ORIGINAL ARTICLES

Maternal short-chain fatty acids are associated with metabolic parameters in mothers and newborns

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During the course of pregnancy, dynamic remodeling of the gut microbiota occurs and contributes to maternal metabolic changes through an undefined mechanism. Because short chain fatty acids (SCFAs) are a major product of gut microbiome fermentation, we investigated whether serum SCFA levels during pregnancy are related to key metabolic parameters in mothers and newborns. In this prospective study, 20 pregnant women without gestational diabetes were evaluated at 36–38 weeks of gestation, and their newborns were assessed after parturition. In this cohort, which included normal (n = 10) and obese (n = 10) subjects based on prepregnancy body mass index, serum levels of SCFAs (acetate, propionate, and butyrate), maternal adipokines, maternal glucose, and C-peptide were measured at 36–38 weeks of gestation. Maternal weight gain and newborn anthropometrics were also determined. Data were analyzed using linear regression to test for associations, adjusting for prepregnancy obesity. In this cohort, serum acetate levels were associated with maternal weight gain and maternal adiponectin levels. In addition, serum propionate correlated negatively with maternal leptin levels, newborn length, and body weight. Taken together, this study observed that novel relationships exist among maternal SCFA levels and multiple interrelated maternal/newborn metabolic parameters. (Translational Research 2014;164:153–157)

Abbreviations: BMI = body mass index; SCFA = short-chain fatty acid

Pregnancy is a dynamic metabolic state that must allocate nutritional resources between mother and fetus. These metabolic changes include alteration in insulin sensitivity and secretion, along with fatty acid mobilization from the adipose depots. Each of these changes occurs dynamically throughout pregnancy to meet the changing nutritional demands of mother and fetus. For example, increased insulin

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AT A GLANCE COMMENTARY

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Background

The gut microbiome was recently identified as a novel factor involved in metabolic changes during pregnancy.

Translational Significance

As a result of this finding, our study investigated this relationship by studying one of the key factors the gut microbiome generates—short-chain fatty acids—and how they may be related to metabolic parameters in mothers and newborns.

secretion occurs during early pregnancy, initially in the setting of unchanged insulin sensitivity.[1] During mid pregnancy, insulin resistance increases, and insulin secretion increases to match this change.[1] Along with changes in insulin sensitivity/secretion, maternal adiposity stores increase during early pregnancy, whereas in mid to late pregnancy, adipose depots are diminished.[1] Playing a role in these metabolic changes, adipocyte-specific hormones, called "adipokines" (ie, adiponectin and leptin) have been identified for their role in metabolic response during pregnancy because they contribute to the regulation of satiety, adiposity, and insulin resistance.[2] More importantly, the metabolic health of the mother has important implications for the health of the infant. For example, it is well established that maternal obesity is a factor in newborn birth weight that, consequently, has lasting metabolic effects throughout the life of the infant.[3]

Although much is known about metabolism during pregnancy, an intriguing new factor, the gut microbiome, has been identified for its role in contributing to metabolic changes throughout pregnancy.[4] In their report, Koren et al[4] show that major changes occur throughout pregnancy to the gut microbiota. In particular, they suggest that, during the first trimester, the gut microbiome is most similar to that observed in nonpregnant healthy women; however, the third trimester leads to a large degree of gut microbiota dysbiosis, similar to what occurs in metabolic syndromes such as type 2 diabetes.[4] The authors also show these changes contribute to metabolic aberrations, as demonstrated by transfer of human microbiota from either the first-or third-trimester mothers to germ-free mice.[4] However, the factor mediating the gut microbiome effect is unclear.[4] One possible explanation involves the role of gut bacteria in food fermentation.[5] Multiple metabolites are produced during this process, and one of the major products includes short-chain fatty acids (SCFAs).[6]

Considering the recently described relationship between the gut microbiome and the metabolic response during pregnancy, we sought to explore whether a relationship exists between serum SCFA levels during pregnancy and well-described metabolic factors during pregnancy (ie, prepregnancy obesity, maternal weight gain, glucose and select metabolic hormones such as C-peptide, leptin, and adiponectin). Because maternal health strongly impacts newborn outcomes, we also examined how serum SCFAs are related to newborn anthropometrics. Overall, this is the first study to examine whether a relationship exists between serum SCFAs and well-described metabolic measures in pregnancy and newborn outcomes.

METHODS

Subjects. The subjects included in this study were selected from a cohort reported previously.[7] Each of the selected women delivered at The Prentice Women's Hospital of Northwestern Memorial Hospital. Prepregnancy body mass index (BMI) was based on self-reported height and weight, and was confirmed by chart review. From this cohort, 10 obese subjects (prepregnancy BMI, >30 kg/m^2) and 10 normal-weight subjects (prepregnancy BMI, 18–25 kg/m^2), were matched by maternal age and gestation length. Inclusion criteria for this study included singleton-only pregnancy, term pregnancies, and normal blood pressure. Other eligibility criteria were serum glucose level less than 130 mg/dL during their routine 50-g oral glucose challenge test for gestational diabetes screening. Participants provided self-reported race and ethnicity, which was then categorized as African-American/black, white, Hispanic, or Asian. All subjects provided written informed consent, and the study was approved by the Northwestern University Institutional Review Board for conduct of research on human subjects.

Biochemical measures. During the course of the study, maternal blood was collected between 36 weeks and 38 weeks of gestation. All blood was stored at -70°C until assayed. Plasma glucose was measured with Synchron CX Delta Systems instrumentation (Beckman Coulter, Inc., Brea, Calif) using an oxygen rate method with a glucose oxygen electrode, and had an interassay coefficient of variation of 2.0%–2.3%. Maternal triglycerides were measured with the Triglycerides GPO reagent using the Beckman Coulter Unicel DXC800 analyzer (Beckman Coulter). Concentrations of C-peptide, leptin, and adiponectin were assayed using radioimmunoassay kits from Millipore Corporation