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Maternal Gut Microbiome Composition and Gestational Weight Gain in African American Women

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Purpose:

It is estimated that the human intestinal tract harbors 100 trillion bacteria, referred to as the gut microbiota. The specific microbiota colonizing the gut vary among individuals, with some patterns more and others less associated with obesity, a phenomenon believed in part due to some microbes over-harvesting and storing energy compared to others (Aitken & Gewirtz, 2013; Backhed, 2011; Cox & Blaser, 2013). The ratio of two major phyla of bacteria, involving approximately 95% of gut microbes, *Bacteroidetes* (Gram negative) and *Firmicutes* (Gram positive), has been found to be relevant in studies of the gut microbiome that include participants of varying weight categories. The gut microbiome, comprised of bacteria, viruses, archaea, fungi and their genes, has been linked to body weight in non-pregnant populations but there is a dearth of research of the maternal gut microbiome across pregnancy, especially examined by maternal weight (Ursell, Metcalf, Parfrey, & Knight, 2012). Nearly 80% of African American (AA) women of childbearing age report themselves to be overweight or obese, by far the highest of all races (Headen, Davis, Mujahid, & Abrams, 2012). Since the strongest predictor of excessive gestational weight gain (GWG) is prepregnant body mass index (BMI), and 68% of AA women gain excessively, other contributors to racial differences in pre-pregnant weight and inappropriate GWG are now being examined (Bowers et al., 2013; Headen et al., 2012). AA women have been under-represented in human microbiome studies so little is known about the intra-racial differences in the gut microbiome in this population most likely to experience poor birth outcomes and unhealthy GWG (Graham, Mullen, & Whelan, 2015). Maternal prepregnant weight and GWG is closely associated with many obstetric complications, birth weight, postpartum weight retention and risks for the mother and infant to suffer chronic diseases, including obesity, later in life (Cohen & Koski, 2013). The purpose of this study, *The Brain-Gut Axis and Its Influence on Gestational Weight Gain*, is to describe the composition of the gut microbiome across pregnancy in 27 healthy AA women by BMI category delivering term, singleton infants.

Methods:

The study includes a subset of women participating in a larger 5-year parent study, *Biobehavioral Determinants of the Microbiome and Preterm Birth in Black Women*, which prospectively enrolled a socioeconomically-diverse cohort of pregnant AA women at 8-14 weeks gestation and followed them through delivery with data collected via surveys, blood tests, and oral, vaginal, and gut microbiome samples at enrollment and at 24-30 weeks (Corwin et al., 2017). For this sub-study an additional third prenatal patient encounter visit with data collection was added for a subset of 27 women who consented to participate during the period of February 2015 and November 2015. This visit occurred between 35-40 weeks' gestation and involved a third rectal swab to determine late pregnancy gut microbiome and completion of some of the questionnaires on stress, mood, and diet and add data on activity. Chart review after delivery identified additional clinical outcomes. DNA was extracted and sequencing of the V3 and V4 regions of the 16S rRNA gene was determined at each time point. Processing and mapping were completed with QIIME and OTUs were mapped to Greengenes version 13_8. The ratio of *Firmicutes* to *Bacteroidetes* (FTB), a frequently reported indicator of general gut health and weight, was also determined at each time point. Finally, a log 10 transformation of the *Firmicutes* to *Bacteroidetes* ratio was used for the analyses.

Results:

In order to accomplish the primary aim of this sub-study, the relationship between the maternal gut microbiome composition, in this case represented by FTB ratio, and interval and total gestational weight gain was examined. The mean age of the women in this study was 25.2 years; most were publically insured (77.8%); had at least attended some college (55.5%); and were single (85.2%). Of the women who were single, 77.7% were in a relationship, yet varied in whether they lived with their partner (44.4%) or they lived separately (33.3%). While the percent of overweight (11.1%) and obese (44.4%) participants at baseline combined to be the majority of the group, this was lower than the national rate of overweight and obese childbearing-age AA women, which is nearly 80%. Total weight gain over the entire pregnancy was more often either less than recommended (33.3%) or more than recommended (40.7%), a pattern consistent with other studies of gestational weight gain in AA women. Also consistent with the literature, the largest percentage of subjects combined in all BMI categories gained excessively (40.1%) and the next largest group gained inadequately (33.3%). When divided by BMI category, almost half of the combined overweight and obese gained excessively (46.6%) yet an additional percentage gained inadequately (33%).

The study analyses did not indicate any significant relationships existed among the initial BMI or weight or the category of total weight gain of the mother and the change in the FTB ratio during the pregnancy. The associations that were discovered were in the patterns of the ratio of FTB over time. A one-way between-groups analysis of variance was conducted examining the relationship of categories of weight gain at the *midpoint of pregnancy* (20-25 weeks gestation) and the change in FTB ratio during the pregnancy. The participants were categorized as those who by the midpoint had inadequate, adequate, or excessive weight gain according to the recommendations by initial BMI. The category of weight gain at the midpoint was found to be significantly associated at the $p < .05$ level in the change in FTB ratio from the first to the third time points in pregnancy ($f = 3.48$, $p = .05$). The large effect size was calculated using eta squared and equaled .22. Post-hoc comparisons using the Tukey HSD test indicated the mean FTB ratio for inadequate gainers ($M = 1.28$, $SD = 3.27$) was significantly different from the excessive gainers ($M = -17.60$, $SD = 32.68$). The adequate gainers did not differ significantly from either other group. The difference in the change in ratio of FTB also showed a correlation with the ratio at the first time point ($r = -2.71$, $p = .03$), suggesting that the greater the FTB ratio at the start of pregnancy, the greater the decline in the FTB ratio over the pregnancy. This finding supports previous research that *Bacteriodetes* is elevated and rises as overweight and obese women gain weight during pregnancy and that overall diversity in gut microbiome composition declines during pregnancy (Gronlund, Grzeskowiak, Isolauri, & Salminen, 2011; Mokkala et al., 2016). Clinically, it is known that the woman's health prior to and in early pregnancy are important considerations in determining her risk for adverse obstetrical outcomes. These study outcomes reinforce that the initial gut composition and the *weight gain by mid-pregnancy* are significant in the change in gut composition, as well.

Conclusion:

The degree to which the gut microbiome contributes to the overall health of the pregnant woman and her fetus is only now beginning to be measured. Given the potential to alter the gut microbiome with dietary and other lifestyle changes, a better understanding of its contribution to a healthy pregnancy and gestational weight gain is essential, especially considering the global epidemic of obesity. The conclusions of this study may suggest the distinct gestational weight gain patterns (highest inadequate and high rates of excessive when compared to other races) and specific obstetric risks more prevalent in AA women could be related to the intra-racial differences in the gut microbiome that promote weight-related complications more than energy harvest in this and perhaps other similar populations. Obstetric risks may be modifiable if weight gain patterns are normalized to ensure recommended rates by mid-pregnancy and at term, particularly for women entering pregnancy overweight or obese and harboring an unhealthy or "dysbiotic" gut microbiome. Health practices and novel therapies to promote a healthy gut microbiome composition are still to be discovered but will likely prove fundamental in the care of pregnant women throughout the world. This study will advance the science in this poorly understood area of the maternal gut microbiome and gestational weight gain, with particular significance for at-risk AA and perhaps other minority women and their infants.

Title:
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Keywords:
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Abstract Summary:
Nearly 80% of African American (AA) women of childbearing age report themselves to be overweight or obese. While the strongest predictor of excessive gestational weight gain is prepregnant weight, other

contributors to racial differences in weight gain, such as gut microbiome composition, are now being examined.

Content Outline:

I. Introduction

A. The gut microbiome, comprised of bacteria, viruses, archaea, fungi and their genes, has been linked to body weight in non-pregnant populations but there is a dearth of research of the maternal gut microbiome across pregnancy, especially examined by maternal weight.

B. Nearly 80% of African American (AA) women of childbearing age report themselves to be overweight or obese, by far the highest of all races. Since the strongest predictor of excessive gestational weight gain (GWG) is prepregnant body mass index (BMI), and 68% of AA women gain excessively, other contributors to racial differences in pre-pregnant weight and inappropriate GWG, such as gut microbiome composition, are now being examined

II. Body

A. This study describes the composition of the gut microbiome across pregnancy in 27 healthy AA women by BMI category delivering term, singleton infants.

1. This is a sub-study of a larger study which enrolled a socioeconomically-diverse cohort of pregnant AA women at 8-14 weeks gestation and followed them through delivery with data collected via surveys, blood tests, and oral, vaginal, and gut microbiome samples at enrollment and at 24-30 weeks
2. For this sub-study an additional third prenatal patient encounter visit with data collection was added for a subset of 27 women who consented to participate during the period of February 2015 and November 2015. This visit occurred between 35-40 weeks' gestation and involved a 3rd rectal swab to determine late pregnancy gut microbiome and to repeat completion of some of the questionnaires. The ratio of *Firmicutes* to *Bacteroidetes* (FTB), a frequently reported indicator of general gut health and weight, was also determined at each time point.

B. One of the primary aims of this sub-study was to describe the relationship between the maternal gut microbiome composition, in this case represented by FTB ratio, and interval and total gestational weight gain in AA women.

1. The study findings did not indicate any significant relationships exist among the initial BMI or weight or the category of total weight gain of the mother and the change in the FTB ratio during the pregnancy.
2. The associations that were discovered were in the patterns of the ratio of FTB over time. The category of weight gain at the midpoint was found to be significantly associated at the $p < .05$ level in the change in FTB ratio from the first to the third time points in pregnancy.

C. The difference in the change in ratio of FTB also showed a correlation with the ratio at the first time point ($r = -2.71$, $p = .03$), suggesting that the greater the FTB ratio at the start of pregnancy, the greater the decline in the FTB ratio over the pregnancy.

1. This finding supports previous research that Bacteriodetes is elevated and rises as overweight and obese women gain weight during pregnancy and that overall diversity in gut microbiome composition declines during pregnancy.

2. These study outcomes reinforce that the initial gut composition and the weight gain by mid-pregnancy are significant in the change in gut composition, as well.

III. Conclusion

Given the potential to alter the gut microbiome with dietary and other lifestyle changes, a better understanding of its contribution to a healthy pregnancy and gestational weight gain is essential, especially considering the global epidemic of obesity.

A. The conclusions of this study may suggest the distinct gestational weight gain patterns and specific obstetric risks more prevalent in AA women could be related to the intra-racial differences in the gut microbiome that promote weight-related complications more than energy harvest in this and perhaps other similar populations.

B. Obstetric risks may be modifiable if weight gain patterns are normalized to ensure recommended rates by mid-pregnancy and at term, particularly for women entering pregnancy overweight or obese and harboring an unhealthy or “dysbiotic” gut microbiome.

C. This study will advance the science in this poorly understood area of the maternal gut microbiome and gestational weight gain, with particular significance for at-risk African American and perhaps other minority women and their infants.

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