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Racial discrimination predicts greater systemic inflammation in pregnant African American women

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Abstract

Purpose—Chronic exposure to racial discrimination by pregnant African American women may lead to allostatic overload; thereby, predisposing women to systemic inflammation. Thus, the goal of this study was to examine if experiences of racial discrimination are related to systemic inflammation in pregnant African Americans.

Methods—A sample of 96 African American women from Chicago completed questionnaires and had blood drawn during the second trimester of pregnancy (19.7 ± 2.5 weeks).

Results—Experiences of racial discrimination were associated with higher cytokine levels of interleukin(IL)-4 (*B*=2.161, 95% CI =1.02–3.30, $p<.001$) and IL-6 (B = 1.859, 95% CI = .61–3.11, $p= .004$) when controlling for covariates.

Conclusion—These findings suggest that experiences of racial discrimination may cause physiological wear and tear on the body leading to alteration of immune functions. Nurses should

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inquire about women's experiences of racial discrimination and make referrals for community or church support groups for women who report racial discrimination.

Keywords

Racial discrimination; cytokines; inflammation; pregnancy; African American; depressive symptoms

Introduction

Pregnant African American women are more likely to experience racial discrimination, defined as being hassled or made to feel inferior due to one's race, ethnicity, or color (Krieger et al., 2010), compared with pregnant non-Hispanic white women (Dominguez, Dunkel-Schetter, Glynn, Hobel, & Sandman, 2008). Chronic exposure to racial discrimination in African American women may cause physiological wear and tear on the body known as allostatic load (McEwen, 2012). The theory of allostatic load describes acute stress as an adaptive physiological process that helps the individual overcome (or avoid) a stressor, and maintain balance or allostasis. In contrast, chronic or cumulative stress increases one's allostatic load (dysregulation of the adaptive system that can lead to disease) and alters allostasis, leading to alteration of immune functions and negative health outcomes.

Chronic exposure to racial discrimination has been related to higher levels of inflammation in non-pregnant minority populations. In one study of a multiethnic sample of women, greater everyday discrimination predicted higher C-reactive protein (CRP), a well-established marker of systemic inflammation (Beatty Moody, Brown, Matthews, & Bromberger, 2014). Similarly, African American women reporting 1 or 2 experiences of racial discrimination had higher levels of CRP compared with those reporting no experiences of racial discrimination (Cunningham et al., 2012). In a study of elderly African American women and men, greater self-reported experiences of racial discrimination related to higher CRP levels (Lewis, Aiello, Leurgans, Kelly, & Barnes, 2010). In another study, African American adolescents exposed to racial discrimination had higher levels of inflammation [composite of IL-1β, IL-6, IL-8, and IL-10, tumor necrosis factor (TNF)-α, interferon (IFN)-γ] when assessed three years later (Brody, Yu, Miller, & Chen, 2015). However, one study found no relationship between racial discrimination and IL-6 in African American and Latina non-pregnant women (Ratner, Halim, & Amodio, 2013). Although there is a clear relationship between higher levels of racial discrimination and greater systemic inflammation in non-pregnant populations, no study has examined the relationship between racial discrimination and inflammation in pregnant women.

The immune system during pregnancy is regulated by a complex array of cytokines that protect the fetus and promote placental development (Chatterjee, Chiasson, Bounds, & Mitchell, 2014; Schminkey & Groer, 2014). The second trimester (14–27 weeks) is a predominantly anti-inflammatory period which is promoted by an increase in progesterone-induced anti-inflammatory cytokines [e.g., interleukin (IL)-10]; these in turn contribute to uterine quiescence and maintenance of pregnancy (Chatterjee et al., 2014; Schminkey & Groer, 2014). Toward the end of pregnancy pro-inflammatory cytokines (e.g., IL-1β, IL-6,

IL-8) induce prostaglandin synthesis in the placenta that stimulates uterine contractions resulting in cervical ripening, rupture of membranes, labor and birth (Chatterjee et al., 2014; Giurgescu, Engeland, Zenk, & Kavanaugh, 2013; Schminkey & Groer, 2014). While this is a normal process, higher inflammation during the second trimester may lead to premature rupture of membranes, preterm labor, and preterm birth (<37 completed weeks gestation) (Coussons-Read et al., 2012; Giurgescu et al., 2013; Vogel et al., 2007). Pregnant African American women are more likely to have greater systemic inflammation in the second trimester compared with pregnant white women (Blackmore et al., 2014; Christian, Glaser, Porter, & Iams, 2013). We postulate that the chronic exposure to racial discrimination may lead to allostatic overload thereby predisposing women to systemic inflammation. Hence, the purpose of this study was to examine whether experiences of racial discrimination are associated with systemic inflammation in the second trimester of pregnancy in African American women.

Materials and Methods

Design and Sample

This study used a cross-sectional design among pregnant African American women from a midwifery practice of a medical center in Chicago. Participants were enrolled if they were at least 18 years of age; had singleton pregnancy; were in the second trimester of pregnancy; and had a low-risk pregnancy. Women with medical complications (e.g., chronic hypertension, diabetes) or receiving steroid treatment were excluded since these factors may influence inflammatory levels. A sample of 114 women was enrolled into the study. Seven women did not complete the questionnaires or the questionnaires were lost in the mail. Of the 107 women who completed the questionnaires, 11 women did not have blood samples collected or the samples were not processed within three hours of venipuncture and were not included in the analysis. A final sample of 96 women had completed questionnaire data and had useable blood samples.

Variables and Instruments

Maternal characteristics—Maternal characteristics included socio-demographic and obstetrical characteristics and depressive symptoms. Maternal socio-demographic and obstetrical characteristics (e.g., maternal level of education, employment, income, prior pregnancies, medical history, smoking during pregnancy, and body mass index [BMI]) were collected from self-administered questionnaires or medical records. BMI (kg/m^2) was calculated using pre-pregnancy weight and height from medical records.

Depressive symptoms were measured by the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977). This scale assesses the presence of salient symptoms of depression within the past seven days. The CES-D does not provide a diagnosis of clinical depression, but a customary cutoff score of 16 or higher is used to identify those with elevated (e.g., clinically relevant) levels of depressive symptoms. The instrument has been used with good reliability in prior research with pregnant African American women (Garfield et al., 2015; Giurgescu et al., 2015). In the current study the Cronbach's alpha was 0.87.

Experiences of racial discrimination—The Experiences of Discrimination (EOD) instrument measures self-reported experiences of racial discrimination in one's lifetime (Krieger, Smith, Naishadham, Hartman, & Barbeau, 2005). The EOD asks about 9 situations of experienced discrimination due to race, ethnicity, or color (e.g., at school; at work; getting medical care). For each situation, respondents may reply *yes* = 1 or *no*= 0. The sum of all 9 situations equals the total score (range 0–9). EOD has established construct validity in a sample of African American adults (Krieger et al., 2005). The instrument has been used in prior research with postpartum African American women (Giurgescu et al., 2012). In the current sample the Cronbach's alpha was 0.83. Because of extreme positive skewness EOD was used as dichotomous variable [0=no (0 situations); 1=yes (1–9 situations)] in regression models.

Systemic Inflammation—Plasma levels of IL-1β, IL-2, IL-4, IL-6, IL-8 and IL-10 were measured by multiplex bead immunoarrays (Life Technologies, Grand Island, NY). Compared with ELISAs, these multiplex arrays provide simultaneous measurement of interrelated cytokines, high sensitivity, and reductions in inter-plate variability. The minimal detection limit is <0.5 pg/ml for each analyte and the inter-assay coefficients of variation were 4.4%–8.6%.

Procedures

The study was approved by the Institutional Review Board at the participating medical center. Women who received prenatal care at the midwifery practice and fit the inclusion criteria of the study were invited to participate. Women completed an informed consent process prior to data collection. Women completed the questionnaires in a private room in the clinic or at home and returned them in an envelope provided by the research staff. The participant's venous blood was drawn by a registered nurse or medical assistant through antecubital venipuncture (within 30 sec. of venipuncture) into a sterile serum separator tube (10 ml) and placed on ice. This was done in the afternoon (1:00 p.m. – 5:00 p.m.) to control for the influence of circadian rhythm on variations in cytokine levels. Many serum cytokines show a circadian rhythm opposite to that of cortisol, with highest values during sleep periods and lower values during wakefulness (Vgontzas et al., 2005). Participants received a monetary incentive of $25 for their participation and time. The blood samples were transported on ice to the laboratory where they were centrifuged (1500g × 15min at 4°C) and aliquoted (400μl per tube) within three hours of withdrawal. The aliquoted samples were frozen at −80°C. The assays were performed by a laboratory technician in duplicate according to manufacturer's specifications and under the supervision of one of the study co-authors (CGE).

Data analysis

Data were entered, cleaned and prepared for analysis on an ongoing basis by the principal investigator or research staff using SPSS 22.0 (SPSS Inc., Chicago, IL). Twelve samples for IL-1β, 17 samples for IL-2, 18 samples for IL-6, 18 samples for IL-8, and 22 samples for IL-10 were below the limits of detection in duplicate wells. This occurred without sampling errors (Luminex, Riverside CA) indicating that the values were valid but below detection threshold, therefore these values were replaced with zero. Cytokine values were positively

skewed; therefore, natural log transformations for cytokine data were conducted to normalize the distributions. Descriptive statistics were used to describe the maternal characteristics, experiences of racial discrimination and cytokine levels. Pearson's *r* correlation coefficient and point-biserial correlations were used to examine relationships among maternal characteristics, experiences of racial discrimination and cytokines. Hierarchical multiple linear regression analyses were conducted to examine if experiences of racial discrimination predicted systemic inflammation in the second trimester of pregnancy in African American women when controlling for maternal characteristics [low levels of education (coded as yes= high school or lower; and no=some college or higher), unemployment (coded as yes vs. no), smoking during pregnancy (coded as yes vs. no), BMI, gestational age at time of data collection, and clinically relevant levels of depressive symptoms (coded as no= CES-D scores of 15 or lower; and yes=CES-D scores of 16 or higher)]. The rationale for these covariates is that low levels of education were related to experiences of racial discrimination; and unemployment was related to IL-4. Smoking and BMI were included since smoking and obesity have each been related to higher levels of inflammation (Gonçalves et al., 2011; Wang & Ye, 2015). Gestational age at data collection was included in the analysis given limited data suggesting that IL-6 and IL-10 increase across pregnancy (Christian & Porter, 2014; Coussons-Read, Okun, & Nettles, 2007). Depressive symptoms were included in the analysis given that depressive symptoms have been related to greater systemic inflammation in pregnant women (Cassidy-Bushrow, Peters, Johnson, & Templin, 2012; Christian, Franco, Glaser, & Iams, 2009).

Results

Maternal Characteristics

Women had a mean age of 24 years and a mean gestational age at data collection of 20 weeks. The majority of women were multigravida, single, living with the father of the baby, and unemployed. Women had a mean CES-D score of 12.72±9.53. Twenty-nine (30.2%) women had CES-D scores of 16 or higher which are used to identify those with elevated (e.g., clinically relevant) levels of depressive symptoms (see Table 1). Women had a mean score for situations of racial discrimination of 1.47±1.95 (range 0–9). Fifty-one women (53.1%) reported one or more experiences of racial discrimination. The most frequently reported situations of racial discrimination were *getting service in a store or restaurant; getting hired or getting a job; on the street or in a public setting*; and *from police or in the courts* (see Table 2). Blood cytokine levels are presented at the bottom of Table 3.

Women who reported experiencing racial discrimination were more likely to be educated beyond high school (r=.209, p=.043) and to report higher levels of depressive symptoms (r=.281, p=.006). Women with higher levels of IL-4 were more likely to be unemployed (r=.234, p=.022). There were no other relationships between experiences of racial discrimination or cytokine levels and maternal characteristics of age, BMI, multigravida, single marital status, living with the baby's father, annual household income and smoking during pregnancy.

Bivariate Associations between Experiences of Racial Discrimination and Inflammation

As shown in Table 3, women who reported one or more experiences of racial discrimination had higher levels of IL-4 (r=.270, p=.008) and IL-6 (r=.236, p=.021). Cytokines were highly correlated with each other.

Multivariable Associations with Inflammation

Given that experiences of racial discrimination were related to IL-4 and IL-6 in the bivariate analysis, we performed hierarchical multiple linear regression analyses to determine the contribution of experiences of racial discrimination to cytokine expression independent of potential confounding by maternal characteristics. For IL-4 (see Table 4), none of the covariates were associated with IL-4 levels (model 1). Experiences of racial discrimination were added in model 2. There was a 13% change in R^2 between the first and the second model. Twenty-seven percent of variance in IL-4 was explained by the combined impact of the independent variables. Experiences of racial discrimination were positively associated with IL-4 (B=2.161, 95% CI =1.02–3.30, p<.001) when controlling for covariates. For IL-6 (see Table 5), none of the covariates were associated with IL-6 (model 1). Experiences of racial discrimination were added in model 2. There was an 8% change in R^2 between the first and the second model. Twenty-two percent of variance in IL-6 levels was explained by the combined impact of the independent variables. Experiences of racial discrimination were positively associated with higher levels of IL-6 (B = 1.859, 95% CI = .61–3.11, p= .004) when controlling for covariates.

Discussion

To our knowledge this is the first study to examine the relationship between experiences of racial discrimination and systemic inflammation in pregnant women. Racial discrimination predicted higher levels of IL-4 and IL-6 during the second trimester of pregnancy in African American women. Prior studies found that racial discrimination was related to inflammation in non-pregnant populations (Brody et al., 2015; Cunningham et al., 2012; Lewis et al., 2010). According to the allostatic load chronic or cumulative stress results in dysregulation of the adaptive system leading to alteration of immune functions and negative health outcomes (McEwen, 2012). Chronic exposure to racial discrimination in African American women may cause physiological wear and tear on the body leading to alteration of immune functions and inflammation, which can lead to negative birth outcomes (e.g., preterm birth). Indeed, research suggests there is a higher risk for preterm birth in women who report experiences of racial discrimination (Giurgescu, McFarlin, Lomax, Craddock, & Albrecht, 2011; Misra, Strobino, & Trabert, 2010) or who have higher levels of inflammation during the second trimester (Cassidy-Bushrow et al., 2012; Coussons-Read et al., 2012; Gargano et al., 2008; Vogel et al., 2007). Inflammation may act as a mediator between racial discrimination and preterm birth. Future research needs to examine this possibility.

Women with higher levels of education reported experiencing one or more situations of racial discrimination. Other researchers also reported that African-American women ages 40–79 with more than 12 years of education were more likely to report racial discrimination compared with African American women with 12 years of education or less (Dailey, Kasl,

Holford, Lewis, & Jones, 2010). Women with higher levels of education may feel more empowered to recognize racial discrimination and thus may report more experiences of racial discrimination (Ertel et al., 2012). Women with higher levels of education may also live or spend time in areas or contexts with more whites and thus are more likely to be exposed to racial discrimination. Indeed, Dailey and colleagues (2010) found that African American women living in less disadvantaged neighborhoods and neighborhoods with the lowest percentages of African Americans were more likely to report experiences of racial discrimination than African American women living in more disadvantaged neighborhoods and neighborhoods with the highest percentages of African Americans. Similarly, Ertel and colleagues (2012) found that women living in more affluent neighborhoods reported more experiences of racial discrimination compared with women living in more economically deprived neighborhoods (78% and 54%, respectively).

In this study of pregnant African Americans, women who reported more experiences of racial discrimination also reported higher levels of depressive symptoms. This is similar to findings from studies among pregnant (Ertel et al., 2012) and non-pregnant (McNeil, Fincham, & Beach, 2014; Schulz et al., 2006) African American women. Ertel and colleagues (2012) found that experiences of racial discrimination were differentially associated with risk for depressive symptoms in two cohorts of pregnant African American women with positive associations in the lower socioeconomic cohort and no association found in the higher socioeconomic cohort. These results and our findings suggest that experiencing racial discrimination is a unique psychosocial stressor that can influence the mental health of pregnant African American women.

There are few limitations for this study. The sample size was small and majority of women were from lower socioeconomic status. Women with low-risk pregnancy were recruited from one midwifery practice. The results cannot be generalized to African American women with higher socioeconomic status, high-risk pregnancy or from other settings. Data were collected one time during the pregnancy. Limited data suggest that cytokine levels change across pregnancy (Christian & Porter, 2014; Coussons-Read et al., 2007). Future studies need to employ longitudinal designs, as multiple measures across pregnancy would allow for a better understanding of the impact of experiences of racial discrimination on systemic inflammation during pregnancy and associated negative birth outcomes (e.g., preterm birth). Despite these limitations, the findings suggest that experiences of racial discrimination are related to alterations in immune functions in pregnant African American women.

Fifty-three percent of pregnant African American women in our study reported one or more situations of racial discrimination. Nurses should inquire about women’s experiences with racial discrimination and make referrals for community or church support groups for women who report racial discrimination. The most frequent racial discrimination situation (34%) occurred when getting service in a store or restaurant. Policies and programs to promote African American ownership of and employment at business including stores and restaurants may help to alleviate this form of discrimination. More generally, policy and other interventions to reduce racism or combat its deleterious effects are needed to reduce racial discrimination.

Conclusion

Pregnant African American women from our study who experienced racial discrimination had alterations in immune functions and greater systemic inflammation. This may be one pathway by which African American women have higher rates of preterm birth compared with non-Hispanic white women. Future research needs to assess, at multiple time points across pregnancy, the pathways by which racial discrimination and inflammation contribute to the health disparity that exists in preterm birth for African American women.

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Table 1

Maternal characteristics (N=96)

Variable		
	M (*SD*)	Range
Age	23.60 (5.13)	18–41
Gestational age at data collection (weeks)	19.73 (2.54)	15–26
Body Mass Index[a]	27.45 (6.63)	17–50
CES-D[b]	12.72 (9.53)	
	N (%)	
Multigravida	69 (71.9)	
Single	83 (86.5)	
Living with the baby's father	49 (51.0)	
Education		
Less than high school	14 (14.6)	
Graduated high school	26 (27.1)	
Some college	38 (39.6)	
Associate degree	7 (7.3)	
Bachelor degree	9 (9.4)	
Graduate program	2 (2.1)	
Unemployed	49 (51.0)	
Annual household income[c]		
Less than $10,000	48 (50.0)	
$10,001–20,000	12 (12.5)	
$20,001–30,000	17 (17.7)	
More than $30,001	13 (13.5)	
Smoking during pregnancy	7 (7.1)	
Clinically relevant depressive symptoms (CES-D≥ 16)	29 (30.2)	

[a] Body Mass Index available for 93 women

[b] CES-D: Center for Epidemiological Studies Depression

[b] Household income available for 90 women

Table 2

Frequency of situations of racial discrimination (N=96)

Situations of racial discrimination*	
Getting service in a store or restaurant	34.4%
Getting hired or getting a job	20.0%
On the street or in a public setting	20.0%
From police or in the courts	18.8%
At work	17.0%
Getting credit, bank loans, or a mortgage	10.4%
At school	10.6%
Getting housing	7.4%
Getting medical care	6.3%

* the frequency represents responses of “yes” to each situation

Table 3

Relationships among experiences of racial discrimination and cytokines (N=96)

Variables	EOD	IL-1β	IL-2	IL-4	IL-6	IL-8	IL-10
EOD[a]	—	.137	.169	.270**	.236*	.077	.120
IL-1β			.838**	.654**	.757**	.721**	.819**
IL-2				.803**	.846**	.742**	.855**
IL-4					.841**	.632**	.800**
IL-6						.682**	.835**
IL-8							.806**
M (SD)	0.53 (0.50)	20.15 (4.83)	3.78 (8.07)	8.74 (18.28)	3.34 (5.51)	12.27 (18.58)	6.14 (12.43)

*$p<.05$;

**$p<.001$, two-tailed

[a]EOD: Experiences of Discrimination [scored as 0=0 situations and 1=1–9 situations); mean (sd) is the percent of women who experienced racial discrimination]; IL: interleukin; M: mean; SD: standard deviation; cytokines measured in pg/ml.

Table 4

Multiple linear regression predicting IL-4 levels (N=96)

	B	S.E.	*β*	*t*	*p*	95%CI
Model 1[a]						
Low levels of education	1.012	.640	.185	1.58	.118	−.263, 2.286
Unemployed	−1.088	.640	−.204	−1.70	.093	−2.362, .187
Low household income	−.865	.653	−.162	−1.33	.189	−2.164, .434
Gestational age at data collection	.197	.114	.184	1.73	.088	−.030, .424
Body Mass Index	−.056	.043	−.136	−1.28	.204	−.142, .031
Smoking during pregnancy	−1.144	1.159	−.109	−.99	.327	−3.452, 1.163
CES-D	−.011	.033	−.039	−.34	.735	−.077, .055
Model 2[b]						
Low levels of education	.742	.597	.136	1.24	.217	−.445, 1.930
Unemployed	−1.191	.593	−.223	−2.01	.048	−2.372, −.010
Low household income	−1.277	.614	−.239	−2.08	.041	−2.498, −.055
Gestational age at data collection	.249	.106	.233	2.34	.022	.037, .461
Body Mass Index	−.057	.040	−.139	−1.41	.162	−.137, .023
Smoking during pregnancy	−1.140	1.073	−.108	−1.06	.291	−3.278, .995
CES-D	−.052	.032	−.179	−1.61	.113	−.117, .013
EOD	2.161	.272	.404	3.78	.000	1.023, 3.299

[a]Note: Low levels of education (scored as no= some college education or higher; and yes= high school graduate or lower); unemployed (no vs. yes); low household income (scored as no ≥$10,000; and yes <$10,000); smoking during pregnancy (no vs. yes); clinically relevant depressive symptoms [scored as no=CES-D (Center for Epidemiological Studies Depression) ≤15; and yes=CES-D≥16]; Experiences of racial discrimination (scored as no=0 situations; and yes=1–9 situations).

[a]Model 1 predicted 13% of variance in IL-4 ($F_{(7,86)}$ =1.722, p=.116, R^2=.132).

[b]Model 2 predicted 27% of variance in IL-4 ($F_{(8,86)}$=3.546, p=.002, R^2=.267, Δ R^2=.134).

Table 5

Multiple linear regression predicting IL-6 levels (N=96)

	B	S.E.	*β*	*t*	*p*	95%CI
Model 1[a]						
Low levels of education	.1.351	.683	.232	1.98	.051	−.008, 2.711
Unemployment	−1.010	.683	−.178	−1.48	.143	−2.369, .350
Low household income	−.602	.696	−.106	−.86	.390	−.987, .784
Gestational age at data collection	.100	.122	.088	.82	.413	−.142, .342
Body Mass Index	−.084	.046	−.193	−1.82	.073	−.177, .008
Smoking during pregnancy	−1.619	1.237	−.145	−1.31	.194	−4.080, .843
CES-D	−.002	.035	−.006	−.05	.961	−.072, .068
Model 2[b]						
Low levels of education	1.120	.657	.192	1.71	.092	−.008, 2.711
Unemployment	−1.098	.653	−.193	−1.68	.096	−.187, 2.427
Low household income	−.955	.675	−.168	−1.42	.161	−2.299, .389
Gestational age at data collection	.145	.117	.127	1.24	.219	−.142, .342
Body Mass Index	−.085	.044	−.196	−1.93	.058	−.173, .003
Smoking during pregnancy	−1.615	1.180	−.144	−1.37	.175	−3.965, .734
CES-D	−.037	.036	−.119	−1.03	.305	−.108, .034
EOD	1.859	.629	.327	2.96	.004	.607, 3.111

[a]Note: Low levels of education (scored as no= some college education or higher; and yes= high school graduate or lower); unemployed (no vs. yes); low household income (scored as no ≥$10,000; and yes <$10,000); smoking during pregnancy (no vs. yes); clinically relevant depressive symptoms [scored as no=CES-D (Center for Epidemiological Studies Depression) ≤15; and yes=CES-D≥16]; Experiences of racial discrimination (scored as no=0 situations; and yes=1–9 situations).

[a]Model 1 predicted 13% of variance in IL-6 ($F_{(7,86)}$ =1.653, p=.133, R^2=.128).

[b]Model 2 predicted 22% of variance in IL-6 ($F_{(8,86)}$=2.680, p=.012, R^2=.216, Δ R^2=.088).