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Maternal and neonatal metabolomic profile in pregnancies following bariatric surgery

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Objective

Pregnancy following bariatric surgery is associated with a reduction in large for gestational age neonates, gestational diabetes but also an increased risk of small for gestational age neonates and shorter gestation. We've used a multi-omic approach to investigate the maternal and neonatal metabolic and gut microbial profiles of pregnancies following bariatric surgery compared to those without surgery.

Methods

This was a prospective observational study. Pregnant women were seen at 11-14 (T1), 20-24 (T2), 28-30 (T3), 30-32 (T4), 35-37 (T5) weeks gestation and delivery. At each visit, maternal characteristics, BMI and BP were recorded, maternal blood (insulin resistance was calculated at T3), urine and stool samples were obtained and fetal growth scans were performed. At delivery, birthweight was recorded and neonatal cord blood and urine were obtained. Global metabolic profiles (maternal and neonatal) were acquired by 1H NMR and data were modelled using orthogonal partial least squares discriminant analysis (OPLS-DA). Metabolites whose concentration was significantly increased in a study group were identified. DNA was extracted from maternal faecal samples and 16S rRNA gene sequencing was performed to identify bacterial taxa whose relative abundance was increased in malabsorptive patients. Relationships between discriminatory metabolites and microbes as well as relationships between metabolites/microbes and clinical data were assessed by Spearman correlation analysis.

Results

The study included 118 pregnant women without surgery and 47 women with previous bariatric surgery (21 with a restrictive and 26 with a previous malabsorptive procedure). Compared to the no-surgery group, pregnant women with previous malabsorptive procedure were characterised by lower concentrations of proteinogenic branched-chain amino acids, a decrease in products of valine degradation, and an increase in excreted urinary microbial co-metabolites; metabolites phenylacetylglutamine (PAG), p-cresol sulfate (PCS), indoxyl sulfate (IS), p-hydroxyphenylacetate (PHPA), produced by protein putrefaction in the gut, remained significantly elevated ($p < 0.05$) throughout pregnancy. This corresponded to a shift in maternal gut microbial community structure toward facultative anaerobes, with a particular increase in the genera Escherichia ($p < 0.05$), Streptococcus ($p < 0.05$), and Enterococcus ($p < 0.01$). Urinary PAG and PCS concentrations negatively correlated with maternal fasting insulin (T3; PAG: $\rho = -0.46$, $p = 0.0004$ and PCS: $\rho = -0.42$, $p = 0.0013$). Estimated fetal weight negatively correlated with PAG (T2; $\rho = -0.31$, $p = 0.02$), PCS (T2; $\rho = -0.29$, $p = 0.03$), and IS (T5; $\rho = -0.32$, $p = 0.02$). PAG and IS concentrations at delivery also negatively correlated with birthweight (PAG: $\rho = -0.36$, $p = 0.02$ and IS: $\rho = -0.4$, $p = 0.01$). There was no difference in the metabolic profile of cord blood serum, but the neonatal urinary PAG concentrations were higher in those born from malabsorptive mothers compared to those born from women without surgery ($p < 0.05$).

Conclusion

Malabsorptive bariatric surgery results in a significant change in the maternal metabolic phenotype; the altered gut microbiota results in a change in microbial metabolism which may be linked to improved insulin sensitivity, seen in this population and have a transgenerational effect to the neonate.