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Title The Effect of Race-related Stress on Risk for Adverse Pregnancy Outcomes in Black

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Degree Master of Science

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The Effect of Race-related Stress on Risk for Adverse Pregnancy Outcomes in Black Pregnant Persons

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B.A., University of Michigan, 2018

M.Sc., Emory University, 2025

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An abstract of a thesis submitted to the Faculty of the James T. Laney School of Graduate Studies of Emory University in partial fulfillment of the requirements for the degree of Master of Science in Clinical Research

2025

Abstract

The Effect of Race-related Stress on Risk for Adverse Pregnancy Outcomes in Black Pregnant Persons
By: Sydni Williams, M.Sc., M.D.

Low birth weight (LBW) and preterm birth (PTB) are significant contributors to infant mortality in the United States that disproportionally impact Black pregnant persons and their offspring. Although these outcomes have been linked to chronic stress, the contribution of race-related stress to these disparities remains largely understudied. We investigated the effect of race-related stress on weight and gestational age at birth in a prospective cohort of 192 pregnant Black persons recruited at Grady Memorial Hospital in Atlanta, Georgia. The Index of Race-Related Stress Brief (IRRS-Brief), sociodemographic characteristics, and blood cortisol levels were collected at study enrollment during the first trimester of pregnancy. Neonatal birth weights and gestational age were collected via standardized medical record abstraction. We conducted multiple regressions to determine whether greater race-related stress was associated with lower birth weight and gestational age while controlling for sociodemographic factors identified by DAG. We conducted Generalized Additive Models (GAM) to predict first-trimester cortisol using IRRS subscales. Race-related stress was not significantly associated with LBW or PTB and no significant predictors of the outcomes emerged from the regressions, including the interaction term between pediatric sex and IRRS. Significant non-linear associations were observed between institutional racism ($p = 0.03$, $r^2 = 0.749$) and cultural race-related stress ($p = 0.02$, $r^2 = 0.931$) and first-trimester cortisol levels, with education and income emerging as important predictors. These results suggest that race-related stress contributes to physiological stress responses, which may have downstream effects. Future studies are necessary to explore how race-related stress might contribute to these adverse birth outcomes. These studies should aim to better understand the relationship between race-related stress and cortisol and to inform their potential downstream impact on maternal and fetal health.

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Introduction

Low birth weight (LBW) is a significant public health challenge defined as birth weight < 2500 grams. LBW is associated with a wide range of both short- and long-term consequences, the most consequential of which is increased infant mortality. In 2020, infant mortality rates were 22 times higher for LBW infants than for infants with birth weights ≥ 2,500 grams[1]. A retrospective cohort study established that the incidence ratio for risk of death was positively associated with birth weight, with extremely low birth weight infants (< 1000 grams) almost 200 times more likely to die within the first year of life [2], implicating LBW as a strong determinant of first-year mortality. Similarly, preterm birth (PTB) is a concerning pregnancy outcome that affects nearly 15 million births yearly that is defined as the birth of an infant before 37 completed weeks of gestation[3]. In the short term, PTB increases the risk of neonatal respiratory distress and sepsis, and in the long term, it causes poor neurodevelopment, including hearing and vision delays[4].

LBW and PTB are pathological in all populations, not only because of their strong association with infant and neonatal mortality but also because of their role as a marker for maternal health and its impact on long-term child health outcomes[3] [5]. However, racial inequities in outcomes related to LWB and PBW exist, as these both disproportionately affect minoritized Black persons and their offspring at greater rates [6,6,7]. Black pregnant persons are more likely to deliver LBW and pre-term infants and are also disproportionately impacted by the high infant mortality rates[7]. In Black infants, the risk for LBW is 2.3 times higher than for White infants [1] and the rate of mortality in these LBW infants is 214.4 per 100,000 live births compared to a rate of 56.4 in non-

Hispanic Whites [7]. Likewise, a systematic review reported two times the odds of PTB in those of Black race when compared to non-Hispanic whites.

Considering the documented racial disparities in PTB and LWB, many studies have attempted to understand individual maternal risk factors that may confer risk in Black pregnancy persons, including low income, low education, unmarried marital status, and short interpregnancy interval. However, when individual risk factors, exposures, and protective factors are accounted for, the risk for PTB and LBW in Black pregnant persons remained twice that of White persons [1,6,89], suggesting that maternal factors account for some but not all the racial disparities. Additionally, the disproportionate risk for PTB and LBW have been found to persist in samples of women with similar access to healthcare across races, such as those in the military[10], making it clear that while some of the disparity may be attributed to sociodemographic differences, many of these at-risk deliveries are unexplained by these factors.

Given these unexplained disparities, researchers have explored differences in chronic stress exposure between Black and non-Black persons as a plausible explanation. The cumulative physiologic impact of chronic stress exposure, first described by McEwen and Stellar as allostatic load[11], is strongly associated with poor health outcomes including cardiovascular disease, cancer, and diminished quality of life[12]. Elevated cortisol concentration is a known biomarker of chronic stress that is the hallmark of glucocorticoid resistance (GR), a state that develops when chronic elevated levels of cortisol in the setting of chronic stress exposure result in the tissues being less sensitive to cortisol[13]. In GR, this persistent exposure to cortisol causes binding of cortisol to the glucocorticoid receptor to be impaired, making the body less sensitive to the effects of cortisol [13]. In pregnancy, greater allostatic load due to chronic stress exposure, also known as weathering, is associated with more adverse pregnancy and birth outcomes, including PTB and LBW [14]. Studies have tried to elucidate the root cause underlying the relationship between chronic stress and adverse pregnancy outcomes and examined additional factors contributing to chronic stress as a potential explanation. However, when accounting for the effects of acute, financial, and relationship stressors, the increased risk of LBW and PTB in Black persons was lessened but did not fully account for the racial/ethnic differences [15,16].

On a global measure combining exposure to stressors in five domains (occupation, finances, relationships, racial bias, and violence), Black individuals reported significantly higher levels of stress than any other race/ethnicity[17]. In pregnancy, Black pregnant individuals experience significantly higher levels of stress compared to their non-Hispanic White counterparts, influenced by various factors including racial discrimination and systemic inequities[18]. Additionally, increased psychophysiological hyperarousal due to chronic trauma exposure disproportionately impacts minoritized Black persons[19] and is associated with greater systemic inflammation[20]. Although stress is multifactorial, one stressor unique to marginalized minorities is that of race-related stress, which is a significant contributor to Black women's every day, global psychological distress[17,21].

To further explain the differences in risk for LBW that are not fully explained by chronic stressors, researchers have sought to establish the relationship between lifetime exposure to race-related stress, and its impact on LBW and PTB. A recent study found that more lifetime everyday discrimination and exposure to interpersonal racial discrimination were associated with LBW [15]. Specifically, when lifetime discrimination of women who deliver very low birthweight (<1500 grams) infants was evaluated across 5 domains: work, securing employment, seeking medical care, receiving service at a restaurant or store, maternal lifetime exposure to interpersonal racism in 3 or more domains was associated with a 3-fold increase in odds of LBW. Importantly, this association persisted across maternal sociodemographic, biomedical, and behavioral characteristics [22]. In PTB, racism amplifies the degree of effect of weathering on PTB, highlighting racism as a potential accelerator of risk for PTB[23]. Several studies have supported this claim, finding that for each one-unit increase in the incidence of racial discrimination in childhood, adolescence, and adulthood, the odds of PTB increased by at least 48%[24]. However, while these studies have examined lifetime exposure to discrimination/racism, they have not focused on the intrapartum period, a unique period during which the mother and the fetus are inherently symbiotic. Additionally, previous studies have noted that their utilized instruments of lifetime discrimination lacked sensitivity [25] and that their study design prevented researchers from broadly evaluating confounders such as specific biological measurements, health complications, and other types of everyday stress [22]. Thus, further research is needed to better understand the relationship between individual experiences of race-related stress during pregnancy, LBW, and PTB and the mechanisms by which race-related stress confers risk for LBW and PTB specifically in Black pregnant persons.

In the current study, we examined the association between race-related stress and LBW and PTW, and cortisol levels during the 1st trimester of pregnancy among Black pregnant persons recruited as a part of a longitudinal cohort study at Grady Memorial Hospital, a large safety-net hospital servicing a larger underserved, underinsured, and uninsured population (**Figure 1**). We hypothesized that increased race-related stress in Black pregnant persons in pregnancy would be associated with greater and risk of LBW and PTB and cortisol concentrations during the first trimester of pregnancy.

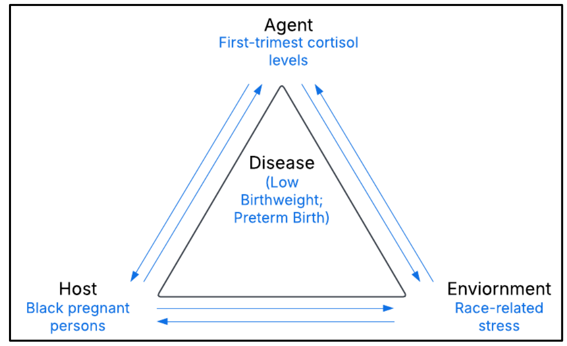

***Figure 1**: A conceptual model the gaps in knowledge*

Materials and Methods

Ethical Oversight: All procedures in the current study were approved by the Institutional Review Board of Emory University.

Study Sample: We leveraged data collected as part of a completed longitudinal cohort study of neuroendocrine mechanisms underlying alterations in psychophysiology during pregnancy (MH115174; PI: Michopoulos). Female participants were recruited from 2018-2022 at random from a pool of patients receiving prenatal care at the Gynecology and Obstetrics clinic at Grady Memorial Hospital (GMH). GMH is a publicly funded, tertiary care center serving a predominantly socioeconomically disadvantaged and racially marginalized inner-city population. Trained staff approached potential participants in the obstetrics clinics regarding potential participation. During the COVID-

19 pandemic, potential participants were identified via electronic medical records and invited to participate via telephone. Inclusion criteria included: singleton pregnancy, between 8-16 weeks' gestation, Black/African American race, English fluency, and between 18 and 40 years old with deliveries at GMH and race-related stress data.

Exclusion criteria included: mental retardation, active psychosis, hospitalization for mental health reasons within the past month, and acute impairment from drugs or alcohol such that they cannot provide informed consent. 192 participants who met inclusion and exclusion criteria were identified and included in the final analysis.

Experimental Design:

We conducted a longitudinal cohort study. Individuals were identified via electronic health record, approached, and screened by clinical research coordinators. Participants who met the inclusion criteria thereafter completed their first study visit in which a clinical interview and surveys were collected, and an initial cortisol measurement was taken. Thereafter, participants completed one study visit per trimester, which were scheduled at the time of their regular clinic visit. During the second and third trimester, cortisol measurements were repeated, and surveys were re-administered.

Measures:

Exposure variables:

Blood collection and cortisol measurement. Cortisol concentrations were collected via blood draw by trained phlebotomists. Participants' blood was drawn at 9:30 AM after a 30-minute rest period to minimize the effects of cortisol variation throughout the day. Participants were told to eat breakfast before the study. Cortisol concentrations were assayed using mass spectrometry at the Emory National Primate Research Center Biomarkers Core[26].

Measure of race-related stress. The Index of Race-Related Stress Brief (IRRS-B) is a 22-item validated[27] measure of the stress associated with specific experiences of racism and discrimination in African Americans. This survey is validated in the Black/African American population thus, only individuals in this racial group were included in the study.

The IRRS-B consists of the following four racism subscales: Cultural Racism, Institutional Racism, Individual Racism, and Collective Racism. A Global Racism measure can also be computed based on a combined score from the four subscales. The IRRS-B requires respondents to indicate whether they have experienced a given racism-related event and the degree of stressfulness on a four-point summated rating scale (0 = event never happen, 1 = event happened but not upset, 2 = event happened, and I was slightly upset, 3 = event happened, and I was upset, and 4 = event happened, and I was extremely upset). The primary independent variable for our data analysis will be Global Racism (range: 0 to 88) with a higher score indicating more race-related stress. The primary exposure was Global Racism and the secondary exposures were: Cultural Racism, Institutional Racism, and Individual Racism.

Outcome variables:

Medical Chart Abstraction for birth weight and gestational age. Medical data was abstracted by a team of trained clinicians. Birth weight and gestational age were abstracted by weight in grams according to the extraction criteria of the International Classification of Diseases v.9 (ICD-9)[28], recently validated for research on preterm and low-weight births. Birth weight and gestational age were analyzed on a continuous scale to preserve the granularity of the data and on a categorical scale to align with clinically meaningful risk thresholds.

Covariates:

Demographic data, and measures of current perceived stress, ongoing trauma exposure, substance use, and any other variables not available for electronic health record abstraction were measured during a structured clinical interview at enrollment.

<u>Statistical Analysis</u>:

We first explored the demographic and descriptive characteristics of those included in our study, stratified by the primary outcome (LBW).

We conducted bivariate analyses to evaluate differences in birthweight and gestational age by IRRS subscales using Pearson's Correlation and t-tests for continuous variables and chi-square (or Fisher's exact test in the event of low cell counts) for categorical variables. To visually assess these relationships, we generated box plots to compare IRRS subscale distributions across LBW status (LBW vs. no LBW) and PTB status

(PTC vs. no PTB) and scatter plots to evaluate distributions across the continuous birthweight and gestational age, identifying a line of best fit.

Third, we used multiple linear regression to further examine the relationship between the exposure and outcome variables on a continuous scale and multiple logistic regression to examine the relationship on a dichotomous scale. These models were controlled for potential confounders which were identified using DAGs informed by literature review (**Figure 2, Figure 3**). The models predicting birthweight were adjusted for the following covariates: age, race, smoking. On the other hand, the models predicting gestational age were adjusted for the following covariates: age, race, insurance

Together, these analyses examine the impact of race-related stress on birthweight and gestational age, both dichotomously and continuously.

For the subgroup analysis, we first examined the relationship between race-related stress subscales and first-trimester cortisol levels using Pearson's Correlation test. Next, we used generalized additive models to flexibility capture nonlinear relationships between IRRS scales and first-trimester cortisol levels while adjusting for the following confounders based on literature review: employment status, age, education, income level, smoking status.

Analyses were conducted using R Studio (Version 2023.06.2+561) using the following packages: dplyr, table1, stats, ggplot2, gam.

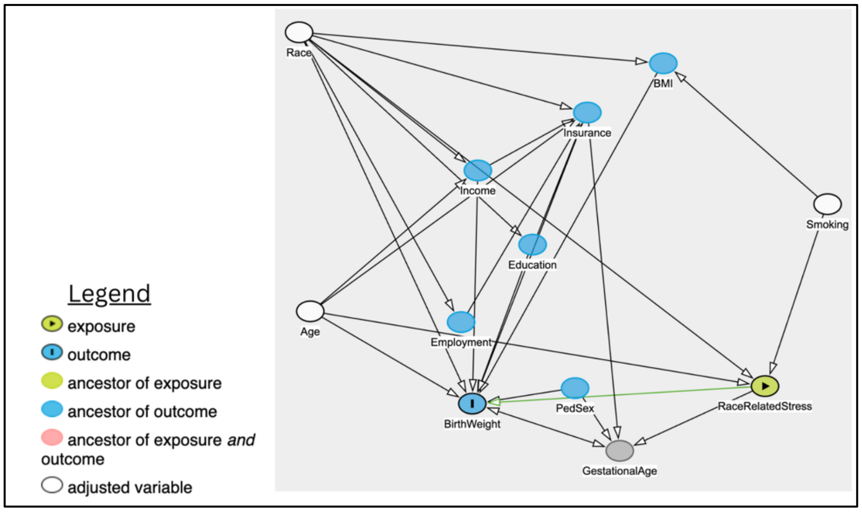

Figure 2: *DAG of factors influencing relationship between race-related stress and birthweight*

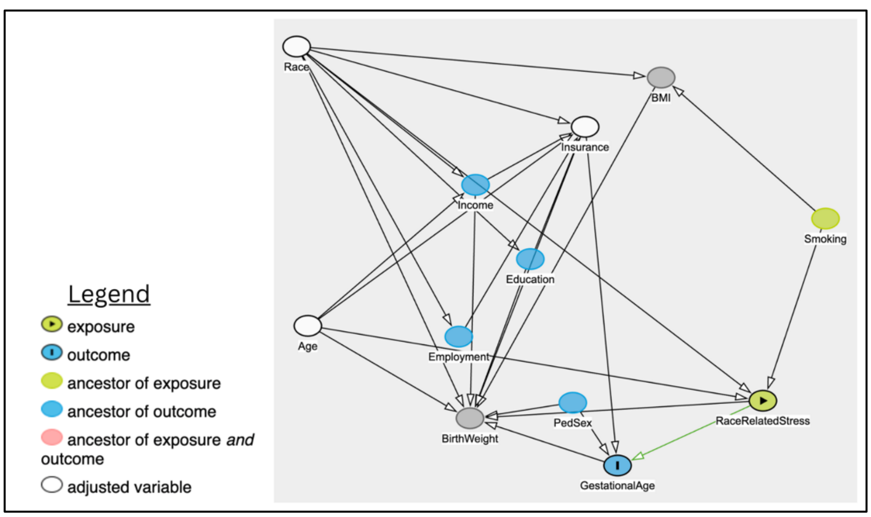

Figure 3: *DAG of factors influencing relationship between race-related stress and gestational age*

Results

Descriptive statistics for the women included in our study are presented in ***Table 1.*** 192 women were included in our study, 36 of which delivered a LBW infant, and 156 participants who delivered infants of normal birthweight. The age of participants ranged from 18 to 40 years old, with the mean age for participants being 27.6 years (SD 5.42). 178 (92.7%) participants identified as non-Hispanic/Latinx. 92 (47.9%) participants reported an income level of more than $999.00 per month, while 38 (19.8%) reported less than $500 per month and 20 (10.4%) reported less than $1,000 per month. 42 (21.9%) did not report an income level. The mean BMI of the cohort was 32.5 (SD 9.37). The normal birthweight cohort had a mean BMI of 32.2 (SD 8.89) and the low birthweight cohort had a mean BMI of 34.1 (SD 11.2), there was not a statistically significant difference between the BMIs of the groups. The study cohort was largely uninsured or underinsured. 143 (74.5%) of participants reported having Medicaid insurance, 18 (9.4%) reported no insurance coverage, and 19 (9.9%) reported having private insurance, with no significant difference in insurance status between the groups. The average number of previous pregnancies was 3.23 (SD 2.17), with no significant difference in number of previous pregnancies between the two groups. The mean global racism score from the IRR-B was 52.3 (SD 22.3). The mean gestational age of participants' infants was 37.5 weeks (SD 2.44 weeks). The mean gestational age of those in the LBW group was 34.2 (SD 3.44 weeks) while those without LBW had a mean gestational age of 38.3 (SD 1.20 weeks), with the difference being statistically significant (p-value: 215e-09). The mean birthweight of the normal birthweight group was 3160 grams (SD 362 grams), while the mean birthweight of the LBW group was 1970 grams (SD 540 grams). The mean birthweight of the entire cohort was 2930 grams (SD 614 grams).

Table 1: *Sociodemographic Characteristics of Study Participants by Low vs. Normal Birth Weight*

Table 1: Sociodemographic Characteristics of Study Participants by Low vs. Normal Birth Weight

	Not Low Birth Weight (N=156)	**Low Birth Weight (N=36)**	**Total (N=192)**
Sex			
Male	0 (0%)	0 (0%)	0 (0%)
Female	156 (100%)	36 (100%)	192 (100%)
Age			
Mean (SD)	27.7 (5.49)	27.4 (5.19)	27.6 (5.42)
Median [Min, Max]	27.5 [18.0, 40.0]	26.5 [18.0, 36.0]	27.0 [18.0, 40.0]
Ethnicity			
Hispanic/Latinx	3 (1.9%)	2 (5.6%)	5 (2.6%)
Not Hispanic/Latinx	146 (93.6%)	32 (88.9%)	178 (92.7%)
Missing	7 (4.5%)	2 (5.6%)	9 (4.7%)
Race			

[1] Low Race-Related Stress refers to an IRRS total score < 51 | [2] Low Birth Weight describes babies born weighing less than 5 pounds, 8 ounces (2500 grams)

<u>Table 1:</u> Sociodemographic Characteristics of Study Participants by Low vs. Normal Birth Weight

	Not Low Birth Weight (N=156)	Low Birth Weight (N=36)	Total (N=192)
African American/Black	149 (95.5%)	36 (100%)	185 (96.4%)
Hispanic/Latino	1 (0.6%)	0 (0%)	1 (0.5%)
Asian	0 (0%)	0 (0%)	0 (0%)
Caucasian/White	0 (0%)	0 (0%)	0 (0%)
Mixed	4 (2.6%)	0 (0%)	4 (2.1%)
Other	2 (1.3%)	0 (0%)	2 (1.0%)
Education Level			
Less than High School	17 (10.9%)	5 (13.9%)	22 (11.5%)
High School or GED	71 (45.5%)	19 (52.8%)	90 (46.9%)
More than HS	67 (42.9%)	12 (33.3%)	79 (41.1%)
Missing	1 (0.6%)	0 (0%)	1 (0.5%)
Income Level			
Less than $500 per month	29 (18.6%)	9 (25.0%)	38 (19.8%)
Less than $1,000 per month	17 (10.9%)	3 (8.3%)	20 (10.4%)
More than $999.00 per month	79 (50.6%)	13 (36.1%)	92 (47.9%)
Missing	31 (19.9%)	11 (30.6%)	42 (21.9%)
BMI			
Mean (SD)	32.2 (8.89)	34.1 (11.2)	32.5 (9.37)

Table 1: Sociodemographic Characteristics of Study Participants by Low vs. Normal Birth Weight

	Not Low Birth Weight (N=156)	Low Birth Weight (N=36)	Total (N=192)
Median [Min, Max]	31.0 [17.0, 64.0]	32.0 [21.0, 71.0]	31.0 [17.0, 71.0]
Missing	2 (1.3%)	1 (2.8%)	3 (1.6%)
Health Insurance			
No	13 (8.3%)	5 (13.9%)	18 (9.4%)
Yes - Medicaid	118 (75.6%)	25 (69.4%)	143 (74.5%)
Yes - Private Insurance	15 (9.6%)	4 (11.1%)	19 (9.9%)
Missing	10 (6.4%)	2 (5.6%)	12 (6.3%)
Previous Pregnancies			
Mean (SD)	3.22 (2.21)	3.31 (2.00)	3.23 (2.17)
Median [Min, Max]	3.00 [1.00, 10.0]	3.00 [1.00, 8.00]	3.00 [1.00, 10.0]
Race-Related Stress Total Score			
Mean (SD)	51.8 (22.5)	54.5 (21.7)	52.3 (22.3)
Median [Min, Max]	49.0 [22.0, 105]	56.0 [22.0, 106]	51.0 [22.0, 106]
Race-Related Stress Individual Score			
Mean (SD)	12.9 (7.11)	14.2 (7.27)	13.1 (7.14)
Median [Min, Max]	10.0 [6.00, 30.0]	12.5 [6.00, 30.0]	10.0 [6.00, 30.0]

Table 1: Sociodemographic Characteristics of Study Participants by Low vs. Normal Birth Weight

	Not Low Birth Weight (N=156)	Low Birth Weight (N=36)	Total (N=192)
Race-Related Stress Institutional Score			
Mean (SD)	10.2 (5.80)	11.7 (5.97)	10.5 (5.84)
Median [Min, Max]	8.00 [6.00, 29.0]	12.0 [6.00, 30.0]	8.00 [6.00, 30.0]
Missing	0 (0%)	1 (2.8%)	1 (0.5%)
Race-Related Stress Cultural Score			
Mean (SD)	28.8 (12.4)	28.9 (11.1)	28.8 (12.1)
Median [Min, Max]	30.0 [10.0, 50.0]	32.0 [10.0, 46.0]	31.0 [10.0, 50.0]
Missing	1 (0.6%)	0 (0%)	1 (0.5%)
Perceived Stress Scale			
Mean (SD)	15.8 (7.39)	15.8 (7.76)	15.8 (7.43)
Median [Min, Max]	15.0 [1.00, 32.0]	15.0 [4.00, 36.0]	15.0 [1.00, 36.0]
Missing	59 (37.8%)	13 (36.1%)	72 (37.5%)
Stressful Life Events in Last 6mo			
Mean (SD)	1.54 (1.65)	1.49 (1.40)	1.53 (1.60)
Median [Min, Max]	1.00 [0, 7.00]	1.00 [0, 5.00]	1.00 [0, 7.00]

Table 1: Sociodemographic Characteristics of Study Participants by Low vs. Normal Birth Weight

	Not Low Birth Weight (N=156)	Low Birth Weight (N=36)	Total (N=192)
Missing	10 (6.4%)	1 (2.8%)	11 (5.7%)
TEI Total Types Trimester 1			
Mean (SD)	3.01 (2.67)	2.53 (2.13)	2.92 (2.58)
Median [Min, Max]	2.00 [0, 10.0]	2.00 [0, 7.00]	2.00 [0, 10.0]
Missing	58 (37.2%)	13 (36.1%)	71 (37.0%)
Pediatric Birth Weight in Grams			
Mean (SD)	3160 (362)	1970 (540)	2930 (614)
Median [Min, Max]	3140 [2500, 4230]	2180 [550, 2480]	3030 [550, 4230]
Pediatric Gestation Age			
Mean (SD)	**38.3 (1.20)**	**34.2 (3.44)**	**37.5 (2.44)**
Median [Min, Max]	39.0 [35.0, 41.0]	35.0 [24.0, 38.0]	38.0 [24.0, 41.0]
Pediatric Sex			
Female	85 (54.5%)	14 (38.9%)	99 (51.6%)
Male	71 (45.5%)	22 (61.1%)	93 (48.4%)

Table 2 depicts the correlations between the different subscales of the IRRS and birthweight and gestational. There was no statistically significant correlation between any IRRS scales/subscales and birthweight or gestational age at the significance level of $p<0.05$.

***Table 2**: Bivariate correlations among IRRS variables, r (p-value)*

	Birthweight	Gestational Age
Global Racism	-0.05 (0.49)	-0.12 (0.79)
Individual Racism	-0.08 (0.25)	-0.04 (0.63)
Institutional Racism	-0.10 (0.15)	-0.09 (0.20)
Cultural Racism	0.00 (0.98)	0.03 (0.81)

Figure 2 and **Figure 3** boxplots depicting the distribution of global, individual, institutional, and cultural race-related stress by birthweight and gestational age.

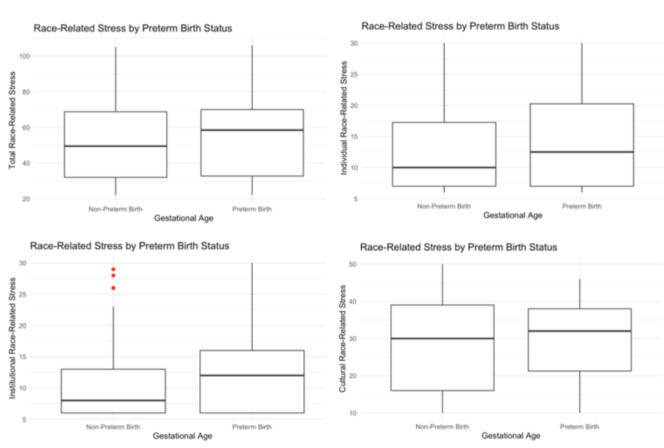

***Figure 4:** Boxplots depicting the distribution of race-related stress by gestational age*

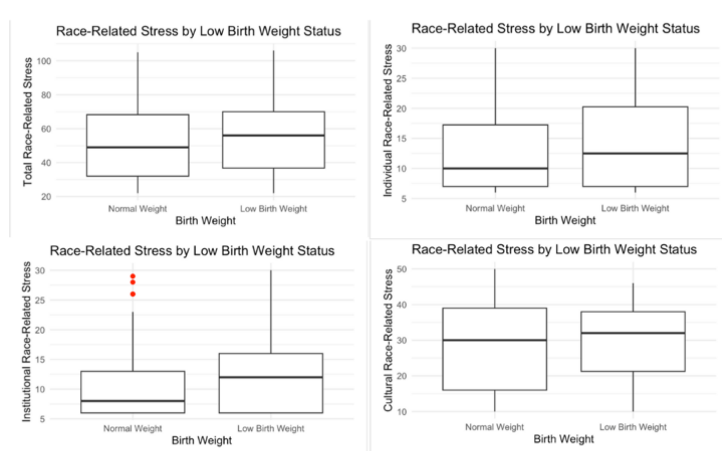

***Figure 5**: Box plots depicting the distribution of race-related stress by birthweight*

Figure 4 and Figure 5 are scatterplots of the correlation between IRRS scales and birthweight and gestational age on a continuous scale, with the line of best fit depicted.

The results of the multiple regression model(s) predicting the outcome is shown in **Table 3**. In these models, there is no significant association between the IRRS scales and the outcome variables. None of the parametric coefficients or interaction terms were significant.

The models predicting birth weight were adjusted for: pediatric gestational age and those predicting gestational age were adjusted for pediatric sex. The models predicting gestational age was adjusted for: age, race, and smoking status, with pediatric sex included as an interaction term. The models predicting birthweg were adjusted for: age, race, and insurance status.

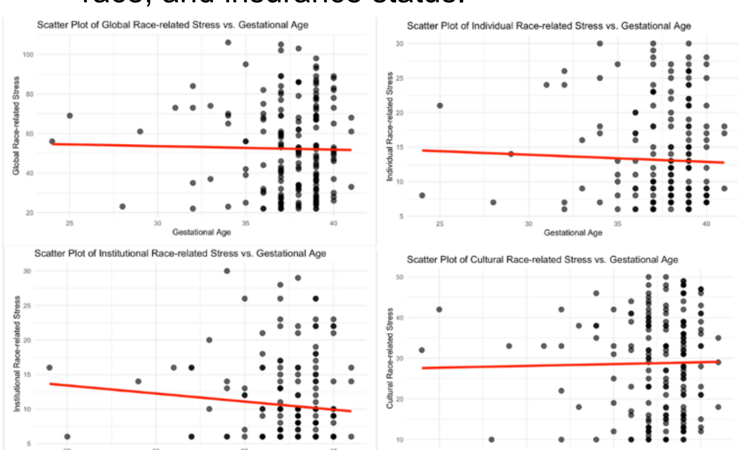

***Figure 7**: Scatter plots of race-related stress vs. gestational age*

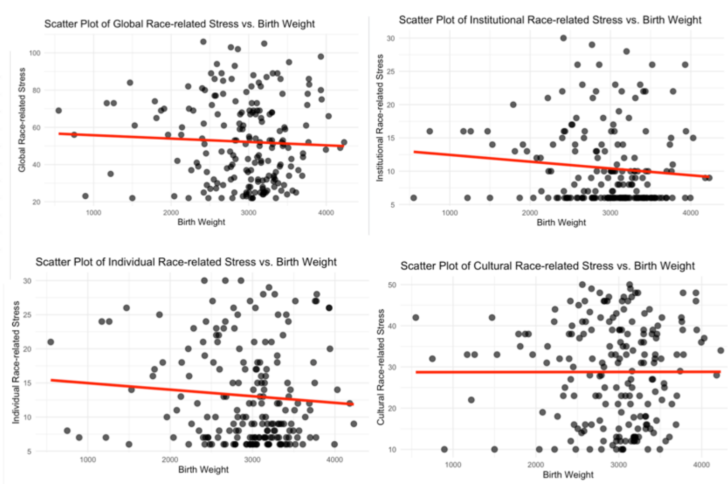

***Figure 6**: Scatter plots of race-related stress vs. birth weight*

__Table 3__: Regressions for outcome variables

Predictor Variables	Beta Coefficient	Standard Error	p-value
3a. Predicting Birthweight as a continuous variable, n= 171			
IRRS – Total	-1.85 grams	3.23	0.57
IRRS – Individual	-1.20 grams	9.94	0.91
IRRS – Institutional	-14.27 grams	11.70	0.22
IRRS – Cultural	-2.29 grams	5.86	0.70
3b. Predicting LBW as a dichotomous variable, n= 171			
IRRS – Total	0.01	0.02	0.56
IRRS – Individual	-0.01	0.05	0.80
IRRS – Institutional	0.06	0.06	0.26
IRRS – Cultural	0.02	0.03	0.54
3c. Predicting Gestational Age as a continuous variable, n= 181			
IRRS – Total	-0.0 weeks	0.01	0.60
IRRS – Individual	-0.02 weeks	0.03	0.51
IRRS – Institutional	-0.05 weeks	0.03	0.10
IRRS – Cultural	6.03e-05 weeks	1.57e-02	1.0
3c. Predicting Gestational Age, as a dichotomous variable n= 182			
IRRS – Total	0.01	0.01	0.30
IRRS – Individual	0.04	0.03	0.18
IRRS – Institutional	0.07	0.03	**0.04***

IRRS – Cultural	0.01	0.02	0.73

Subgroup Analysis

Of the 192 women included in our study, 33 women had first-trimester cortisol levels available. The correlations between race related stress subscales and 1st trimester cortisol were non-linear and non-significant (**Figure 8**).

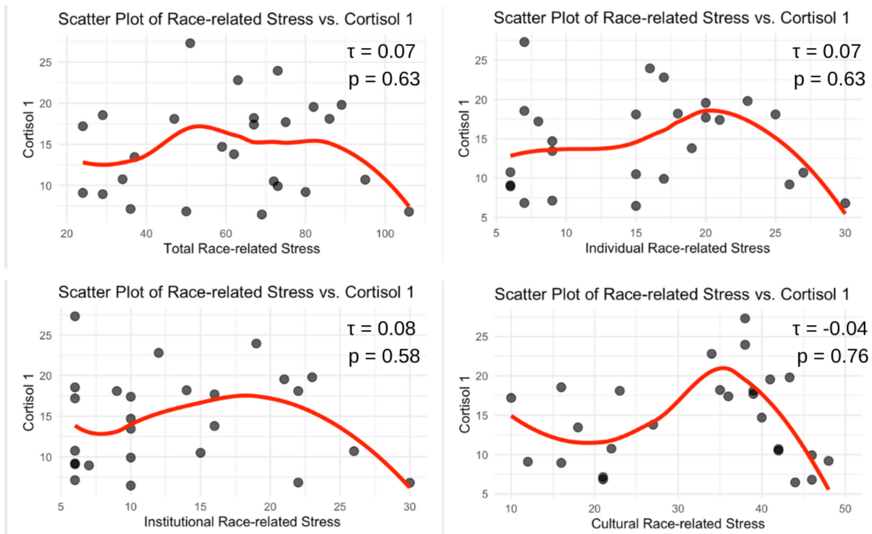

Figure 8: *Scatter plots of race-related stress vs. first-trimester cortisol levels*

The Generalized Additive Models (GAM) predicting cortisol using Global and individual race-related stress and controlling for employment, age, education, income, and smoking status show a non-significant relationship between 1st trimester cortisol and the global racism (p-value = 0.70) and individual racism subscales (p-value = 0.93). However, the GAM for institutional racism shows that effect institutional racism on cortisol levels changes at different levels of cultural race-related stress, rather than following a simple linear pattern. This model displays very significant (p-value = 0.03) non-linear association where institutional racism accounts for 47.4% of the variance in cortisol levels and 74.9% of the deviance. In this model, education, specifically having a GED and being a Technical School Graduate were significant predictors of cortisol levels with p-values of 0.03 and 0.2 respectively. In the model of cultural race-related stress, the association was again highly significant (p-value = 0.02), and the model was a very good fit (r^2 = 0.931, Deviance explained = 99.1%). In this model, income level greater than $999 per month was a significant predictor of cortisol levels (p-value = 0.07), with those in lower income brackets having higher cortisol levels (estimate = -6.92).

Table 4: *Summary of Generalized Additive Models*

GAM Models, n=33				
Family	**Link Function**	**Formula**	**Adjusted R^2**	**Deviance Explained**
Gaussian	Identity	Cortisolµg/dL.1 ~ s(IRRSITotSum1) + employment + age + education + income_three_cat + smoke_tobacco_current	0.331	68.2%
Gaussian	Identity	Cortisolµg/dL.1 ~ s(IRRSInd_sum1) +	0.202	62%

		employment + age + education + income_three_cat + smoke_tobacco_current		
Gaussian	Identity	Cortisolμg/dL.1 ~ s(IRRSInst_sum1) + employment + age + education + income_three_cat + smoke_tobacco_current	0.474	74.9%
Gaussian	Identity	Cortisolμg/dL.1 ~ s(IRRScul_sum1) + employment + age + education + income_three_cat + smoke_tobacco_current	0.931	99.1%
Parametric Coefficients | β estimate (p-value)				
Variable	**Model 1 (GlobalRRS)**	**Model 2 (Individual RRS)**	**Model 3 (Institutional RRS)**	**Model 4 (Cultural RRS)**
Intercept	22.1762 (0.0718)	23.1017 (0.0975)	25.4609 (0.0286*)	9.7586 (0.2486)

Employment: Employed	3.4202 (0.2319)	2.8796 (0.3511)	4.2905 (0.1079)	3.0066 (0.1714)
Age	-0.1863 (0.5215)	-0.2308 (0.4724)	-0.2646 (0.3154)	0.2238 (0.2689)
Education: High School Graduate	-0.2221 (0.9510)	-1.0317 (0.8044)	-0.4329 (0.8928)	3.5335 (0.2212)
Education: GED	-11.6095 (0.1262)	-12.0216 (0.1626)	**-16.3291 (0.0339*)**	-28.9126 (0.0909)
Education: Some College	-6.8033 (0.1880)	-6.1301 (0.2820)	-7.0951 (0.1231)	-8.0620 (0.0633)
Education: Technical School Graduate	-13.3638 (0.0774)	-11.3902 (0.1624)	**-17.5932 (0.0228*)**	-7.6379 (0.0719)
Education: College Graduate	-3.6574 (0.4212)	-3.1807 (0.5294)	-6.4981 (0.1519)	0.5161 (0.8282)
Income: Less than $1,000/month	6.5907 (0.2871)	6.2650 (0.3599)	8.0585 (0.1503)	11.2849 (0.0926)

Income: More than $999/month	-3.7748 (0.3994)	-2.8567 (0.5588)	-5.0411 (0.2223)	**-6.9234 (0.0442*)**
Smoking Tobacco: Yes	6.1924 (0.2299)	5.7532 (0.3148)	6.5203 (0.1584)	23.1770 (0.0660)
Approximate Significance of Smooth Terms				
	Edf	**Ref. df**	**Chi. Sq**	**p-value**
GlobalRRS	1	1	3.056	0.111
Individual RRS	1	1	0.942	0.355
Institutional RRS	1	1	6.591	**0.028***
Cultural RRS	8.401	8.882	13.81	**0.0271***

Discussion & Conclusion

In the current prospective study, we investigated the relationship between race-related stress, birth weight, and gestational age in a cohort of 192 Black pregnant persons recruited at Grady Memorial Hospital in Atlanta, Georgia. Our main aim was to determine if there was an association between race-related stress, LBW, and PTB. Our results show that there was no significant relationship between race-related stress, birthweight, and gestational age when controlling for factors identified by DAG. These findings are not consistent with prior findings showing that perceived racism, both in childhood and adulthood, predicts birthweight, irrespective of medical and sociodemographic control variables [29]. Additionally, accumulating evidence suggests that infants born to Black mothers are more likely to be born LBW and PTB, with stress being a significant contributor [15,17,23,29]. While our findings do not align with prior research linking race-related stress to adverse birth outcomes, the high level of missingness in key variables likely reduced the statistical power of our analysis. This limitation may have contributed to our inability to detect significant associations.

Prior research has found differences in risk for LBW by pediatric sex with females having greater odds of being born LBW[30,31]. Our multivariable regressions predicting LBW included pediatric sex as an interaction term and found no significant difference in LBW status by pediatric sex in our sample. This inconsistency with comparable research may be due to sample size limitations that impacted the statistical power of our analysis. While this relationship is well-established in the existing body of literature, future studies aiming to clarify the role of pediatric sex in risk for LBW ensure adequate power to detect these associations.

We also conducted a subgroup analysis of the relationship between race-related stress and first-trimester cortisol values in 33 Black pregnant persons who had cortisol and race-related stress data. Bivariate correlations using Pearson's Correlation revealed nonsignificant nonlinear relationships between first-trimester cortisol and all IRRS scales. Given these non-linear relationships, GAMs were used to model the relationship between first-trimester cortisol and IRRS cortisol and revealed significant non-linear associations for institutional race-related stress and cultural race-related stress, with education emerging as an important predictor in the model for institutional race-related stress and income emerging as an important predictor in the model for cultural race-related stress. Existing literature shows a significant positive relationship between race-related stress and cortisol. Our results expand on this evidence, suggesting that this association may be strongest for cultural and institutional race-related stress. Though we did not find the relationship between race-related stress and our outcomes to be significant in the current sample, our evidence of the relationship between race-related stress and cortisol supports the work of others which suggests inflammation as a potential mediator to the relationship between race-related stress, LBW, and PTB [33]. This large literature review emphasizes proteome and lipidome profile, telomere shortening, and other markers of systemic inflammation as potential mediators which were not evaluated in the current study and should be examined in further research.

Though our findings are informative, our study has several limitations. Given the overlap of our recruitment period with the COVID-19 pandemic, our sample includes many individuals for whom we did not have IRRS or outcome data, making it likely that we were underpowered to detect a difference amongst this sample of individuals with similar trauma exposure. Missingness in this dataset was handled via listwise deletion, which may not have been sufficient to address this issue. Further research should explore methods of imputation to account for missingness in the outcome data. Similarly, our analysis of the relationship of cortisol and race-related stress only included 33 individuals, which may have resulted in overfitting of the data. Future studies should be well-powered to examine this relationship and should include other markers of systemic inflammation which are associated with increased psychophysiological hyperarousal including C-Reactive Protein (CRP)[34] and the ratio of Interleukin (IL) – 6 and IL-10[35,36] . Additionally, we assessed our aims in a unique sample of individuals recruited at a large safety new hospital who are largely under- or uninsured, making it unlikely that our findings are generalizable to the larger population. However, given that this population of pregnant persons is largely underrepresented in research and at increased risk for the outcomes, the value of this population far outweighs any limitations of generalizability. Lastly, the current study uses a validated survey instrument to assess race-related stress. However, the use of this self-reported tool may have introduced responder bias. To our knowledge, there is no other validated method to assess race-related stress, though promising methods of approximately structural racism are emerging [37,38] and should be employed in future research to minimize potential bias.

To our knowledge, the IRRS has never been employed in Black pregnant persons. This cohort includes Black pregnant persons recruited at a large, public safety new hospital and, thus a unique population of Black pregnant persons with a high incidence of trauma exposure, making this an ideal sample to address the specified aims. Additionally, though data was only available in a small subgroup, our research integrates blood cortisol levels with a subjective survey instrument to get a fuller understanding of this relationship. Previous studies examining this relationship have found that Black women who experience greater lifetime racism had greater CRP response and had higher cortisol stress reactivity with acute racial stressors [39,40] .

However, to our knowledge, no studies have evaluated this relationship in the context of adverse pregnancy outcomes. The results of this study contribute to the growing body of literature seeking to understand racial disparities in risk for LBW and PTB. This study justifies the need for future research to further explore the relationship between race-related stress and adverse pregnancy outcomes. Further research stands to inform clinical practice and guide practices that mitigate risk for LBW and PTB in Black pregnant persons.

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None

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