Full-length Article

Lifetime stressor exposure, systemic inflammation during pregnancy, and preterm birth among Black American women

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ABSTRACT

Although Black American mothers and infants are at higher risk for morbidity and mortality than their White counterparts, the biological mechanisms underlying these phenomena largely remain unknown. To investigate the role that lifetime stressor exposure, perceived stressor severity, and systemic inflammatory markers might play, we studied how these factors were interrelated in 92 pregnant Black American women. We also compared inflammatory marker levels for women who did versus did not go on to give birth preterm. During the early third trimester, women completed the Stress and Adversity Inventory for Adults to assess the stressors they experienced over their lifetime. Women also provided blood samples for plasma interleukin (IL)-6, IL-8, IL-1β, and tumor necrosis factor (TNF)-α quantification. Preterm births were identified by medical record review. Controlling for relevant covariates, there were significant positive associations between average levels of both overall and acute perceived stressor severity and plasma IL-1β levels. Controlling for perceived stress at assessment and exposure to racial discrimination did not affect these results. Mediation models revealed that exposure to more chronic stressors was related to higher plasma IL-1β levels, as mediated by higher average levels of overall perceived stressor severity. Exposure to fewer acute stressors was related to higher plasma IL-1β levels, as mediated by higher average levels of acute perceived stressor severity. Finally, women who went on to give birth preterm had higher levels of plasma IL-6. These data thus highlight the potential importance of assessing and addressing lifetime stressor exposure among mothers before and during maternal-infant care.

1. Introduction

Black American mothers are at greater risk for maternal morbidity and mortality than their White counterparts (Joseph et al., 2021; Thompson & Suter, 2020). Moreover, Black American infants are more than twice as likely to die as compared to White American infants (Ely & Driscoll, 2020; Thompson & Suter, 2020). Despite increasing acknowledgement that “race as biology is fiction, racism as a social problem is real,” (Smedley & Smedley, 2005) racial disparities in pregnancy outcomes have persisted and even widened. Indeed, racism cuts across structures, systems, and individual interactions, shaping the health of Black Americans (Boyd, Lindo, Weeks, & McLemore, 2020). For example, though largely cross-sectional, available data suggest that Black American women are exposed to more life stressors than White women and White and Black men, including racial and gender discrimination but also many other types of stressors (Assari, 2020; Gordon et al., 2020; Gur et al., 2020; Kim, Im, Liu, & Ulrich, 2020; White, Bell, Huang, & Williams, 2020). Black American women are also

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to maternal risk (e.g., by altering immune processes (e.g., Gomes et al., 2019). Further, whereas some data suggest that anxiety during pregnancy receive mental health support with any consequence (American College of Obstetricians and Gynecologists, 2018). Interestingly, though, even when perinatal mental health conditions are treated, risk for pregnancy complications often remain elevated (Snapper, Hart, Venkatesh, Kaimal, & Perlis, 2018; Venkatesh, Ferguson, Smith, Cantonwine, & McElrath, 2019). Such findings suggest that there could be an added benefit to addressing other effects of lifetime stressor exposure that go unrecognized by healthcare providers within the parameters of current clinical practice.

To address this issue, we examined associations among lifetime stressor exposure, lifetime perceived stressor severity, and systemic inflammatory markers during pregnancy among Black Americans, who experience a disproportionate burden of stressors. We also investigated possible differential effects of chronic versus acute stressors. Grounded in the Allostatic Load Framework (McEwen, 1998; McEwen & Seeman, 1999; McEwen, 2007; McEwen & Gianaros, 2010) and informed by Social Safety Theory (Slavich, 2020), we also tested whether associations among stressor exposures and systemic inflammatory markers were mediated by levels of perceived stressor severity, controlling for pertinent covariates (Fig. 1). Finally, we compared levels of prenatal inflammatory markers for women who did versus did not go on to give birth preterm.

Based on the literature summarized above, we hypothesized that greater lifetime stressor exposure and greater perceived stressor severity would be associated with higher levels of systemic inflammatory markers. In addition, we hypothesized that these associations would be strongest for chronic stressors, and, moreover, that perceived stressor severity would mediate the link between stressor exposure and levels of systemic inflammation. Finally, we hypothesized that women who went on to give birth preterm would exhibit higher levels of systemic inflammatory markers than those who did not. We tested these hypotheses in a unique observational cohort study of Black American women who were enrolled early in their third trimester of pregnancy and prospectively followed to enable post-birth medical record review.

2. Method

2.1. Participants

This study was conducted from 2013 to 2015 using a convenience sample of women recruited from a populous Midwestern city during

![Fig. 1. Pathways linking lifetime stressor exposure to systemic inflammatory markers as mediated by lifetime perceived stressor severity. We propose a framework for empirical testing positining that lifetime stressor exposure affects biology relevant to health as mediated by individuals' perceptions of how stressful or threatening a stressor is perceived. In testing this model in the present study, we focused on systemic inflammatory markers that were assessed during pregnancy and the occurrence of preterm birth, while controlling for relevant covariates.](image-url)
prenatal care. Participants were recruited using direct solicitation by a
member of the research team, waiting area flyers, examination room
flyers, flyers posted in community locations (e.g., daycares, community
events), and through electronic recruitment messages (e.g., Research-
Match.org, StudySearch, social media). Since a primary goal of this
research was to address disparities in pregnancy complications wit-
nessed among Black Americans, participants had to self-report as Black,
non-Hispanic, and U.S.-born and raised. Inclusion criteria also included
a current singleton pregnancy, completion of dating and anatomy ul-
trasounds, maternal age 18–34, pre-pregnancy body mass index (BMI)
18.5–39, and self-reported non-smoking status or smoking cessation by
the second trimester. At the time of recruitment, women who reported
receiving a diagnosis of a chronic immune-related condition (e.g.,
chronic hypertension) or major complication of pregnancy (e.g., gesta-
tional diabetes, a gestational hypertensive disorder) during the assessed
pregnancy were not eligible to enroll. However, several women were
diagnosed with complications after enrollment and were retained in
the sample. Women regularly taking medications with immune implications
(e.g., corticosteroids) or self-reporting alcohol or illicit drug use after
the first trimester were excluded.

Of the 96 pregnant women enrolled in this prospective cohort study,
all had complete lifetime stressor and systemic inflammatory marker
data except for three participants. One additional participant was lost
to follow up prior to the completion of pregnancy. This left a final
analytical sample of 92 participants. Due to the study design and
enrollment criteria, all participants were pregnant with one baby \(M =
30 \text{ weeks}, 3 \text{ days} (SD = 10.27 \text{ days}) \) gestation at enrollment and
collection. All participants (100%) self-reported as Black, non-
Hispanic, and U.S.-born. As shown in Table 1, women were primarily
in their twenties (68.48%), employed at least part time (73.91%),
and did not hold private insurance (67.39%). Some women reported
smoking in early pregnancy but quitting by the second trimester (23.91%),
with all other women self-reporting as non-smokers. Mean values for
pre-pregnancy BMI are also shown in Table 1, with 64.13% of women
exhibiting a BMI in the overweight (BMI = 25–29) or obese (BMI > 30)
category. Most participants did not experience a major complication of
pregnancy (e.g., gestational diabetes (0%), gestational hypertension
(9.78%), preeclampsia (3.26%), and preterm birth (7.61%)).

2.2. Data collection
Participants completed a study visit between 28 weeks 0 days and 32
weeks 6 days of pregnancy (i.e., the early third trimester), at which time
the informed consent process was completed and demographic, behav-
ioral, and stressor-related data were collected by self-report and
entered using direct electronic data capture. At the end of the study visit,
whole blood was collected by antecubital or distal venipuncture stan-
dardized to the hours of 1100–1600 to reduce potential for confounding
by diurnal variation (Nilsson, Lekander, Akerstedt, Axelsson, & Ingre,
2016). Sampling time of day was recorded and used as a covariate. If a
participant reported a cold- or flu-like illness, antibiotic use, or
vaccination, the study visit was rescheduled for at least seven days later.
Oral temperature was also measured, with no participants showing signs
of fever. The protocol for the study was approved by The Ohio State
University Biomedical and OhioHealth Institutional Review Boards.
Participants received $50 in gift cards at the study visit.

2.3. Measures

2.3.1. Demographic, behavioral, and clinical characteristics
Demographic (e.g., age, marital status, education, employment sta-
tus, insurance status), behavioral (e.g., smoking status), and clinical (e.
ge., pre-pregnancy weight, parity) characteristics were determined by
self-report using standardized instruments. Height was also measured
to enable calculation of pre-pregnancy BMI. Complications of pregnancy
were determined by manual abstraction of data from a detailed review
of prenatal, labor and delivery, and newborn medical records after
the birth of the baby, including all provider notes.

2.3.2. Lifetime stressor exposure and lifetime perceived stressor severity
Lifetime stressor exposure and lifetime perceived stressor severity
were assessed using the Stress and Adversity Inventory for Adults (Adult
STRAIN) (Slavich & Shields, 2018). The Adult STRAIN is a National
Institute of Mental Health/Research Domain Criteria Initiative-
recommended electronic instrument developed as an efficient and reli-
able method for assessing exposure to acute and chronic stressors
occurring over the entire lifespan (https://www.strainsetup.com). Un-
like investigator-based methods that require several hours for inter-
viewing participants and conducting expert panel consensus ratings, the
Adult STRAIN uses extensive intelligent logic to assess stressors expe-
rienced from the earliest memories of childhood up to the date of
assessment, with an average administration time of approximately 18
min. The Adult STRAIN shows great concurrent, discriminant, and
predictive validity, and excellent test–retest reliability of up to 0.953
over one month, including in primarily female samples (Cazassa, Oli-
veira, Spahr, Shields, & Slavich, 2020; Dooley, Slavich, Moreno, &

2.3.2.1. Stressor exposure versus perceived stressor severity. The Adult
STRAIN (Slavich & Shields, 2018) systematically assesses participants’
exposures to 55 different moderate-to-severe stressors that are known to
substantially affect health. Follow-up questions assess each reported
stressors’ frequency, timing, duration, and perceived severity. The sum
of lifetime stressors endorsed was used for analysis, with higher scores
indicating greater lifetime stressor exposure (possible range = 0–166,
given how frequency is calculated). Participants’ perception of the
severity of each stressor experienced was also assessed using a 0 (very
slightly or not at all) to 5 (extremely) scale (possible range = 0–265).
The sum of perceived stressor severity scores (i.e., “total severity”) and
average of perceived stressor severity scores (i.e., “average severity”)
were used for analysis, with higher scores indicating greater lifetime
perceived stressor severity.

2.3.2.2. Chronic versus acute stressor exposure. The Adult STRAIN sys-
tematically probes for two main types of lifetime stressor exposure: chronic
difficulties and acute life events. Chronic difficulties are persistent stressors that include situations such as prolonged housing,
financial, or marital problems that typically last for at least one month
but are frequently present for several months or years. In contrast, acute
life events are episodic in nature and include situations such as receiving
bad news or getting into an accident. Twenty-nine questions assess
chronic difficulties and 26 questions assess acute life events. Lifetime
stressor exposures and lifetime perceived stressor severity variables
were created for all exposures (i.e., “overall”), for chronic difficulties (i.
e., “chronic”), and for acute life events (i.e., “acute”).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Participant characteristics ((N = 92)).</th>
</tr>
</thead>
<tbody>
<tr>
<td>( M \pm SD )</td>
<td>Count (%)</td>
</tr>
<tr>
<td>Maternal age</td>
<td>26.36 ± 4.47</td>
</tr>
<tr>
<td>Married (yes)</td>
<td>22 (23.91%)</td>
</tr>
<tr>
<td>Bachelor’s degree or greater (yes)</td>
<td>24 (26.09%)</td>
</tr>
<tr>
<td>Employed (yes)</td>
<td>68 (73.91%)</td>
</tr>
<tr>
<td>Private insurance (yes)</td>
<td>30 (32.61%)</td>
</tr>
<tr>
<td>Non-smoker (yes)</td>
<td>70 (76.09%)</td>
</tr>
<tr>
<td>Pre-pregnancy body mass index</td>
<td>28.32 ± 5.71</td>
</tr>
<tr>
<td>Nulliparity (yes)</td>
<td>29 (31.52%)</td>
</tr>
<tr>
<td>Gestational diabetes (yes)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Gestational hypertension (yes)</td>
<td>9 (9.78%)</td>
</tr>
<tr>
<td>Preeclampsia (yes)</td>
<td>3 (3.26%)</td>
</tr>
<tr>
<td>Preterm birth (yes)</td>
<td>7 (7.61%)</td>
</tr>
</tbody>
</table>
2.3.3. Perceived stress at the time of assessment

Perceived stress levels at the time of assessment were quantified using the Perceived Stress Scale (PSS)-14 and used as a covariate (Cohen, Kessler, & Underwood Gordon, 1995). The PSS-14 asks participants to indicate if, over the past month, they have never, almost never, sometimes, fairly often, or very often had each of a possible 14 experiences (e.g., felt difficulties were piling up so high that you could not overcome them). Items are scored from 0 to 4, with reverse scoring applied as appropriate. Higher scores indicate greater perceived stress over the past month, which can range from 0 to 56. The PSS has been widely validated, including during pregnancy (Bann et al., 2017; Zhang et al., 2019). The PSS has an internal consistency of 0.88–0.89 and intraclass correlation of 0.60 across pregnancy (Bann et al., 2017). Higher PSS scores have been related to more perinatal depressive symptoms and poorer perinatal health (Zhang et al., 2019).

2.3.4. Racial discrimination

Exposures to racial discrimination was quantified using the Experiences of Discrimination Scale (EOD) and used as a covariate (Krieger, 1990; Krieger & Sidney, 1996). The EOD asks participants to indicate if, over their lifetime, they have ever experienced discrimination based on their race, ethnicity, or color across nine assessed situations (e.g., at work, getting medical care). If a situation is endorsed, participants are asked to indicate whether the racial discrimination has occurred once, 2–3 times, or 4 or more times. Frequency scores can be calculated, with higher scores indicating greater discrimination exposure. The EOD has an internal consistency of 0.86 and test–retest reliability of 0.70 (Krieger, Smith, Naishadham, Hartman, & Barbeau, 2005). Higher EOD scores have been related to more depressive symptoms among Black American women of childbearing age (Millender et al., 2021).

2.3.5. Systemic inflammation during pregnancy

During the early third trimester study visit, venous whole blood was collected into heparinized vacutainers, placed on ice, and immediately transported to the laboratory for processing. Samples were centrifuged at 1200g at 15 °C for 10 min. Heparinized plasma was aspirated and stored in aliquots at –80 °C until thawed in batches. All plasma cytokine values for this report were determined following first thaw. Plasma levels of the pro-inflammatory cytokines interleukin (IL)-6, IL-8, IL-1ß, and tumor necrosis factor (TNF)-α were determined in duplicate as pg/mL using a multi-spot MSD 4-plex immunoassay and the Sector Imager 2400 per manufacturer instructions (Meso Scale Discovery, Gaithersburg, MD). Briefly, this assay uses electrochemiluminescence to capture and quantify levels of multiple proteins simultaneously. Calculated intra-assay coefficients of variation were 7.1%, 4.0%, 15.5%, and 3.9% for IL-6, IL-8, IL-1ß, and TNF-α, respectively. Calculated inter-assay coefficients of variation averaged across low and mid-calibration curve values, which most closely approximated sample values, were 5.1%, 4.8%, 2.7%, and 9.2% for IL-6, IL-8, IL-1ß, and TNF-α, respectively. Since all plasma cytokine distributions were positively skewed, log transformations were applied to improve the distribution of error terms when plasma cytokines served as dependent variables.

2.3.6. Preterm birth

Cases of preterm birth were identified by manual abstraction of data derived from a detailed review of prenatal and labor and delivery records after the birth of the baby, including all healthcare provider notes. Preterm birth was defined as a birth before 37 weeks 0 days of pregnancy based on the obstetric estimate of due date and actual date of birth. All participants completed a dating ultrasound before 15 weeks of pregnancy, which confirmed or set the estimated due date.

2.4. Data analysis

Participants’ demographic, behavioral, and clinical characteristics were described according to mean and standard deviation or count and frequency as appropriate. Descriptive statistics were generated for the primary variables of interest, and distributions and Spearman rank-order associations were examined.

Next, multivariate multivariable linear regression models were built to examine associations among lifetime stressor exposure, lifetime total and average perceived stressor severity, and log-transformed plasma levels of the key cytokines IL-6, IL-8, IL-1ß, and TNF-α. Subscale analyses were then conducted by repeating the above series of analyses with stressor exposure and perceived stressor severity partitioned into chronic versus acute. To address issues of multiple comparisons when testing these planned, a priori hypotheses, we conducted joint significance testing that investigated associations with all four cytokines simultaneously. To examine whether associations between perceived severity of stressors encountered over the lifetime and levels of systemic inflammatory markers were driven by perceived stress levels at the time of assessment or exposures to racial discrimination, significant models were repeated while adjusting for participants’ PSS-14 and EOD scores.

Based on the associations observed between lifetime stressor exposure, perceived stressor severity, and plasma cytokine levels in the above-described models, potential mediational pathways linking lifetime stressor exposure to plasma cytokine levels through lifetime perceived stressor severity were tested using the PROCESS macro developed by Hayes (2013). Briefly, this macro estimates the effect of a predictor on an outcome without considering a proposed mediator (i.e., total effect), controlling for a proposed mediator (i.e., direct effect), and through a proposed mediator (i.e., indirect effect). Statistical inference for testing of the indirect effect involves constructing 10,000 bias-corrected bootstrap confidence intervals, with replacement. Finally, multivariable linear regression models were built to examine if log-transformed plasma IL-6, IL-8, IL-1ß, or TNF-α levels differed for women who did versus did not go on to give birth preterm.

STATA 15.0 (College Station, TX) was used for the primary analyses. SPSS 27.0 (New York, NY) was used for testing mediation. Significance was set to α = 0.05 for all tests. Post-estimation diagnostics were performed to review assumption satisfaction. Based on data from our laboratory and published studies (Gillespie, Mitchell, Kowalsky, & Christian, 2018; Lam, Chiang, Chen, & Miller, 2021; Nilsonne et al., 2016), we also considered maternal age, socioeconomic status (operationalized as insurance status), smoking status, pre-pregnancy BMI, parity, and sampling time of day as potential confounders and held these covariates constant in all models.

3. Results

3.1. Descriptive statistics and bivariate associations

Spearman rank-order associations among lifetime stressor exposures, lifetime total perceived stressor severity, lifetime average perceived stressor severity, and plasma pro-inflammatory cytokine levels during the early third trimester of pregnancy are shown in Table 2. Median and interquartile ranges for each variable are also presented. Median values and interquartile ranges for plasma cytokine levels among women falling in the low, mid-, and high tertiles for average perceived stressor severity are also shown in Supplemental Table 1.

3.2. Lifetime stressor exposure and lifetime perceived stressor severity

As would be expected, the covariate-adjusted regression models revealed that experiencing more overall, chronic, and acute stressors was associated with higher total overall, chronic, and acute perceived stressor severity (p ≤ 0.001). Interestingly, the covariate-adjusted regression model did not reveal an association between experiencing more overall stressors and participants’ average levels of overall perceived stressor severity [$\beta = 0.008$, SE = 0.006, t(84) = 1.24, p = 0.219]. However, greater chronic stressor exposure was related to experiencing greater average levels of overall perceived...
stressor severity \(\text{Coef.} = 0.047, SE = 0.018, \beta = 0.267, t(84) = 2.65, p = 0.010\) and more acute stressor exposure was related to experiencing lower average levels of acute perceived stressor severity \(\text{Coef.} = -0.033, SE = 0.012, \beta = -0.292, t(84) = -2.67, p = 0.009\).

### 3.3. Lifetime stressor exposure, lifetime perceived stressor severity, and systemic inflammation during pregnancy

Covariate-adjusted multivariate multivariable regression models did not reveal evidence of associations among overall stressor exposure nor total overall perceived stressor severity and plasma levels of IL-6, IL-8, IL-1β, or TNF-α during pregnancy \(p > 0.207\). Likewise, associations were not significant when the effects of chronic and acute stressors were analyzed separately \(p \geq 0.133\).

In contrast, joint tests of significance for covariate-adjusted multivariate regression models revealed that average levels of overall and acute perceived stressor severity were related to plasma cytokine levels \(F(4,83) = 2.5, p = 0.049\) and \(F(4, 83) = 3.28, p = 0.015\), respectively.

Specifically, there was a significant association between greater average levels of overall perceived stressor severity and higher log-transformed plasma IL-1β levels \(\text{Coef.} = 0.168, SE = 0.071, \beta = 0.238, t(84) = 2.34, p = 0.022\). Subscale analyses revealed that this association was significant for average levels of acute perceived stressor severity \(\text{Coef.} = 0.139, SE = 0.061, \beta = 0.230, t(84) = 2.26, p = 0.026\) but not average levels of chronic perceived stressor severity \(\text{Coef.} = 0.050, SE = 0.052, \beta = 0.103, t(84) = 0.97, p = 0.336\). Subscale analyses also revealed an association between greater average levels of acute perceived stressor severity and higher log-transformed plasma IL-8 levels \(\text{Coef.} = 0.117, SE = 0.056, \beta = 0.218, t(84) = 2.09, p = 0.040\).

Given that average levels of perceived stressor severity (but not stressor count nor total perceived stressor severity) were associated with plasma IL-1β and IL-8 levels, it is possible that higher average levels of perceived stressor severity may simply be a reflection of experiencing more perceived stress at the time of assessment. Therefore, we repeated these analyses while controlling for participants’ PSS-14 scores. However, this did not affect the results: higher average levels of overall perceived stressor severity continued to be related to higher plasma IL-1β levels \(\text{Coef.} = 0.159, SE = 0.075, \beta = 0.226, t(83) = 2.14, p = 0.036\); likewise, higher average levels of acute perceived stressor severity continued to predict higher plasma IL-1β levels \(\text{Coef.} = 0.141, SE = 0.061, \beta = 0.234, t(83) = 2.30, p = 0.024\) and IL-8 \(\text{Coef.} = 0.118, SE = 0.056, \beta = 0.221, t(83) = 2.11, p = 0.038\) levels. Moreover, for each of these models, unlike scores from the Adult STRAIN, PSS-14 scores were not significantly related to participants’ plasma pro-inflammatory cytokine levels \(p \geq 0.109\).

In addition, we investigated if average levels of perceived stressor severity over the lifetime were associated with plasma IL-1β and IL-8 levels over and above associations that may be explained by experiencing racial discrimination. To accomplish this, we repeated the above-described analyses while controlling for participants’ EOD scores. However, this did not affect the results: higher average levels of overall perceived stressor severity continued to be related to higher plasma IL-1β levels \(\text{Coef.} = 0.180, SE = 0.072, \beta = 0.254, t(83) = 2.50, p = 0.014\); likewise, higher average levels of acute perceived stressor severity continued to be related to higher plasma IL-1β \(\text{Coef.} = 0.136, SE = 0.062, \beta = 0.225, t(83) = 2.20, p = 0.030\) and IL-8 \(\text{Coef.} = 0.121, SE = 0.056, \beta = 0.227, t(83) = 2.17, p = 0.033\) levels. Similar to the PSS-14, unlike the Adult STRAIN, EOD scores were not significantly related to participants’ plasma pro-inflammatory cytokine levels in each of these models \(p s \geq 0.193\).

### 3.4. Indirect effects of lifetime stressor exposure on systemic inflammation during pregnancy as mediated by average levels of lifetime perceived stressor severity

The above analyses revealed associations among experiencing more chronic stressors and higher average levels of overall perceived stressor severity and, in turn, higher average levels of overall perceived stressor severity and greater plasma IL-1β levels. Because of these findings, we examined the indirect effect of chronic stressor exposure on plasma IL-1β levels as mediated by average levels of overall perceived stressor severity. As shown in Fig. 2, covariate-adjusted tests of mediation revealed an indirect effect of experiencing more chronic stressors on greater plasma IL-1β levels as mediated by higher average levels of overall perceived stressor severity \(\text{ab} = 0.002, 95\% CI 0.002, 0.005\). Covariate-adjusted tests of mediation did not reveal an association between chronic stressors and plasma IL-1β levels without considering the proposed mediator \(\text{total effect: ab} = 0.005, t(85) = 1.24, p = 0.217\) and controlling for the proposed mediator \(\text{direct effect: c'} = 0.003, t(84) = 0.76, p = 0.449\).

The above analyses also revealed associations between experiencing fewer acute stressors and higher average levels of acute perceived stressor severity and, in turn, higher average levels of acute perceived stressor severity and greater plasma IL-1β and IL-8 levels. Therefore, we examined the indirect effects of acute stressor exposure on plasma IL-1β and IL-8 levels as mediated by average levels of acute perceived stressor severity. As shown in Fig. 3, covariate-adjusted tests of mediation revealed an indirect effect of experiencing fewer acute stressors on greater plasma IL-1β levels as mediated by higher average levels of acute perceived stressor severity \(\text{ab} = -0.002, 95\% CI -0.006, 0.002\).
versus did not go on to give birth preterm did not show significantly different log-transformed plasma IL-6 levels during pregnancy, as mediated by average levels of overall and acute lifetime perceived stressor severity among Black American women. These effects remained significant while controlling for both perceived stress at the time of assessment (i.e., PSS-14 scores) and participants’ exposure to racial discrimination (i.e., EOD scores), indicating that experiencing lifetime stressors is predictive over and above the effects attributable to these variables. Moreover, plasma IL-6 levels were higher during the early third trimester among women who did versus did not go on to give birth preterm. These findings thus suggest that assessing lifetime perceived stressor severity may be important for understanding the effects that major life stressors have on health-relevant biology. Although perceived stress, depressive symptoms, and symptoms of anxiety in adulthood are well-established correlates of lifetime stressor exposure (McLoughlin, Fletcher, Slavich, Arnold, & Moore, 2021; Toussaint, Shields, Dorn, & Slavich, 2016), such snapshots of mental health during clinical care fail to provide a comprehensive picture of individuals’ experiences.

We found that Black American women exposed to more chronic stressors experienced higher average levels of overall perceived stressor severity. Higher average levels of overall perceived stressor severity mediated the association between experiencing more chronic stressors and greater plasma IL-1β levels during pregnancy. These findings are consistent with prior research suggesting that chronic stressor exposure may be particularly deleterious, including for immune-related health outcomes (Dhabhar, 2014). For example, individuals managing chronic health conditions often report a progressive toll on their coping capacity, including their ability to manage other stressors (Bryl et al., 2021; Tracy et al., 2021). Individuals in the midst of ongoing crises have reported feelings of demoralization and hopelessness that contributed to their growing emotional distress (Braun-Lewensohn, Abu-Kaf, & Kalagy, 2021; Elnakib et al., 2021). Some psychoeducational interventions are now focusing on empowering participants that are facing chronic stressors, including racial discrimination (Brown et al., 2017; Saban et al., 2021). Preliminary results from these studies suggest potential for health benefits (Brown et al., 2017; Saban et al., 2021), including for immune-related health (Shields, Spahr, & Slavich, 2020).
We also found that Black American women exposed to fewer acute stressors experienced higher average levels of acute perceived stressor severity. Higher average levels of acute perceived stressor severity mediated the association between experiencing fewer acute stressors and having greater plasma IL-1β levels during pregnancy. These findings are interesting and may be consistent with prior research suggesting the potential for a resilience phenotype in which certain stressors build psychological strength and provide biological protection – but only when experienced in limited doses and under certain circumstances (Dooley et al., 2017; Seery, Leo, Lupien, Kondrak, & Almonte, 2013; Shields et al., 2017). For example, undergraduate students exposed to some (versus few or many) lifetime stressors report lower pain intensity during a cold pressor test (Seery et al., 2013). Cancer survivors exposed to some (versus few or many) lifetime acute (but not chronic) stressors report less frequent cancer-related intrusive thoughts and more positive affect (Dooley et al., 2017). Such findings highlight the complexity of the stressor exposure-health link across the life course.

In addition, we found that average levels of perceived stressor severity but not stressor exposure, total perceived stressor severity, or perceived stress at the time of assessment, was associated with plasma IL-1β and IL-8 levels for the pregnant Black American women assessed here. These findings may suggest that levels of inflammatory markers are dynamically regulated by current perceptions of lifetime stressor severity. If that is the case, systemic levels of some inflammatory markers may be particularly susceptible to interventions such as cognitive behavioral therapy, which aims to reframe how individuals think to improve health (Moraes, Miranda, Loures, Mainieri, & Mar-mora, 2018; Shields et al., 2020). Indeed, studies describing the beneficial effects of such therapies is growing and improved immune profiles may be a potential mechanism of action (Lau, Cheng, Wong, Yen, & Cheng, 2021; Pearlstein, Staudenmaier, West, Geraghty, & Cosgrove, 2020). What should also be noted is that this report provides evidence that lifetime stressor exposure appears to shape average levels of perceived stressor severity at recall. Such effects, over time, cannot simply be erased, and personal resilience cannot be expected to replace perceived stressor severity at recall. Such effects, over time, cannot be assumed. Moreover, although several well-known correlates of stress and systemic inflammatory markers (e.g., smoking status, BMI) were included as covariates, some data suggest that health-related behaviors partially mediate associations between stress and health outcomes (e.g., Woods-Giscombe et al., 2021). Focused investigations on such pathways are thus important. Third, although the Adult STRAIN partitions lifetime stressors into chronic difficulties versus acute life events, acute life events can have lasting effects. Indeed, rumination and hyperarousal have been observed following discrete yet traumatic events but were not assessed here (Szabo, Warnecke, Newton, & Valentine, 2017). Fourth, only seven women fit the case definition of preterm birth in this sample. As such, the exploratory nature of these analyses should be acknowledged and replication is required. Finally, this report focused on pregnant Black American women, who reported greater lifetime perceived stressor severity than prior studies of pregnant women completing the STRAIN (Smith et al., 2020). This is consistent with prior research showing that pregnant Black Americans report more lifetime stressors than pregnant White Americans (Malat et al., 2020). However, the difference must also be considered in terms of generalizability.

5. Conclusion

In conclusion, this study provides new data showing that greater lifetime stressor exposure is related to higher levels of the key inflammatory cytokines IL-1β and IL-8 during pregnancy among Black American women and that this association is mediated by average levels of lifetime perceived stressor severity. These findings may point to factors driving the substantial health disparities evident in this population. Furthermore, we found that plasma IL-6 levels were higher among women who did versus did not go on to give birth preterm. These findings are consistent with frameworks such as allostatic load and Social–Emotional–Environmental Theory (McEwen, 1998; McEwen & Seeman, 1999; McEwen, 2007; McEwen & Gianaros, 2010; Slavich, 2020), which posit that an individual’s perceptions of stressor severity over the lifetime is an important process linking stressor exposures and health. These data thus highlight the potential importance of assessing and addressing lifetime stressor exposure among the mother during the provision of prenatal care as well as the societal and institutional inequities that place a disproportionate burden of stress on Black American women.