births (p<0.05). GLP-1 levels also positively correlated to higher birthweights in both cohorts (Figure 2).
• No significant differences in LGA and AGA pregnancies for concentrations of insulin, leptin, adiponectin, IL-6, TNF-α, PIGF, VEGF-A, VEGF-D, or FLT3L.

Umbilical Cord Plasma:

• Insulin levels were insignificantly increased in LGA infants compared to AGA (p>0.05) (Figure 3).
• GLP-1 levels were higher in LGA compared to AGA neonates.

Placenta:

• Localization of GLP-1R in the syncytiotrophoblast microvillous membrane (MVM) (Figure 4).

CONCLUSIONS

We identified, for the first time, increased maternal plasma GLP-1 as a strong correlate with accelerated fetal growth in pregnancies complicated by maternal obesity (Figure 2). We also localized the GLP-1 receptor to the syncytiotrophoblast MVM with immunohistochemistry (IHC) (Figure 4). This data suggests that maternal GLP-1 levels influence placenta function to increase nutrient flux to the fetus, accelerating fetal growth.

We speculate that higher fetal insulin in the LGA cord blood (Figure 3) may be related to higher fetal GLP-1 levels which contributes to fetal insulin resistance; however, the exact mechanism remains unknown.

ACKNOWLEDGEMENTS

I would like to thank Dr. Powell for being an incredible mentor, who made this project possible.

Thank you to Jerad Dumolt for further investigating so much of these findings.

Thank you to Anita Kramer and Kathryn Erickson for both providing so much guidance in the lab.

REFERENCES