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Full Length Article

The association of maternal obesity and race with serum adipokines in pregnancy and postpartum: Implications for gestational weight gain and infant birth weight

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ABSTRACT

Adiponectin and leptin are hormones known to play roles in maternal metabolism during pregnancy. Levels of these hormones have been demonstrated to vary based on adiposity and race. However, there is a lack of data concerning the relationship between race and the change of adiponectin and leptin throughout pregnancy. The purpose of this study was to examine serum levels of adiponectin, leptin, and leptin-to-adiponectin ratio (LAR) throughout pregnancy and to assess their association with gestational weight gain (GWG) and infant birth weight while considering the effects of race and pre-pregnancy body mass index (BMI). Serum levels of adiponectin, leptin, gestational weight gain, and infant birth weight were measured in 80 pregnant women at early (12.4 ± 1.3 weeks gestation), mid (20.6 ± 1.3 weeks gestation), late pregnancy (29.2 ± 1.4 weeks gestation), and 7–11 weeks postpartum (8.8 ± 0.8 weeks). In women overall, serum adiponectin decreased across pregnancy and increased at postpartum ($p = 0.17$.) At each prenatal timepoint, both black race and obesity were associated with lower adiponectin ($ps < 0.05$). In women overall, serum leptin increased across pregnancy, and declined at postpartum. At every assessment, a stepwise increase in leptin was observed in relation to BMI class. Black women with obesity had markedly higher LAR in mid- and late pregnancy and postpartum than all other groups ($p < 0.05$). Serum leptin during pregnancy was significantly associated with total GWG in both black and white women ($ps < 0.005$). Neither adiponectin, leptin, nor LAR were associated with infant birth weight. Race and BMI both have significant effects on serum adiponectin, leptin, and LAR levels in pregnancy and postpartum. Notably, the combined effects of race and BMI result in markedly higher LAR among black women with obesity. Implications for racial disparities in metabolic syndrome and postpartum weight retention remain to be explicated.

1. Introduction

Adiponectin is a hormone that directly affects vascular function and modulates several metabolic processes, including glucose regulation and fatty acid oxidation. It is secreted from adipose tissues, as well as from the placenta during pregnancy. Plasma levels of adiponectin are inversely correlated with body fat mass in adults and increase in response to weight reduction (Coppola et al., 2009; Mazaki-Tovi et al., 2007). While highly abundant in plasma compared to many other hormones, adiponectin levels in healthy women decrease by approximately 25% from the 1st to the 3rd trimester of pregnancy (Paradisi et al., 2010). Reflecting vascular and metabolic effects of this hormone, adiponectin levels are inversely associated with insulin resistance, triglycerides, and blood pressure as well as cardiovascular morbidity and mortality, although the latter data are inconsistent (Im et al., 2006; Yamamoto et al., 2002; Kadowaki et al., 2006; Pischon et al., 2004; Kumada et al., 2003; Frystyk et al., 2007; Rajpathak et al., 2011; Matsumoto et al., 2008; Wannamethee et al., 2011; Lawlor et al., 2005; Gardener et al., 2012). Of note, the predictive value of adiponectin for cardiovascular disease is found even in normal weight adults, indicating the clinical value of this marker even in the absence of an obese state (Gardener et al., 2012).

In addition, in the context of pregnancy, the adipokine leptin plays a

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particularly important role in the regulation of maternal energy and metabolism. Serum leptin levels are positively correlated with body fat and BMI in non-pregnant (Considine et al., 1996) as well as pregnant adults (Misra et al., 1064; Highman et al., 1998). Serum leptin concentrations nearly double during the course of normal pregnancy, with a steeper trajectory observed among women with normal weight than those with overweight or obesity (Misra and Trudeau, 2011). These increases are believed to be related to the mobilization of maternal fat stores to support fetal growth (Hauguel-de Mouzon et al., 2006).

Adiponectin and leptin regulation is of unique clinical relevance during pregnancy. Lower adiponectin levels have been associated with increased risk of gestational diabetes (Mazaki-Tovi et al., 2005; Williams et al., 2004; Worda et al., 2004; Hedderson et al., 2013; Jenkins et al., 2007). In addition, higher leptin concentrations have been observed in preeclamptic women versus healthy controls at the time of admission for labor (Jenkins et al., 2007; Hendler et al., 2005). These markers also have implications for offspring growth. In a study of 588 mother-child dyads, higher cord blood leptin levels predicted lower BMI and higher leptin in offspring at 3 years of age after controlling for pre-pregnancy BMI, gestational weight gain (GWG) and other relevant factors (Mantzoros et al., 2009). In contrast, higher cord blood adiponectin predicted higher subscapular/triceps skinfold thickness ratio at 3 years, again after controlling for relevant covariates (Mantzoros et al., 2009). Further the ratio of leptin to adiponectin has been shown to be an indicator of insulin resistance (Inoue et al., 2005; Skvarca et al., 2013), is associated with increased obesity (López-Jaramillo et al., 2014; Zhang et al., 2017), and is useful in risk stratification of people with metabolic syndrome (Gauthier et al., 2012).

Importantly, racial differences have been found in both adiponectin and leptin levels. Lower levels of adiponectin have been observed in black versus white adults of both sexes after controlling for obesity status (Gardener et al., 2012; Degawa-Yamauchi et al., 2003). Data have also shown heightened leptin levels in black women compared to white women (Ruhl et al., 2004; Cohen et al., 2012). In addition, some evidence suggests that the association of adiponectin with adverse health outcomes is stronger among blacks versus whites (Nguyen et al., 2008). However, data are lacking about potential interactions between race and body composition in the trajectory of change in adiponectin and leptin across the course of pregnancy. If present, such racial differences may have relevance to the marked racial disparities in adverse perinatal health outcomes such as gestational diabetes, preeclampsia, and low birth weight (Hamilton et al., 2013; Getahun et al., 2008; Lisonkova and Joseph, 2013).

The current study examined changes in serum levels of adiponectin, leptin, and the LAR across pregnancy and into postpartum in relation to maternal race and body mass index (BMI). The association of these markers with total GWG across pregnancy and infant birth weight was determined. Potential interactions for these two outcomes were also examined.

2. Methods

2.1. Study design

This study included 84 pregnant women who were recruited from the Ohio State University Medical Center (OSUMC) Prenatal Clinic. Study visits were conducted during early (Mean = 12.4 ± 1.6 weeks gestation), mid (Mean = 20.6 ± 1.3 weeks gestation), and late (Mean = 29.2 ± 1.4 weeks gestation) pregnancy, as well as 7–11 weeks postpartum (Mean = 8.8 ± 0.8 weeks). At each visit, women provided a blood sample. Two women were excluded due to having only one time point with adiponectin and leptin data, and two women were excluded as outliers for weight change (losses of 49 and 14 pounds), resulting in a final sample size of 80.

2.2. Participants

All women were born and raised in the United States. Women were not eligible if they had current hypertension, diabetes, chronic conditions with implications for immune function (e.g., rheumatoid arthritis, multiple sclerosis, or human immunodeficiency virus), fetal anomaly, illicit drug use or more than two alcoholic drinks per week during pregnancy (per self-report or medical record). Women reporting acute illness (e.g., cold or flu-like symptoms) or antibiotic use within 10 days of a study visit were rescheduled. Each participant completed informed consent and received modest compensation. Prior to beginning the study approval was obtained from the Ohio State University Biomedical Institutional Review Board.

2.2.1. Demographics

Age, race/ethnicity, marital status, education level, annual household income, and number of prior pregnancies (parity) were collected by self-report.

2.2.2. Health parameters

Pre-pregnancy body mass index (BMI; kg/m^2) was calculated using self-reported pre-pregnancy weight and height collected at the first visit. Total GWG and infant birth weight were determined via medical record review after delivery.

2.3. Adiponectin and leptin assays

Serum levels of adiponectin were measured by diluting samples 1:1000 and assaying in duplicate using human adiponectin kits from Meso Scale Discovery (1601 Research Blvd. Rockville, MD). Serum levels of leptin were assayed in duplicate using human leptin kits also from MSD. Plates were read by a MSD Sector Imager 2400 measuring electrochemiluminescence. The lower limits of detection were 64 ng/mL for adiponectin and 137 pg/mL for leptin. Inter- and intra-assay coefficients of variation (CV) for adiponectin were 6.02% and 6.75%, respectively. For leptin, the inter- and intra-assay CVs were 5.79% and 2.76% respectively.

2.4. Statistical analysis

Women were categorized based pre-pregnancy BMI using the following standard ranges: 18.5–24.9 = normal weight, 25–29.9 = overweight, and ≥30 = obese. To evaluate demographic similarity between groups, participant characteristics were compared between groups utilizing either a two-tailed student T test for continuous variables with two groups, an ANOVA omnibus for continuous variables with more than two groups (with Tukey HSD post-hoc tests for paired compairsons), or an extended exact Fisher omnibus for percentages with more than two groups (with Fisher exact tests for paired comparisons). The primary endpoints were serum levels of adiponectin and leptin at three visits during pregnancy as well as once during postpartum. Each endpoint was log transformed for analysis to meet normality assumptions. A linear mixed model was fit to each endpoint across the four visits. The model included main effects for race, BMI group, and study visit, all two-way interactions between BMI group, race, and study visit as well as the three-way interaction between these factors, and a random subject effect to account for correlation among measures from the same subject. Analysis of variance tables were subsequently calculated for each model to determine the significance of main effects and interactions. Least squared means were calculated to determine significant differences between pairwise comparisons of interest. For the outcomes of GWG and infant birth weight, linear models were fit separately for black and white women at each timepoint with adiponectin, leptin, or leptin/adiponectin ratio (LAR) as a main effect and controlling for pre-pregnancy BMI. For models focused on infant birth weight, low birth weights <2500g were excluded from

analysis (n = 5), as these may be indicative of pathological states (such as intrauterine growth restriction), and gestational age at delivery was included as a control variable. All comparisons were performed at α = 0.05 significance level. Analyses and figures were conducted and prepared using R 3.5.3 (Team RDC) and the following packages: nlme, lme4 (Bates et al., 2015), lsmeans (Lenth, 2016), and ggplot2 (Wickham, 2016).

3. Results

3.1. Demographics

In the overall sample, the average age was 25.6 (SD = 4.3; range: 18–33), 48% (n = 38) were black, 43% (n = 34) were married, and 30% (n = 24) reported an income under $15,000. Participant characteristics for each BMI and race group are reported in Table 1 and Table 2, respectively. As shown, there were no significantly differences in age, race, parity, marital status, income, education or smoking history (*ps* > 0.09) between either BMI classifications or between black and white women. There was a notable different in GWG across BMI ($p = 2.15*10^{-3}$) with obese women having significantly less GWG versus normal (p = 0.0026) and overweight (p = 0.012) BMI women, but no difference in infant BW across BMI (p = 0.704) (Table 3). In addition, black versus white women did not differ in total GWG (p = 0.32) or infant birth weight (p = 0.217) (Table 4).

Table 1
Maternal Demographics by BMI classification.

	Overall (n = 80)	Normal BMI (n = 36)	OW BMI (n = 25)	Obese BMI (n = 19)	*p*
Age [Mean (SD)]	25.6 (4.3)	25.4 (4.0)	25.0 (4.9)	26.6 (3.7)	0.42
Race/Ethnicity [n (%)]					0.279
African American	38 (48%)	16 (44%)	15 (60%)	7 (37%)	
European American	41 (51%)	18 (50%)	10 (40%)	11 (58%)	
Hispanic	1 (1%)	0 (0%)	0 (0%)	1 (5%)	
Primigravida [n (%)]	20 (25%)	13 (36%)	4 (16%)	3 (16%)	0.135
Household Income [n (%)]					0.38
<$15,000	24 (30%)	10 (28%)	9 (36%)	5 (26%)	
$15,000-$29,999	24 (30%)	10 (28%)	5 (20%)	9 (47%)	
$30,000 or above	32 (40%)	16 (44%)	11 (44%)	5 (26%)	
Marital Status [n (%)]					0.783
Married	34 (43%)	16 (44%)	9 (36%)	9 (47%)	
Unmarried	36 (45%)	17 (47%)	12 (48%)	7 (37%)	
Single	10 (13%)	3 (8%)	4 (16%)	3 (16%)	
Educational Attainment [n (%)]					0.128
Some Secondary School	7 (9%)	4 (11%)	2 (8%)	1 (5%)	
High School Graduate	16 (20%)	7 (19%)	3 (12%)	6 (32%)	
Some College	29 (36%)	8 (22%)	14 (56%)	7 (37%)	
College Graduate	28 (35%)	17 (47%)	6 (24%)	5 (26%)	
Smoking Status [n (%)]					0.838
Current Smoker	9 (11%)	5 (14%)	2 (8%)	2 (11%)	
Former Smoker	20 (25%)	7 (19%)	8 (32%)	5 (26%)	
Never Smoked	51 (64%)	24 (67%)	15 (60%)	12 (63%)	

3.2. Correlations among key variables

Adiponectin was negatively correlated with leptin at each of the three visits during pregnancy (rs < −0.23, ps < 0.04); this relationship was not significant at postpartum (r = −0.17, p = 0.17). Pre-pregnancy BMI was negatively correlated with adiponectin levels in early pregnancy, mid-pregnancy, and late pregnancy (rs < −0.28, ps < 0.01), but not post-partum (r = −0.22, p = 0.07). Pre-pregnancy BMI was positively

Table 2
Maternal demographics by race.

	Overall (n = 79)[a]	White (n = 41)	Black (n = 38)	*p*
Age [Mean (SD)]	25.6 (4.3)	25.6 (4.8)	25.4 (3.7)	0.824
BMI [Mean (SD)]	26.8 (5.7)	27.1 (6.1)	26.5 (5.4)	0.638
Primigravida [n (%)]	20 (25%)	13 (32%)	7 (18%)	0.204
Household Income [n (%)]				0.091
<$15,000	24 (30%)	9 (22%)	15 (39%)	
$15,000-$29,999	24 (30%)	16 (39%)	7 (18%)	
$30,000 or above	32 (40%)	16 (39%)	16 (42%)	
Marital Status [n (%)]				0.136
Married	33 (42%)	21 (51%)	12 (32%)	
Unmarried	36 (45%)	17 (41%)	19 (50%)	
Single	10 (13%)	3 (7%)	7 (18%)	
Educational Attainment [n (%)]				0.82
Some Secondary School	7 (9%)	4 (10%)	3 (8%)	
High School Graduate	15 (19%)	8 (20%)	7 (18%)	
Some College	29 (36%)	13 (32%)	16 (42%)	
College Graduate	28 (35%)	16 (39%)	12 (32%)	
Smoking Status [n (%)]				0.945
Current Smoker	9 (11%)	5 (12%)	4 (11%)	
Former Smoker	20 (25%)	11 (27%)	9 (24%)	
Never Smoked	50 (63%)	25 (61%)	25 (66%)	

[a] One participant identified as hispanic and was excluded from analysis by race.

Table 3
Gestational Weight Gain and Infant Birth Weight by maternal BMI.

	Overall (n = 80)	Normal BMI (n = 36)	OW BMI (n = 25)	Obese BMI (n = 19)	*p*
GWG (lbs) [Mean (SD)]	23.5 (10.7)	26.2 (9.1)	25.3 (10.6)	16.1 (10.6)	$2.15*10^{-3}$
[Min, Max]	[-1.9, 46.2]	[7.7, 46.2]	[8.9, 45.8]	[-1.9, 40.9]	
Infant BW (g) [Mean (SD)]	3422.6 (368.7)	3402.7 (373.9)	3435.3 (320.3)	3441.4 (432)	0.704
[Min, Max]	[2804,4488]	[2876, 4488]	[2909, 4204]	[2804, 4297]	

Table 4
Gestational wieght gain and infant birth weight by maternal race.

	Overall (n = 79)*	White (n = 41)	Black (n = 38)	*p*
GWG (lbs) [Mean (SD)]	23.5 (10.7)	24.7 (11.8)	22.2 (9.3)	0.32
[Min, Max]	[-1.9, 46.2]	[-1.9, 46.2]	[2.4, 45.8]	
Infant Birth Weight (g) [Mean (SD)]	3422.6 (368.7)	3473.7 (392.3)	3367.1 (338)	0.217
[Min, Max]	[2804,4488]	[2804,4488]	[2850, 4204]	

correlated with leptin levels at all four study timepoints (rs > 0.55, ps < $1*10^{-3}$).

Higher pre-pregnancy BMI was associated with lower total GWG (r = −0.41, p < $1*10^{-3}$). Infant birth weight was not significantly correlated with maternal pre-pregnancy BMI (r = 0.12, p = 0.28) nor GWG (r = 0.13, p = 0.29). The associations between maternal pre-pregnancy BMI, total GWG, and infant birth weight did not differ by race (ps > 0.22).

3.3. Longitudinal changes in adiponectin by BMI and race

As presented in Fig. 1A, in women overall, serum adiponectin decreased from the early to late pregnancy (ps < $1*10^{-3}$) and showed an increasing trend at postpartum (p = 0.17). As hypothesized, significant effects were observed for both race and BMI. With relation to race, a main effect was observed; white women exhibited higher levels than black women in early, mid, and late pregnancy (ps < 0.05). A main effect of BMI was also observed; as compared to women with normal weight, women with obesity exhibited lower serum adiponectin in early, mid, and late pregnancy (ps < 0.02).

In addition, differences in patterns of change over time were observed in relation to both race and BMI. Among white women, adiponectin levels decreased from the early to mid-pregnancy (p < $1*10^{-3}$) and then remained level into late pregnancy (p = 0.94) and postpartum (p = 0.65). In contrast, among black women, adiponectin decreased steadily from the early to late pregnancy (ps < 0.03) before rising at postpartum (p = $3*10^{-3}$).

In relation to BMI, differential trajectories over time were observed (p = 0.04). Among women with normal weight, there was a pattern of decreasing adiponectin from early pregnancy through postpartum. No interactions were observed between race and BMI and levels of adiponectin throughout pregnancy.

3.4. Longitudinal changes in leptin by BMI and race

In women overall (Fig. 1B), serum leptin levels increased from early to mid to late pregnancy (ps < 0.02) and then declined at postpartum (p < $1*10^{-3}$). There was no differential pattern of change across time observed in relation to race (p = 0.50), nor differences by race at any timepoint (ps > 0.12).

In relation to BMI, as expected, women with normal weight had lower leptin than those with overweight or obesity at each visit during pregnancy as well as postpartum (ps < $5*10^{-3}$). In addition, women with overweight exhibited lower serum leptin than those with obesity in early and mid-pregnancy as well as postpartum (ps < 0.02).

Regarding change over time, effects of BMI were observed. Among women with normal weight and overweight, leptin increased from early to late pregnancy (ps < 0.02) and then decreased at postpartum (p < $1*10^{-3}$). In contrast, leptin levels did not change significantly over time among women with obesity (ps ≥ 0.08). No interactions between race and BMI classification were observed with levels of leptin throughout pregnancy.

3.5. Longitudinal changes in LAR by BMI and race

The ratio of leptin to adiponectin (LAR) increased in the entire cohort of women from early to mid-pregnancy (p = $1*10^{-4}$) and remained stable in late-pregnancy (p = 0.352), see Fig. 1C. When both BMI and race were included in the model, a significant three-way interaction emerged indicating that the interaction between race and BMI varied depending on perinatal stage (p = $1.7*10^{-3}$). As shown in Fig. 1C there were significant within-race differences across time between BMI categories: black women with obesity had higher LAR at mid-pregnancy (ps < $1*10^{-3}$), late pregnancy (ps < $1*10^{-3}$), and postpartum (ps < 0.05) compared to black women with overweight or normal weight. Among whites, women with obesity had higher LAR than those with normal weight in early pregnancy (p < 0.01), mid-pregnancy (p < $1*10^{-3}$) and

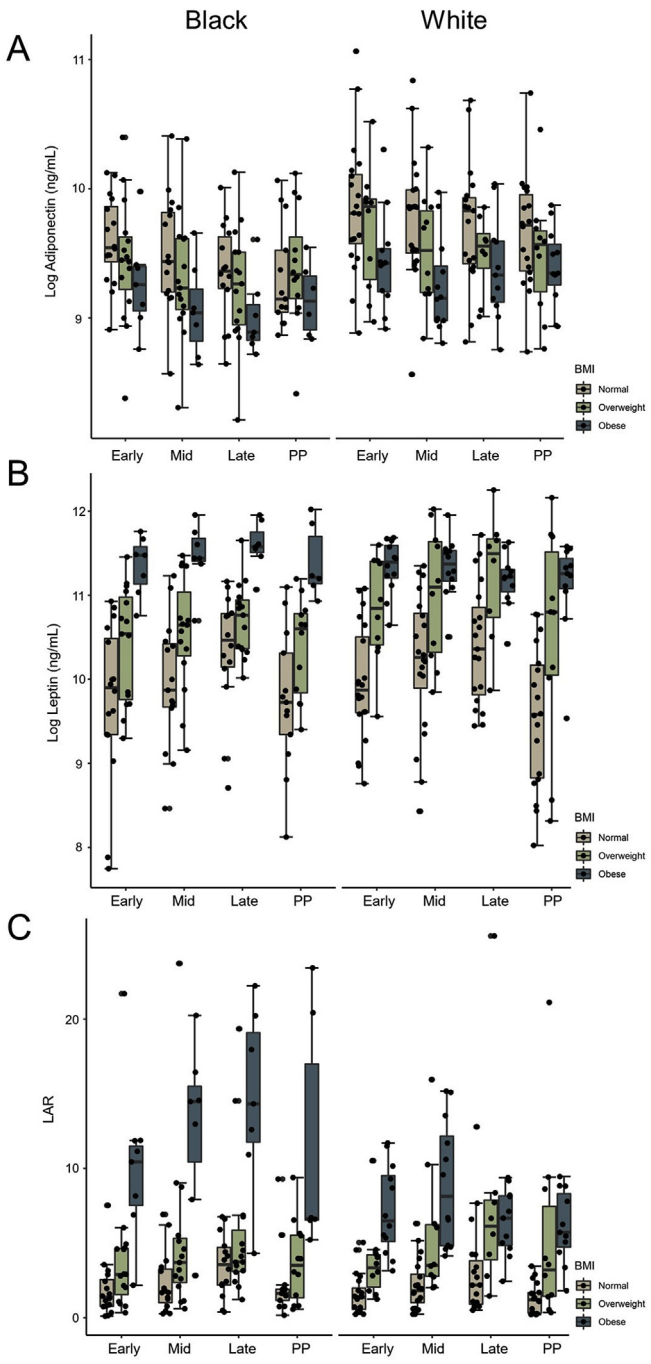

Fig. 1. Adiponectin, Leptin, and LAR throughout pregnancy and into postpartum. A) Adiponectin levels in black (left) and white (right) women throughout pregnancy and into postpartum. Adiponectin levels decreased from early to late pregnancy (p < $1*10^{-4}$). Higher Pre-pregnancy BMI category was associated with lower adiponectin (ps < 0.02). Black women had lower adiponectin levels at all time points versus white women within each BMI category (ps < 0.05). **B)** Serum leptin levels in black (left) and white (right) women throughout pregnancy and into postpartum. Leptin levels increased throughout pregnancy (p < 0.02) and declined in postpartum across both races (p < $1*10^{-3}$). Lower leptin levels were associated with lower BMI categories in a step-wise manner (p < 0.02). **C)** LAR in black (left) and White (right) women throughout pregnancy and into postpartum. LAR demonstrated a significant interaction (p < $2*10^{-3}$) between time, BMI category, and race. Black women with obesity showed higher LAR in mid-pregnancy compared to early pregnancy (p < 0.02) with levels that remained elevated in late pregnancy (p = 0.72) and decreased in postpartum (p < $1*10^{-3}$). In white women LAR did not change across pregnancy (ps > 0.02). PP: postpartum. LAR: Leptin to adiponectin ratio. BMI: Body mass index.

postpartum ($p < 0.01$).

Comparing LAR between race and BMI category within each time point showed that there were no differences between black women with normal BMI and white women with normal BMI (ps > 0.90) nor was there a difference between black versus white women with overweight BMI (ps > 0.92) at any of the assessment points. However, among women with obesity, blacks had significantly higher LAR than whites in late pregnancy ($p = 1*10^{-3}$). Interestingly, LAR over time in black women with obesity followed a different trajectory than LAR in white women with obesity. In black women, LAR increased significantly from early to middle pregnancy ($p = 1.9*10^{-2}$) and remained elevated in late pregnancy ($p = 0.46$) before decreasing significantly in the postpartum period ($p < 1*10^{-3}$). Conversely, in obese white women LAR did not change significantly throughout pregnancy at any time point (ps > 0.20).

3.6. Maternal adipokines & gestational weight gain (GWG)

Total GWG did not differ between black and white women ($t(70) = 1.00$, $p = 0.32$). Data for white and black women were analyzed separately, and models were constructed at each prenatal time point for each adiponectin, leptin, and LAR while adjusting for pre-pregnancy BMI. As shown in Table 5, serum adiponectin in black women was not significantly associated with GWG at any time point (ps > 0.63). Leptin, however, was associated with increased GWG at both middle (estimate: 6.72, $p = 5*10^{-3}$, $R^2 = 0.28$) and late pregnancy (estimate: 6.48, $p = 0.02$, $R^2 = 0.21$) in black women. Likewise, LAR was positively associated with GWG in mid pregnancy (estimate: 0.69, $p = 0.04$, $R^2 = 0.19$).

Among white women, adiponectin as a main effect was not significantly associated with GWG at any time point (ps > 0.24), indicating that pre-pregnancy BMI was the main driver of the association in these cases. Leptin was significantly associated with GWG at early (estimate: 8.93, $p < 5*10^{-4}$, $R^2 = 0.48$), middle (estimate: 7.3, $p < 5*10^{-4}$, $R^2 = 0.49$), and late (estimate: 10.54, $p < 5*10^{-6}$, $R^2 = 0.6$) pregnancy in white women. Likewise, LAR was significantly associated with GWG at early (estimate: 1.63, $p = 0.03$, $R^2 = 0.36$), mid (estimate: 1.52, $p = 2*10^{-3}$, $R^2 = 0.45$), and late (estimate: 1.32, $p < 4*10^{-4}$, $R^2 = 0.49$) pregnancy in white women.

3.7. Maternal adipokines & infant birth weight

For infant birth weight analyses, women delivering infants with clinically low birth weights (<2,500 g, n = 5) were excluded. Models were constructed for black and white women separately at each time-point and controlled for pre-pregnancy BMI and gestational age. There were three pre-term births in the study (birth at < 37 weeks gestational age). Infants of black and white women did not differ in birth weight ($t(70) = 1.25$, $p = 0.22$). Table 6 shows the results of regression analysis for infant birth weight versus adiponectin, leptin, and LAR throughout pregnancy for black (top) and white women (bottom). Infant birth weight was not significantly associated with adiponectin, leptin, or LAR at any of the measured time points during pregnancy.

4. Conclusions

The principal findings of the current study are: first that BMI and race have significant effects on both adiponectin and leptin levels across the course of pregnancy. More specifically, adiponectin levels differed by race, with black women exhibiting lower levels of adiponectin in early, mid, and late pregnancy compared to white women. No race effect was observed in leptin levels across pregnancy and postpartum. However, black women with obesity had significantly elevated level of leptin throughout early, middle, and late pregnancy. This effect was not observed in white women. Additionally, BMI and race appear to have significant interactive effects on the leptin\adiponectin ratio (LAR) that vary throughout pregnancy. Namely this is the finding that black women with obesity had higher LAR in early pregnancy that increased throughout pregnancy (Fig. 1C). Finally, the findings demonstrate that adiponectin and leptin across pregnancy are differentially associated with gestational weight gain (GWG), but not infant birth weight, with the magnitude of the effect influenced by race.

The current data showed meaningful changes in both adiponectin and leptin across the course of pregnancy, as well as significant effects of BMI and race. In terms of typical pregnancy-related changes, these data are consistent with prior data showing decreasing levels of adiponectin and increasing levels of leptin from early to late pregnancy (Paradisi et al., 2010; Anim-Nyame et al., 2000; Catalano et al., 2006; Haghiac et al., 2014). Significant differences were also observed by BMI classification.

Table 5
The Association of serum adiponectin, leptin, and LAR with Gestational Weight Gain.

		Early		Middle		Late	
	Predictor	Est	*p*	Est	*p*	Est	*p*
BLACK	**Adiponectin**	1.88	0.63	0.18	0.96	−1.38	0.73
	95% CI	(-6.02, 9.77)		(-7.69, 8.05)		(-9.53, 6.76)	
	R^2	0.08	0.25	0.08	0.28	0.08	0.26
	Leptin	3.25	0.16	6.72	**$5*10^{-3}$**	6.48	**0.02**
	95% CI	(-1.33, 7.84)		(2.18, 11.26)		(0.97, 12.01)	
	R^2	0.13	0.1	0.28	**$5*10^{-3}$**	0.21	**0.02**
	LAR	0.59	0.16	0.69	**0.04**	0.58	0.1
	95% CI	(-0.24, 1.43)		(0.03, 1.34)		(-0.12, 1.29)	
	R^2	0.13	0.1	0.19	**0.03**	0.15	0.07
		Early		**Middle**		**Late**	
	Predictor	**Est**	***p***	**Est**	***p***	**Est**	***p***
WHITE	**Adiponectin**	4.56	0.24	0.91	0.82	−0.93	0.83
	95% CI	(-3.23, 12.35)		(-7.18, 9.01)		(-9.41, 7.55)	
	R^2	0.29	**$2*10^{-3}$**	0.27	**$4*10^{-3}$**	0.27	**$5*10^{-3}$**
	Leptin	8.93	**$<5*10^{-4}$**	7.3	**$<5*10^{-4}$**	10.54	**$<5*10^{-6}$**
	95% CI	(4.20, 13.65)		(3.49, 11.11)		(6.54, 14.54)	
	R^2	0.48	**$<1*10^{-5}$**	0.49	**$<9*10^{-6}$**	0.6	**$<2*10^{-6}$**
	LAR	1.63	**0.03**	1.517	**2*10–3**	1.318	**$<4*10^{-4}$**
	95% CI	(0.18, 3.09)		(0.62, 2.42)		(0.63, 2.00)	
	R^2	0.36	**$<5*10^{-4}$**	0.45	**$<3*10^{-5}$**	0.49	**$<8*10^{-6}$**

Est: Parameter estimate. 95% CI: (5%, 95%) confidence interval. Significance determined at $p < 0.05$.

Table 6
The association of serum adiponectin, leptin, and LAR with Infant Birth Weight.

		Early		Middle		Late	
	Predictor	Est	*p*	Est	*p*	Est	*p*
BLACK	**Adiponectin**	−132.33	0.38	−158.14	0.29	−156.85	0.33
	95% CI	(-432.87, 168.20)		(-457.38, 141.11)		(-479.8, 166.10)	
	R^2	0.07	0.54	0.07	0.5	0.08	0.44
	Leptin	112.95	0.2	113.89	0.24	171.02	0.13
	95% CI	(-62.56, 288.46)		(-78.56, 306.32)		(-50.03, 392.07)	
	R^2	0.09	0.38	0.08	0.45	0.13	0.25
	LAR	3.55	0.84	4.37	0.74	16.91	0.23
	95% CI	(-30.72, 37.83)		(-22.57, 31.30)		(-10.96, 44.77)	
	R^2	0.04	0.87	0.04	0.73	0.1	0.36
	Predictor	**Early Est**	***p***	**Middle Est**	***p***	**Late Est**	***p***
WHITE	**Adiponectin**	3.9266	0.98	−21.57	0.89	−50.58	0.77
	95% CI	(-297.47, 305.33)		(-331.46, 288.32)		(-394.93, 293.77)	
	R^2	0.03	0.79	0.03	0.79	0.03	0.81
	Leptin	22.47	0.84	24.69	0.78	60.12	0.59
	95% CI	(-195.9, 240.84)		(-153.09, 202.47)		(-163.35, 283.59)	
	R^2	0.03	0.78	0.03	0.78	0.04	0.76
	LAR	2.67	0.93	9.8	0.62	60.5	0.71
	95% CI	(-57.35, 62.69)		(-30.32, 49.93)		(-26.87, 38.96)	
	R^2	0.03	0.79	0.04	0.74	0.03	0.79

Est: Parameter estimate. 95% CI: (5%, 95%) confidence interval. Significance determined at $p < 0.05$.

Specifically, lower adiponectin and higher leptin levels were observed in women with obesity compared to women with normal weight in early, mid, and late pregnancy. This is in line with prior data showing decreased adiponectin and increased leptin levels in women with obesity compared to women of normal weight (Misra and Trudeau, 2011; Hendler et al., 2005). Notably, the longitudinal design of the current study provides for stronger interpretation of change across pregnancy and into postpartum. The finding that black women with obesity had significantly elevated levels of leptin throughout pregnancy also extends prior data showing lower adiponectin levels in black non-pregnant adults and children compared to whites (Gardener et al., 2012; Degawa-Yamauchi et al., 2003; Cohen et al., 2012).

Regarding leptin, some prior data have shown higher leptin levels in non-pregnant black women compared to whites (Ruhl et al., 2004). However leptin is known to be produced from the placenta and thought to play key roles in nutrient regulation and mitogenesis during pregnancy (Tessier et al., 2013). Thus, it is possible that physiological adaptations across pregnancy obscure any racial effect. The observed interaction between BMI, race, and leptin level indicates that in the obese state leptin levels may be differentially regulated between black and white women. Of note, prior data from others, as well as our group, indicates that the predictive value of BMI varies based on race (Gillespie and Christian, 2016). For example, prior data from our group show that BMI is more strongly associated with both serum cytokine levels and birthweight among pregnant European American than black women (Gillespie and Christian, 2016). It has been suggested that this may be due to differential fat distribution in women of different races. Specifically, black women may be more likely to carry excess fat in the lower body while European American women may be more likely to carry excess fat in the abdominal region (Katzmarzyk et al., 2010). There have been reported ethnic differences in serum leptin in early pregnancy, independent of BMI classification, which were associated with increased subcutaneous fat deposition in women of South Asian descent (Sommer et al., 2015). Thus, even at the same BMI, the health implications of excess weight may vary between races.

The current findings show that greater leptin levels were associated with increased GWG across pregnancy. As pregnancy progressed, each change in leptin was associated with an even greater increase in weight, as shown by the increasingly positive parameter estimates throughout pregnancy (Table 2). The positive directionality of this finding has been supported with other data in pregnant women (Lacroix et al., 2016; Franco-Sena et al., 2016; Stein et al., 1998; Jansson et al., 2008). This directionality did not differ by BMI classification or race. This contrasts with some literature showing that the relationship between leptin and weight gain may be more pronounced in women of normal weight (Lacroix et al., 2016; Franco-Sena et al., 2016). Additionally, the current findings support that leptin levels are positively associated with GWG at an earlier timepoint in pregnancy in white women than black women (Table 2). The positive association between leptin and GWG, but not adiponectin and GWG, is not surprising as it is well known that in obese states there are increased free leptin levels as the hypothalamic satiety centers become overwhelmed by leptin produced in peripheral adipose tissue resulting in a state of leptin resistance (Zhou and Rui, 2013). Further, during pregnancy leptin may serve an additional role of ensuring the maternal body meets the energy demands of the developing fetus by modulating peripheral insulin resistance (Tessier et al., 2013).

Interestingly, the LAR has been shown to be useful in correlating with insulin resistance in non-diabetic white adults (Finucane et al., 2009) and in patients with type 2 diabetes mellitus where it has been suggested that LAR is a more sensitive indicator of insulin resistance than HOMA-IR (Inoue et al., 2005). Likewise, in pregnancy, the LAR has been shown to be inversely correlated with HOMA-IR (Skvarca et al., 2013). Increased LAR is also known to be associated with increased abdominal obesity, a core feature of metabolic syndrome, in patients with coronary artery disease (López-Jaramillo et al., 2014) and is a female specific predictor of obesity even in non-obese children (Zhang et al., 2017). The racial difference in LAR observed in the current study may be one mechanism that explains the racial differences in postpartum weight retention. For example, higher pre-pregnancy BMI is a risk factor for greater postpartum weight retention (Gore et al., 2003) and, in the US, black women exhibit 2–3X greater weight retention at one year postpartum than white women, including 2-fold greater risk of retaining ≥ 10 lbs and $\geq$20 lbs (Keppel and Taffel, 1993; Parker and Abrams, 1993; Smith et al., 1994).

The main strengths of the current study are that it provides a longitudinal analysis of leptin and adiponectin levels across pregnancy and into post-partum and specifically focuses on the effects of BMI and race. The current study does have several limitations. First, there was a small number of participants in some subgroups when stratified by race and BMI which limits the power of the analysis. Additionally, parameters

such as fasting lipids, insulin levels, measures of insulin resistance, fat distribution, and post-partum weight retention were not collected during this study limiting our ability to expand upon the effects of the measured adipokines. Further, large cohort studies of the association between gestational diabetes mellitus and race have indicated that being born outside of the US (despite identifying as a specific race) increases risk of GDM in several racial groups including blacks and non-Hispanic whites (Hedderson et al., 2013). This implies that geographic birth place (which was not collected in the current study) rather than only self-reported race may be useful in understanding the relationship between metabolic states and weight gain. Finally, this study sample was predominately low income, with representation of only black and white women, limiting generalizability.

In conclusion, the current study provides data suggesting that in addition to BMI, race affects adiponectin and leptin levels throughout pregnancy with black women with obesity having higher LAR throughout pregnancy than white women. These differences appear to be related primarily to differences in circulating adiponectin levels. Further, leptin levels were associated with total GWG in both black and white women, but with the relationship present at an earlier timepoint in white women. These relationships may have important implications for racial disparities in metabolic syndrome and postpartum weight retention. Future studies should focus on establishing these findings in a larger population of pregnant women while examining outcomes of insulin resistant and fat distribution and including race as a primary mediator.

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Declaration of competing interest

The authors report no conflicts of interest.

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