Title
Maternal subjective social standing is related to inflammation during pregnancy

Authors
Scholaske, Laura
Buss, Claudia
Wadhwa, Pathik D
et al.

Publication Date
2020-08-01

DOI
10.1016/j.bbi.2020.05.023

Peer reviewed

HHS Public Access

Author manuscript

Brain Behav Immun. Author manuscript; available in PMC 2021 August 01.

Published in final edited form as:

Brain Behav Immun. 2020 August ; 88: 711–717. doi:10.1016/j.bbi.2020.05.023.

Maternal subjective social standing is related to inflammation during pregnancy

Laura Scholaske[a,b,c], **Claudia Buss**[a,d], **Pathik D. Wadhwa**[d], **Sonja Entringer**[a,d]

[a]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health (BIH), Institute for Medical Psychology, 10117 Berlin, Germany

[b]Department of Psychology, Humboldt-Universität zu Berlin, Institute of Psychology, Unter den Linden 6, 10099 Berlin, Germany

[c]German Center for Integration and Migration Research, Mauerstr. 76, 10117 Berlin

[d]Development, Health and Disease Research Program, University of California, Irvine, 837 Health Sciences Drive, Irvine, California, 92697, United States

Abstract

Background.—The association of socioeconomic status (SES) with health and disease risk is well established. Low-grade inflammation represents a key pathway believed to underlie this association. Previous research has suggested that subjective social standing (SSS) is more consistently associated with health outcomes than objective measures of SES such as income and education. Given the importance of maternal inflammatory state in a wide array of pregnancy, birth and fetal/child developmental and health outcomes, we examine here the independent association of maternal SSS relative to objective SES with pro-inflammatory state during pregnancy.

Methods.—We conducted a longitudinal study of an ethnically diverse sample of 250 pregnant women with 3 study visits in early, mid and late gestation. We obtained objective measures of SES (income, education), and SSS with reference to the community and to the nation using the MacArthur Scale of Subjective Social Status. At each study visit, a composite maternal pro-inflammatory score was derived from circulating levels of inflammatory markers (IL-6, CRP, TNF-α).

Results.—In hierarchical linear models, SSS but not objective SES was significantly and negatively associated with maternal inflammatory state. Moreover, the relationship between SSS and inflammatory state remained significant after accounting for objective SES. SSS with

Correspondence should be addressed to Sonja Entringer, Institute for Medical Psychology, Charité Berlin, Luisenstr. 57, 10117 Berlin, Germany, phone: +49 30 450 529 216, sonja.entringer@charite.de OR Pathik D. Wadhwa, MD, PhD., Director, UC Irvine Development, Health and Disease Research Program, University of California, Irvine, School of Medicine, 3117 Gillespie Neuroscience Research Facility (GNRF), 837 Health Sciences Road, Irvine, CA 92697, Tel: (949) 824-8238, Fax: (949) 824-8218, pwadhwa@uci.edu.

reference to the community was a stronger predictor of inflammatory state than SSS with reference to the nation.

Discussion.—Our finding adds to the scientific literature on SSS and health, highlights the importance of including SSS measures in this context, and supports future research on the relative role and biological pathways by which SSS may impact pregnancy, birth and fetal/child development and health.

Keywords

inflammation; socio-economic status (SES); subjective social standing; pregnancy

Introduction

Socioeconomic status (SES) is among the most consistent and important determinants of health and disease risk (Braveman, Cubbin, Egerter, Williams, & Pamuk, 2010; J. P. Smith, 2004). Individuals of lower SES are at higher risk for an array of adverse health outcomes, including cardiovascular disease, obesity, diabetes, depression, and lower life expectancy (Everson, Maty, Lynch, & Kaplan, 2002; Kanjilal et al., 2006; Miech & Shanahan, 2000; National Center for Health Statistics, 2012). These health disparities may not only endure over the index individual's lifespan but also may be transmitted across generations via the process of developmental programming (Aizer & Currie, 2014). Offspring of mothers with lower SES have been shown to develop health disparities that manifest by the time of birth itself (e.g., preterm birth, low birth weight; [Parker, Schoendorf, & Kiely, 1994; L. K. Smith, Draper, Manktelow, Dorling, & Field, 2007, and for a review see Blumenshine, Egerter, Barclay, Cubbin, & Braveman, 2010]). Moreover, SES has been shown to partially account for racial/ethnic disparities in the prevalence of adverse developmental, birth and infant/child health outcomes (Culhane & Goldenberg, 2011).

The pathways by which SES impacts health are diverse and include structural barriers to the health care system that emerge as a consequence of financial and educational constraints. In addition, several studies have established that the effects of SES on health also are related to chronic stress that is consequent to lower social standing (Baum, Garofalo, & Yali, 1999). Biological pathways implicated in the chronic activation of the biological stress response such as low-grade inflammation have been proposed to play a key role in the underlying relationships between SES, stress and health. Indeed, several studies have demonstrated that SES is inversely associated with levels of pro-inflammatory markers of the immune system, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α) (Gruenewald, Cohen, Matthews, Tracy, & Seeman, 2009; Hänsel, Hong, Cámara, & von Känel, 2010; Owen, Poulton, Hay, Mohamed-Ali, & Steptoe, 2003; Steptoe, Owen, Kunz-Ebrecht, & Mohamed-Ali, 2002). Several other studies have established that stress-related physiological alterations such as pro-inflammatory state may be antecedents of many of the adverse physical and mental health outcomes related to lower SES (Bertoni et al., 2010; Choi, Joseph, & Pilote, 2013; Li et al., 2018; Liu, Wang, & Jiang, 2017; Raison, Capuron, & Miller, 2006).

Indicators of SES such as income and educational level have also been shown to relate to maternal inflammatory state during pregnancy (Finy & Christian, 2018; Miller et al., 2017). Maternal inflammation during pregnancy represents among the most important determinants of pregnancy complications such as gestational hypertension (Sharma et al., 2018) and preeclampsia (Perucci, Corrêa, Dusse, Gomes, & Sousa, 2017), adverse birth outcomes such as preterm-birth (Romero et al., 2006; Wadhwa, Culhane, Rauh, & Barve, 2001) and low birth weight (Denson et al., 2017), and newborn, infant and child neurodevelopmental and other health outcomes including childhood obesity (Entringer et al., 2012), asthma (Remes, S. T., & Pekkanen, 2005), newborn brain connectivity and working memory (Rudolph et al., 2018), amygdala volume and impulse control (Graham et al., 2018), schizophrenia (Brown & Derkits, 2010; Ellman et al., 2010), cognitive impairment (Rasmussen et. al., 2019), and attention deficit disorder (Instanes et al., 2017). Thus, maternal inflammation during pregnancy likely represents a key pathway by which the effects of maternal socioeconomic disadvantage on health are transferred from one generation to the next (Slopen et al., 2015).

One potential source of stress in the context of lower SES is the subjective perception of one's social standing (Adler, Epel, Castellazzo, & Ickovics, 2000). Kraus and colleagues have proposed a model in which they attribute particular importance to an individual's perceived rank in society for health and disease risk (Kraus, Tan, & Tannenbaum, 2013). They suggest that individuals who perceive their rank position as lower than that of others experience less predictability and controllability of their social environment (Keltner, Gruenfeld, & Anderson, 2003), and consequently more social constraint, helplessness, and uncertainty (Hemingway, Nicholson, Stafford, Roberts, & Marmnot, 1997; Sapolsky, 2005) – that is, psychological distress, – whereas individuals who perceive their rank position as higher than others experience greater autonomy due to a feeling of more predictability and controllability of the environment. These authors propose that individuals draw information on their rank position involuntarily from chronic societal and situation-specific characteristics in social interactions, whereby social comparisons carry weight. According to social comparison theory, proximity is a relevant criterion for choosing a comparison group, such that individuals are more likely to compare themselves with groups that are closer to them (e.g., neighborhood) than with those far away or too abstract (e.g., nation) (Zell & Alicke, 2010).

Consistent with this model, a number of studies have reported that perceived rank position is a more consistent predictor of health-related outcomes than objective SES measures (Euteneuer, 2014), even when adjusting for objective SES. A commonly used measure of perceived rank position is the *MacArthur Scale of Subjective Social Status* or "social ladder scale," wherein participants are asked to indicate their perceived position on a ladder in which people who have most money, most education and best jobs are at the top rung of the ladder, whereas people with the least money, least education and worst or no jobs are at the bottom of the ladder. Respondents are instructed to reference their status relative to either others in their own community ("community subjective social status") or to others in the nation in which they live ("nation subjective social status"). This scale was introduced by Adler et al. (2000) and high test-retest reliability and predictive utility were established (Operario, Adler, & Williams, 2004).

Several studies have reported that after adjusting for objective measures of SES (i.e., income, education, occupational status) measures of subjective social status are related to a broad range of health outcomes, including psychological functioning, depression, cardiovascular parameters, diabetes, sleep, body fat distribution, and cortisol habituation to repeated stress (Adler et al., 2000; Demakakos, Nazroo, Breeze, & Marmot, 2008; Singh-Manoux, Marmot, & Adler, 2005). However, only few studies have addressed the role of subjective social status in the context of pregnancy and pregnancy-related outcomes. There is some evidence that subjective social status is related to self-rated health, physical functioning, depression and smoking status during pregnancy (Maxson, Edwards, Ingram, & Lynn Miranda, 2012; Ostrove, Adler, Kuppermann, & Washington, 2000; Stewart, Dean, Gregorich, Brawarsky, & Haas, 2007). In one study (Finy & Christian, 2018), the association of maternal SES (income, educational level, perceived social class) with inflammation during pregnancy was shown, however, the effects of objective and subjective measures have not been disentangled.

To sum up, subjective social standing appears to be a more consistent predictor of health outcomes than objective SES and also has been associated with pro-inflammatory status in non-pregnant adults. However, its role in the context of pregnancy and in the intergenerational transmission of health disparities is poorly understood. Therefore, the aim of our study was to examine the relationships between objective SES and subjective social standing with maternal inflammation during pregnancy in an ethnically diverse population. We tested the hypotheses that:

1) subjective social standing (SSS) is inversely related to levels of maternal systemic inflammation during pregnancy;

2) the relationship between SSS and inflammation during pregnancy remains significant after adjusting for objective SES; and

3) SSS with reference to the community is a stronger predictor of inflammation during pregnancy than SSS with reference to the nation.

We also sought to determine whether the hypothesized relationships between maternal SSS / objective SES and maternal inflammation during pregnancy persist over and beyond that of various potential SES-related psychological, biophysical and behavioral sequelae during pregnancy by controlling for maternal race/ethnicity, body mass index (Christian & Porter, 2014), stress and depressive symptoms (Christian, 2014; Christian, Franco, Glaser, & Iams, 2009).

Methods

Sample

The study sample consisted of $N = 250$ pregnant women with singleton, intrauterine pregnancies who were participants in a prospective cohort study at the University of California, Irvine, Development, Health and Disease Research Program. Exclusion criteria were uterine anomalies, pre-existing major medical co-morbidities (hypertension, infection or diabetes), use of antenatal systemic corticosteroids, antenatal administration of glucocorticoids, or illicit drug use. Subjects who developed obstetric conditions during the

course of the study were not excluded, but we adjusted our statistical analyses for the occurrence of obstetric risk conditions in the index pregnancy in (see below).The study comprised three visits during pregnancy at 9-17 (T1, early pregnancy), 18-24 (T2, mid pregnancy) and 29-35 weeks gestation (T3, late pregnancy). Sample characteristics are presented in Table 1. The study was approved by the UC Irvine Institutional Review Board, and all participants provided written, informed consent.

Measures

Maternal pro-inflammatory composite score (based on IL-6, TNF-α, CRP).— Maternal antecubital venous blood samples were collected at each study visit in serum tubes (BD Vacutainer). Blood samples were collected at each of the three study visits in the morning between 7:30 and 9:00 am. Blood samples were allowed to clot for 30 minutes at room temperature and were centrifuged at 4 °C at 1500 x g. Serum was then separated and stored at −80 °C. IL-6 concentrations were determined using a commercial high sensitivity ELISA (eBioscience) with a sensitivity of 0.03 pg/ml. The intra- and inter-assay coefficients of variability for IL-6 measurements were 10% and 14% respectively. TNF-α concentrations were quantified using a commercial Multiplex Bead-Based Kit, the V-PLEX Proinflammatory Panel 1 (10-Plex, Milliplex MAP Human Cytokine/Chemokine Kit; Millipore, Billerica, MA, USA) in accordance with the kit-specific protocols provided by the manufacturer. Assay sensitivity was 3.2 – 10000 pg/mL. The assay yielded reliable values for the assessed cytokines: coefficient of variation (*CV*)<2.97, lower limit of detection (LLD)=0.06 pg/mL. Plates were read on a Luminex FLEXMAP 3D System and analyzed using xPONENT® software (Luminex). CRP concentrations were determined using a commercial IMMULITE® 2000 High Sensitivity CRP with a sensitivity of <3mg/L.

Inflammation z-score.—A composite maternal pro-inflammatory score was derived from the cytokine concentrations (IL-6, CRP, TNF-α) at each of the three pregnancy visits (see, e. g., Hostinar, Lachman, Mroczek, Seeman, & Miller, 2015; Miller, Brody, Yu, & Chen, 2014). First, values of the pro-inflammatory markers were each winsorized by three standard deviations to bring outliers closer to the mean and normalize the distribution. The values of IL-6, CRP and TNF-α were then converted into z-scores. Finally, the z-scores were averaged into an inflammation z-score for each pregnancy assessment time point when data on at least one of the three markers was available (see Appendix, Table 2 for proportion of inflammation z-scores based on 1, 2 or 3 markers per study visit).

Objective SES.—Maternal sociodemographic characteristics were obtained via a standardized structured interview at T1. Maternal objective SES was defined as a combination (mean) of maternal educational level (originally assessed in categories from *less than high school* to *advanced degree (master's/doctorate)* and then recoded into values from 1 through 5: 1- "less than high school", 2 - "high school degree", 3 - "partial college or specialized training", 4 - "associates or bachelors degree", and 5 - "advanced degree) and household income (originally assessed in categories from ≤ *15,000$* to ≥ *100,000$* and then recoded into values from 1 through 5: 1 - below $15,000, 2 - $15,000-$29,999, 3 - $30,000-$49,999, 4 - $50,000-100,000, and 5 - over $100,000).

Subjective social status (SSS).—Community and nation subjective social status (SSS) were assessed at T1 with the *MacArthur Scale of Subjective Social Status* (Adler et al., 2000). Participants indicated their position with reference to their community and to the nation separately on a ladder given that people who have most money, most education and best jobs are at the top of the ladder while people with least money, least education and worst or no jobs are on the bottom of the ladder. The ladder comprised a scale of rung J (1, lowest position) to rung A (10, highest position).

Covariates.—The statistical models were adjusted for race/ethnicity, body mass index (BMI) at each study visit and gestational age at the time of blood collection. Race/ethnicity was coded as follows: 0, “White non-Hispanic”, 1, “Hispanic” (incl. White, Black, Asian, Multi races and other Hispanic), 2, “Other non-Hispanic” (incl. Black, Asian, Multi races and other non-Hispanic). BMI reflects the maternal current BMI at the respective study visit. In addition, models were adjusted for psychological distress and depressive symptoms during the past four weeks. These were captured by the scale mean scores of the perceived stress scale (PSS) (Cohen, Kamarck, & Mermelstein, 1983) and the Center for Epidemiologic Studies Depression Scale (CESD) (Radloff, 1977) that were administered at each of the three study visits.

Data analysis

Correlations among and between the cytokines were computed, and t-tests were calculated to test for differences in cytokine levels between T1 and T3. Hierarchical linear models (HLM) (e.g. Long, 2012) with random intercepts and fixed slopes that account for the longitudinal data structure were used to quantify the associations between SES / SSS measures and inflammation across pregnancy. Models were fitted with maximum likelihood estimation that is an adequate strategy for dealing with missing values. Missing values were 0.80% in the subjective social standing measures and ranged between 11.60% and 18.80% in the repeatedly measured inflammation score. Repeatedly measured inflammation was the outcome variable, and the intra-class correlation of inflammation suggested that 66.23% of the overall variance in inflammation was between-person variance. The main predictors were community SSS, nation SSS, objective SES (level-2), and all models were adjusted for ethnicity (level-2), and BMI (level-1), gestational age (level-1), PSS (level-1) and CESD (level-1) at measurement. All metric predictors and covariates were grand-mean centered to a mean of 0. Model M1 included the covariates and community SSS, and model M2 included objective SES in addition. Model M3 included the covariates and nation SSS, and objective SES was added to this in model M4. Fit indices of the models were provided for model comparisons, and a χ^2-difference value was derived for comparisons of the models M1 vs. M2 and M3 vs. M4. HLM analyses were run in R using the lme4-package (R Core Team, 2017). Fit indices (AIC, BIC) and Pseudo R^2 indicating explanation of variance by fixed effects are reported for each model.

Results

Descriptive statistics of the cytokine concentrations and the inflammation z-score as well as SSS and objective SES are displayed in Table 1. For each cytokine, the concentrations were

correlated across the three study visits (IL-6: all $r \geq .55$, all $p < .001$; CRP: all $r \geq .72$, all $p < .001$, TNF-α: all $r \geq .41$, all $p < .001$; inflammation z-score: all r ≥ .63, all $p < .001$; for detailed information see Supplement Table 1). Furthermore, cytokines were correlated between each other at every measurement (IL-6 and CRP: all $r \geq .44$, all $p < .001$; IL-6 and TNF-α: all $r \geq .21$, all $p < .01$; CRP and TNF-α: all $r \geq .20$, all $p < .01$; see Supplement Table 1). T-tests indicated that IL-6 and TNF-α significantly increased from T1 to T3, whereas CRP and the inflammation z-score did not significantly change across pregnancy (IL-6: $t(357.26) = -5.06$, $p = .001$; CRP: $t(305) = 0.70$, $p = 0.484$; TNF-α: $t(365.61) = -2.41$, $p = .016$; inflammation z-score: $t(410.95) = 0.37$, $p = 0.712$). The correlations between SSS measures and objective SES were moderate (community and nation SSS: $r = .48$, $p < .001$; community SSS and objective SES: $r = -0.35$, $p < .001$; nation SSS and objective SES: $r = -0.39$, $p < .001$). Ethnicity was not significantly associated with inflammatory levels, however, the different ethnic groups differed in their levels of objective SES and SSS: Hispanic women had significantly lower objective SES ($t(190.44) = 8.00$, $p < .001$), community SSS ($t(194.31) = 3.60$, $p < .001$) and nation SSS ($t(195.85) = 2.73$, $p < .01$) when compared to White non-Hispanic women. There were no significant group differences regarding SES and SSS between White non-Hispanic and other non-Hispanic women.

Lower community SSS was related to higher inflammation z-score (see Figure 1). This relationship was significant in the hierarchical linear models (model M1), and this association remained significant after adjusting for objective SES (model M2). The coefficient of community SSS indicated that each unit decrease in community SSS was associated with a 0.08 unit increase in the inflammation z-score. Pseudo R^2 and fit indices were approximately equal in model M1 and M2, suggesting that objective SES did not explain further variance and did not improve the model fit. The insignificant χ^2-value of the model comparison between M1 and M2 substantiates that there were no major differences between the two models. Similar results emerged for the relationship between nation SSS and the inflammation z-score. Lower nation SSS was associated with higher inflammation z-score (see Figure 2). This association was significant (model M3), also after adjusting for objective SES (M4). The coefficient of nation SSS indicated that the inflammation z-score increased by 0.06 units with every unit decrease in nation SSS. Pseudo R^2 and fit indices were also about equal in model M3 and M4 and the χ^2-value of the model comparison was insignificant, suggesting no improvement of the model by adding objective SES. Objective SES was not significantly related to the inflammation z-score (M2, M4). The coefficients of community SSS were slightly higher compared to the coefficients of nation SSS. However, Pseudo R^2 was only marginally higher in the models with community SSS compared to the models with nation SSS, and fit indices were about the same in all of the four models.

Discussion

In the current study, lower subjective social standing (SSS) was related to higher inflammation during pregnancy, even after adjusting for objective socioeconomic status (SES) and current levels of stress and depressive symptoms. Furthermore, community SSS was a slightly stronger predictor for inflammation during pregnancy than nation SSS.

To our knowledge, this is the first study to investigate the link between subjective measures of SES and inflammation during pregnancy. We replicated findings from previous studies in non-pregnant adults that suggested that indicators of SES were related to pro-inflammatory markers (Finy & Christian, 2018; Miller et al., 2017), and our findings are in line with previously reported observations that SSS is a relevant and even stronger predictor for health outcomes than objective SES measures (Euteneuer, 2014).

Our findings support the notion that adverse experiences in the context of low SES are biologically embedded via pro-inflammatory processes. Among the key mediators believed to underly the link between low SES/SSS and inflammation are stress-related dysregulations of the hypothalamic-pituitary-adrenal (HPA-) axis and health-related behaviors (Hostinar et al., 2015). In response to acute stress, glucocorticoids (cortisol in humans) are released upon activation of the HPA-axis. When glucocorticoids bind to glucocorticoid receptors in immune cells (i.e., monocytes, macrophages), they inhibit the release of pro-inflammatory cytokines (Irwin & Cole, 2011). This immunosuppressive and anti-inflammatory effect helps to downregulate the potentially adverse effects of an accelerated immune response in the organism that is stimulated under acute stress through the activation of the autonomic nervous system. However, chronic stress leads to a prolonged activation of the HPA-axis, which may result in resistance of the glucocorticoid receptors in the immune cells (referred to as glucocorticoid receptor resistance, GCR) (Cohen et al., 2012) and therefore failure to down-regulate inflammatory responses via endogenous cortisol. As a result, higher levels of inflammation emerge under conditions of chronic stress that may play an important role in the onset and progression of a wide range of stress-related diseases. Our results suggest that the association between lower subjective social standing and proinflammatory state was independent of current perceived stress and depressive symptoms, suggesting that other factors that are associated with lower social standing my play additional roles in mediating the observed relationship. These include for example unhealthy dietary patterns, smoking, alcohol and substance abuse that are associated with a pro-inflammatory status in the individual (Hagger-Johnson, Mõttus, Craig, Starr, & Deary, 2012; Raposa, Bower, Hammen, Najman, & Brennan, 2014). Future studies with larger sample sizes should assess all these factors in a comprehensive way and test the various mediating and moderating pathways of SES-related psychological, biophysical and behavioral sequelae.

Based on our and previous findings, SSS seems to be a better predictor for health related outcomes than objective SES. The perception of lack of predictability and controllability of the social environment, social constraint, helplessness, and uncertainty that is associated with low SSS seems to carry more weight in the relationship between social status and health than do actual socioeconomic resources. Objective SES, as based on income and education, was not related to maternal inflammation in our sample, although previous studies showed this relationship in pregnant women (Finy & Christian, 2018; Miller et al., 2017) as well as non-pregnant individuals (Gruenewald et al., 2009; Hänsel et al., 2010; Owen et al., 2003; Steptoe et al., 2002). These studies included samples with more variation in the lower range of SES compared to our sample, which may explain why we did not replicate this association in the current study.

With reference to social comparison theory which argues that individuals compare themselves more likely with groups that are closer to oneself (i.e., have a higher proximity) (Zell & Alicke, 2010) we hypothesized that community SSS will be a better predictor of inflammation than nation SSS. Although a previous meta-analysis could not show significant differences in the predictability of health outcomes by community vs. nation SSS (Zell et al.,2018) , our analyses confirmed this hypothesis. As the community is more proximate, it might constitute a more relevant comparison group to the individual and therefore may be more closely related to stress-related biological alterations than comparison to a more abstract group like the whole nation.

Some limitations of our study have to be noted. First of all, our study design does not permit any causal inferences regarding the role of SSS in inflammation. However, our hypotheses are based on conceptual and biological plausibility, and evidence from previously published studies. In addition, our study sample comprised a low-risk sample with a normative range of inflammatory markers. The variation in birth outcomes (e.g., gestational age at birth, birth weight) was therefore limited in our sample, and we were unable to investigate the potential mediating role of inflammation on the link between maternal SSS and birth as well as infant and child health outcomes.

To conclude, lower subjective social status was related to higher levels of inflammation (indicated by a composite inflammatory score of CRP, IL-6, TNF-α) in an ethnically diverse low-risk sample of pregnant women after adjusting for objective measures of socioeconomic status. These findings support the notion that subjective SES is a reliable predictor of health conditions, thereby highlighting the role of the perceived psychological burden of low social standing in the biological embedding of SES. The findings furthermore support the notion that maternal inflammation during pregnancy may be a key pathway by which the adverse effects of maternal low SES are transferred from one generation to the next. Altogether, this study adds evidence to the role of subjective SES in the intergenerational transmission of health disparities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The preparation of this manuscript was supported by German Research Foundation (DFG) grant EN 851/2-1 to Sonja Entringer and National Institutes of Health (NIH) grant R01 MD-010738 to Sonja Entringer and Pathik D. Wadhwa.

References

Adler NE, Epel ES, Castellazzo G, & Ickovics JR (2000). Relationship of Subjective and Objective Social Status With Psychological and Physiological Functioning: Preliminary Data in Healthy White Women. Health Psychology, 19(6), 586–592. 10.1037/0278-6133.19.6.586 [PubMed: 11129362]

Aizer A, & Currie J (2014). The intergenerational transmission of inequality: Maternal disadvantage and health at birth. Science, 344(6186), 856–861. 10.1126/science.1251872 [PubMed: 24855261]

Baum A, Garofalo JP, & Yali AM (1999). Socioeconomic status and chronic stress. Does stress account for SES effects on health? Annals of the New York Academy of Sciences, 896, 131–144. 10.1111/j.1749-6632.1999.tb08111.x [PubMed: 10681894]

Bertoni AG, Burke GL, Owusu JA, Carnethon MR, Vaidya D, Graham Barr R, … Bertoni AG (2010). Inflammation and the Incidence of Type 2 Diabetes: the Multi-Ethnic Study of Atherosclerosis (MESA). Diabetes Care, 33(4), 804–810. [PubMed: 20097779]

Blumenshine P, Egerter S, Barclay CJ, Cubbin C, & Braveman PA (2010). Socioeconomic disparities in adverse birth outcomes: A systematic review. American Journal of Preventive Medicine, 39(3), 263–272. 10.1016/j.amepre.2010.05.012 [PubMed: 20709259]

Braveman PA, Cubbin C, Egerter S, Williams DR, & Pamuk E (2010). Socioeconomic Disparities in Health in the United States: What the Patterns Tell Us. American Journal of Public Health, 100(Suppl. 1), 186–196. 10.2105/AJPH.2009.166082

Brown AS, & Derkits EJ (2010). Prenatal Infection and Schizophrenia: A Review of Epidemiologic and Translational Studies. American Journal of Psychiatry, 167, 261–280. 10.1176/appi.ajp.2009.09030361 [PubMed: 20123911]

Choi J, Joseph L, & Pilote L (2013). Etiology and Pathophysiology/Obesity Comorbidities Obesity and C-reactive protein in various populations: a systematic review and meta-analysis. Obesity Reviews, 14, 232–244. 10.1111/obr.12003 [PubMed: 23171381]

Christian LM (2014). Effects of stress and depression on inflammatory immune parameters in pregnancy. American Journal of Obstetrics and Gynecology, 211(3), 275–277. 10.1016/j.ajog.2014.06.042 [PubMed: 24956551]

Christian LM, Franco A, Glaser R, & Iams JD (2009). Depressive symptoms are associated with elevated serum proinflammatory cytokines among pregnant women. Brain, Behavior, and Immunity, 23(6), 750–754. 10.1016/j.bbi.2009.02.012

Christian LM, & Porter K (2014). Longitudinal changes in serum proinflammatory markers across pregnancy and postpartum: Effects of maternal body mass index. Cytokine, 70(2), 134–140. 10.1016/jxyto.2014.06.018 [PubMed: 25082648]

Cohen S, Janicki-Deverts D, Doyle WJ, Miller GE, Frank E, Rabin BS, & Turner RB (2012). Chronic stress, glucocorticoid receptor resistance, inflammation, and disease risk. Proceedings of the National Academy of Sciences of the United States of America, 109(16), 5995–5999. 10.1073/pnas.1118355109 [PubMed: 22474371]

Cohen S, Kamarck T, & Mermelstein R (1983). A Global Measure of Perceived Stress. Source Journal of Health and Social Behavior, 24(4), 385–396.

Culhane JF, & Goldenberg RL (2011). Racial Disparities in Preterm Birth. Seminars in Perinatology, 35(4), 234–239. 10.1053/j.semperi.2011.02.020 [PubMed: 21798403]

Demakakos P, Nazroo J, Breeze E, & Marmot M (2008). Socioeconomic status and health: the role of subjective social status. Social Science & Medicine, 67(2), 330–340. 10.1016/j.socscimed.2008.03.038 [PubMed: 18440111]

Denson LA, McDonald SA, Das A, Schendel DE, Skogstrand K, Hougaard DM, … Ehrenkranz RA (2017). Early Elevation in Interleukin-6 is Associated with Reduced Growth in Extremely Low Birth Weight Infants. American Journal of Perinatology, 34(3), 240–247. 10.1055/s-0036-1585419 [PubMed: 27455401]

Ellman LM, Deicken RF, Vinogradov S, Kremen WS, Poole JH, Kern DM, … Brown AS (2010). Structural brain alterations in schizophrenia following fetal exposure to the inflammatory cytokine interleukin-8. Schizophrenia Research, 121(1–3), 46–54. 10.1016/j.schres.2010.05.014 [PubMed: 20553865]

Entringer S, Buss C, Swanson JM, Cooper DM, Wing DA, Waffarn F, & Wadhwa PD (2012). Fetal programming of body composition, obesity, and metabolic function: The role of intrauterine stress and stress biology. Journal of Nutrition and Metabolism, 2012, 1–16. 10.1155/2012/632548

Euteneuer F (2014). Subjective social status and health. Current Opinion in Psychiatry, 27(5), 337–343. 10.1097/YC0.0000000000000083 [PubMed: 25023883]

Everson SA, Maty SC, Lynch JW, & Kaplan GA (2002). Epidemiologic evidence for the relation between socioeconomic status and depression, obesity, and diabetes. Journal of Psychosomatic Research, 53, 891–895. [PubMed: 12377299]

Finy MS, & Christian LM (2018). Pathways linking childhood abuse history and current socioeconomic status to inflammation during pregnancy. Brain, Behavior, and Immunity, 74, 231–240. 10.1016/J.BBI.2018.09.012

Graham AM, Rasmussen JM, Rudolph MD, Heim CM, Gilmore JH, Styner M, … Buss C (2018). Maternal Systemic Interleukin-6 During Pregnancy Is Associated With Newborn Amygdala Phenotypes and Subsequent Behavior at 2 Years of Age. Biological Psychiatry, 83, 109–119. 10.1016/j.biopsych.2017.05.027 [PubMed: 28754515]

Gruenewald TL, Cohen S, Matthews KA, Tracy R, & Seeman TE (2009). Association of socioeconomic status with inflammation markers in black and white men and women in the Coronary Artery Risk Development in Young Adults (CARDIA) study. Social Science & Medicine, 69(3), 451–459. 10.1016/J.S0CSCIMED.2009.05.018 [PubMed: 19524346]

Hagger-Johnson G, Mõttus R, Craig LCA, Starr JM, & Deary IJ (2012). Pathways from childhood intelligence and socioeconomic status to late-life cardiovascular disease risk. Health Psychology, 31(4), 403–412. 10.1037/a0026775 [PubMed: 22309883]

Hänsel A, Hong S, Cámara RJA, & von Känel R (2010). Inflammation as a psychophysiological biomarker in chronic psychosocial stress. Neuroscience and Biobehavioral Reviews, 35(1), 115–121. 10.1016/j.neubiorev.2009.12.012 [PubMed: 20026349]

Hemingway H, Nicholson A, Stafford M, Roberts R, & Marmnot M (1997). The Impact of Socioeconomic Status on Health Functioning as Assessed by the SF-36 Questionnaire: The Whitehall Study 39. American Journal of Public Health, 87(9), 1484–1490. 10.2105/AJPH.87.9.1484 [PubMed: 9314801]

Hostinar CE, Lachman ME, Mroczek DK, Seeman TE, & Miller GE (2015). Additive contributions of childhood adversity and recent stressors to inflammation at midlife: Findings from the MIDUS study. Developmental Psychology, 51(11), 1630–1644. 10.1037/dev0000049 [PubMed: 26389605]

Instanes JT, Halmoy A, Engeland A, Haavik J, Furu K, & Klungsoyr K (2017). Attention-Deficit/Hyperactivity Disorder in Offspring of Mothers With Inflammatory and Immune System Diseases. Biological Psychiatry, 81(5), 452–459. 10.1016/j.biopsych.2015.11.024 [PubMed: 26809250]

Irwin MR, & Cole SW (2011). Reciprocal regulation of the neural and innate immune systems. Nature Reviews Immunology, 11(9), 625–632. 10.1038/nri3042

Kanjilal S, Gregg EW, Cheng YJ, Zhang P, Nelson DE, Mensah G, & Beckles GLA (2006). Socioeconomic Status and Trends in Disparities in 4 Major Risk Factors for Cardiovascular Disease Among US Adults, 1971–2002. Archives ofInternal Medicine., 166(21), 2348 10.1001/archinte.166.21.2348

Keltner D, Gruenfeld DH, & Anderson C (2003). Power, Approach, and Inhibition. Psychological Review, 110(2), 265–284. 10.1037/0033-295X.110.2.265 [PubMed: 12747524]

Kraus MW, Tan JJX, & Tannenbaum MB (2013). The Social Ladder: A Rank-Based Perspective on Social Class. Psychological Inquiry, 24(2), 81–96. 10.1080/1047840X.2013.778803

Li H, Sun K, Zhao R, Hu J, Hao Z, Wang F, … Liu F (2018). Inflammatory biomarkers of coronary heart disease. Frontiers in Bioscience, 10, 185–196.

Liu Y-Z, Wang Y-X, & Jiang C-L (2017). Inflammation: The Common Pathway of Stress-Related Diseases. Frontiers in Human Neuroscience, 11(316), 1–11. 10.3389/fnhum.2017.00316 [PubMed: 28149275]

Long JD (2012). Longitudinal Data Analysis for the Behavioral Sciences Using R. Thousand Oakes, CA: Sage.

Maxson PJ, Edwards SE, Ingram A, & Lynn Miranda M (2012). Psychosocial differences between smokers and non-smokers during pregnancy. Addictive Behaviors, 37, 153–159. 10.1016/j.addbeh.2011.08.011 [PubMed: 22000409]

Miech RA, & Shanahan MJ (2000). Socioeconomic Status and Depression over the Life Course. Journal of Health and Social Behavior, 41(2), 162–176.

Miller GE, Brody GH, Yu T, & Chen E (2014). A family-oriented psychosocial intervention reduces inflammation in low-SES African American youth. Proceedings of the National Academy of Sciences of the United States of America, 777(31), 11287–11292. 10.1073/pnas.1406578111

Miller GE, Culhane J, Grobman W, Simhan H, Williamson DE, Adam EK, … Borders A (2017). Mothers' childhood hardship forecasts adverse pregnancy outcomes: Role of inflammatory,

lifestyle, and psychosocial pathways. Brain, Behavior, and Immunity, 65, 11–19. 10.1016/J.BBI.2017.04.018

National Center for Health Statistics. (2012). Health, United States, 2077: With Special Feature on Socioeconomic Status and Health. Hyattsville, MD.

Operario D, Adler NE, & Williams DR (2004). Subjective social status: reliability and predictive utility for global health. Psychology & Health, 79(2), 237–246. 10.1080/08870440310001638098

Ostrove JM, Adler NE, Kuppermann M, & Washington AE (2000). Objective and subjective assessments of socioeconomic status and their relationship to self-rated health in an ethnically diverse sample of pregnant women. Health Psychology, 79(6), 613–618. 10.1037/0278-6133.19.6.613

Owen N, Poulton T, Hay FC, Mohamed-Ali V, & Steptoe A (2003). Socioeconomic status, C-reactive protein, immune factors, and responses to acute mental stress. Brain, Behavior, and Immunity, 77(4), 286–295. 10.1016/S0889-1591(03)00058-8

Parker JD, Schoendorf KC, & Kiely JL (1994). Associations between Measures of Socioeconomic Status and Low Birth Weight, Small for Gestational Age, and Premature Delivery in the United States. Annals of Epidemiology, 4(4), 271–278. [PubMed: 7921316]

Perucci LO, Correa MD, Dusse LM, Gomes KB, & Sousa LP (2017). Resolution of inflammation pathways in preeclampsia—a narrative review. Immunologic Research, 65(4), 774–789. 10.1007/s12026-017-8921-3 [PubMed: 28391374]

R Core Team. (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing Vienna, Austria.

Radloff LS (1977). The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. Applied Psychological Measurement, 1(3), 385–401.

Raison CL, Capuron L, & Miller AH (2006). Cytokines sing the blues: inflammation and the pathogenesis of depression. Trends in Immunology, 27(1), 24–31. 10.1016/j.it.2005.11.006 [PubMed: 16316783]

Raposa EB, Bower JE, Hammen CL, Najman JM, & Brennan PA (2014). A developmental pathway from early life stress to inflammation: The role of negative health behaviors. Psychological Science, 25(6), 1268–1274. 10.1177/0956797614530570 [PubMed: 24760142]

Rasmussen JM, Graham AM, Entringer S, Gilmore JH, Styner M, Fair DA, … Buss C (2019). Maternal Interleukin-6 concentration during pregnancy is associated with variation in frontolimbic white matter and cognitive development in early life. NeuroImage, 185, 825–835. 10.1016/j.neuroimage.2018.04.020 [PubMed: 29654875]

Remes ST, & Pekkanen J (2005). Perinatal chracteristics and asthma and allergies in offspring In Hodgson D & Coe CL (Eds.), Perinatal Programming (pp. 155–168). London and New York: Taylor & Francis

Romero R, Espinoza J, Kusanovic JP, Gotsch F, Hassan S, Erez O, … Mazor M (2006). The preterm parturition syndrome. BJOG: An International Journal of Obstetrics and Gynaecology, 113(Suppl. 3), 17–42. 10.1021/jf60113a025

Rudolph MD, Graham AM, Feczko E, Miranda-Dominguez O, Rasmussen JM, Nardos R, … Fair DA (2018). Maternal IL-6 during pregnancy can be estimated from newborn brain connectivity and predicts future working memory in offspring. Nature Neuroscience, 21, 765–772. 10.1038/s41593-018-0128-y [PubMed: 29632361]

Sapolsky RM (2005). The Influence of Social Hierarchy on Primate Health. Science, 308(5722), 648–652. 10.1126/science.1106477 [PubMed: 15860617]

Sharma K, Singh R, Kumar M, Gupta U, Rohil V, & Bhattacharjee J (2018). First-Trimester Inflammatory Markers for Risk Evaluation of Pregnancy Hypertension. The Journal of Obstetrics and Gynecology of India, 68(1), 27–32. 10.1007/s13224-017-0988-1 [PubMed: 29391672]

Singh-Manoux A, Marmot MG, & Adler NE (2005). Does subjective social status predict health and change in health status better than objective status? Psychosomatic Medicine, 67(6), 855–861. 10.1097/01.psy.0000188434.52941.a0 [PubMed: 16314589]

Slopen N, Loucks EB, Appleton AA, Kawachi I, Kubzansky LD, Non AL, …Gilman SE (2015). Early origins of inflammation: An examination of prenatal and childhood social adversity in a

prospective cohort study. Psychoneuroendocrinology, 51, 403–413. 10.1016/J.PSYNEUEN.2014.10.016 [PubMed: 25462912]

Smith JP (2004). Unraveling the SES-Health Connection. Population and Development Review, 30, 108–132.

Smith LK, Draper ES, Manktelow BN, Dorling JS, & Field DJ (2007). Socioeconomic inequalities in very preterm birth rates. Archives of Disease in Childhood. Fetal and Neonatal Edition, 92, 11–14. https://doi.org/10.n36/adc.2005.090308

Steptoe A, Owen N, Kunz-Ebrecht S, & Mohamed-Ali V (2002). Inflammatory cytokines, socioeconomic status, and acute stress responsivity. Brain, Behavior, and Immunity, 16, 774–784. 10.1016/S0889-1591(02)00030-2

Stewart AL, Dean ML, Gregorich SE, Brawarsky P, & Haas JS (2007). Race/Ethnicity, Socioeconomic Status and the Health of Pregnant Women. Journal of Health Psychology, 12(2), 285–300. 10.1177/1359105307074259 [PubMed: 17284493]

Wadhwa PD, Culhane JF, Rauh V, & Barve SS (2001). Stress and preterm birth: neuroendocrine, immune/inflammatory, and vascular mechanisms. Maternal and Child Health Journal, 5(2), 119–125. 10.1023/A:1011353216619 [PubMed: 11573837]

Zell E, & Alicke MD (2010). The Local Dominance Effect in Self-Evaluation: Evidence and Explanations. Personality and Social Psychology Review, 14(4), 368–384. 10.1177/1088868310366144 [PubMed: 20435806]

Zell E, Strickhouser JE, & Krizan Z (2018). Subjective social status and health: A meta-analysis of community and society ladders. Health Psychology, 57(10), 979–987. 10.1037/hea0000667

Highlights

- Low subjective social standing (SSS) was related to inflammation during pregnancy.
- Association was stronger for SSS with reference to community than to the nation.
- Relationships persisted after controlling for objective SES.
- Objective SES was not associated with inflammation during pregnancy.

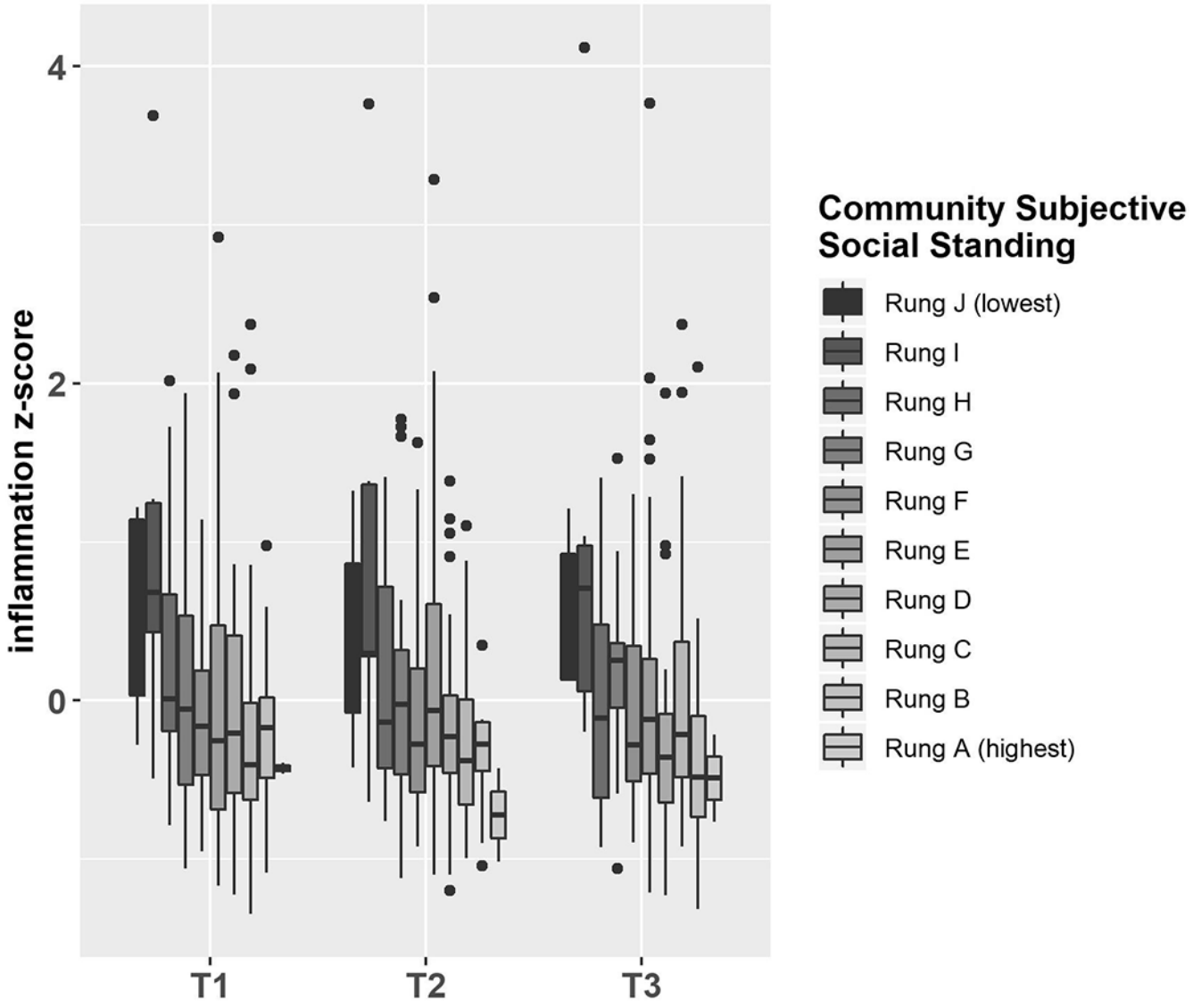

Figure 1.
Relationship between community subjective social standing and inflammation at each pregnancy trimester.

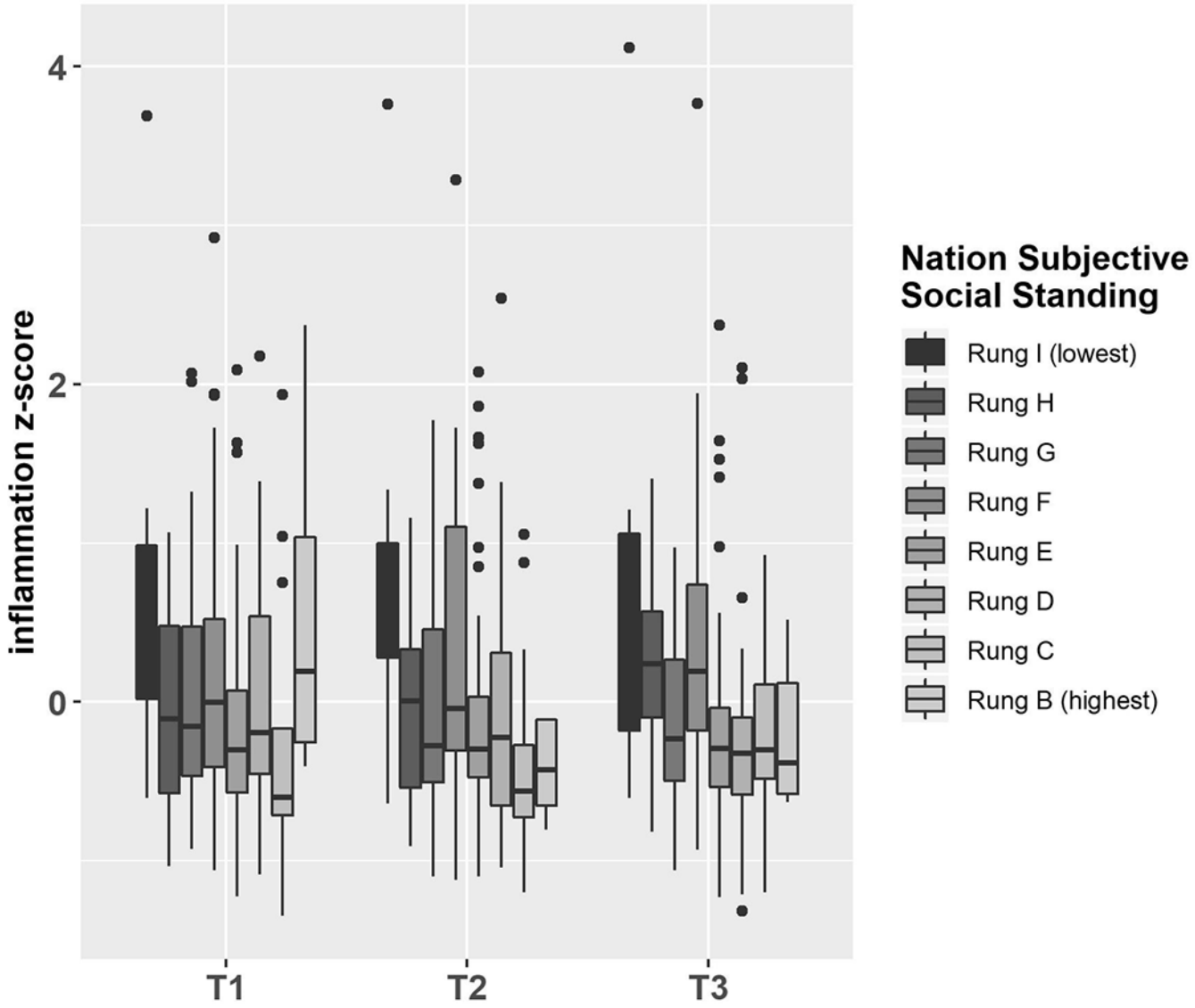

Figure 2.
Relationship between nation subjective social standing and inflammation at each pregnancy trimester.

Table 1.

Sample characteristics (N = 250)

	Mean (SD) [Min, Max]	Frequency
Age	27.8 (5.40) [18.0, 44.0]	
Ethnicity		
White non-Hispanic		92 (36.8%)
Hispanic		107 (42.8%)
Other non-Hispanic		34 (13.6%)
Income		
Below $15,000		20 (8.0%)
$15,000 - $29,999		42 (16.8%)
$30,000 - $49,999		49 (19.6%)
$50,000 - $100,000		92 (36.8%)
Over $100,000		33 (13.2%)
Educational level		
Less than high school		10 (4.02%)
High school degree		48 (19.28%)
Partial college or specialized training		101 (40.56%)
Associates or bachelors degree		62 (24.90%)
Advanced degree		28 (11.24%)
Objective SES	3.23 (0.964) [1.00, 5.00]	
Community SSS	5.89 (1.82) [Rung J, Rung A]	
Nation SSS	5.57 (1.58) [Rung I, Rung B]	
T1 **PSS**	1.52 (0.58) [0.10, 3.30]	
T2 **PSS**	1.41 (0.60) [0.10, 3.50]	
T3 **PSS**	1.48 (0.61) [0.00, 2.90]	
T1 **CESD**	0.70 (0.45) [0.00, 2.60]	
T2 **CESD**	0.64 (0.46) [0.00, 2.45]	
T3 **CESD**	0.70 (0.45) [0.00, 2.40]	
Obstetric risks		46 (18.4%)
Hypertension		9 (3.6%)
Severe infection		21 (8.4%)
Vaginal bleeding		5 (2.0%)
Anemia		12 (4.8%)
Diabetes		10 (4.0%)
T1 **Gestational weeks**	12.9 (1.74) [8.86, 18.0]	
T2 **Gestational weeks**	20.5 (1.42) [16.0, 24.4]	
T3 **Gestational weeks**	30.4 (1.37) [26.9, 34.4]	
T1 **BMI**	27.4 (6.20) [17.1, 49.5]	
T2 **BMI**	28.4 (6.16) [18.6, 50.2]	
T3 **BMI**	30.4 (6.02) [20.9, 52.9]	
T1 **IL-6 (pg/ml)**	0.771 (0.52) [0.03, 2.70]	

	Mean (SD) [Min, Max]	Frequency
T2 **IL-6 (pg/ml)**	0.864 (0.67) [0.03, 3.74]	
T3 **IL-6 (pg/ml)**	1.11 (0.82) [0.00, 4.44]	
T1 **TNF-α (pg/ml)**	8.22 (3.58) [1.14, 19.2]	
T2 **TNF-α (pg/ml)**	8.51 (3.75) [1.16, 20.2]	
T3 **TNF-α (pg/ml)**	9.22 (4.39) [1.35, 28.7]	
T1 **CRP (mg/dL)**	6.06 (5.50) [0.355,22.9]	
T2 **CRP (mg/dL)**	6.04 (5.37) [0.561,22.5]	
T3 **CRP (mg/dL)**	5.65 (4.90) [0.326, 21.3]	
T1 **Inflammation z-score**	0.02 (0.83) [−1.35, 3.69]	
T2 **Inflammation z-score**	0.00 (0.79) [−1.20, 3.76]	
T3 **Inflammation z-score**	−0.01 (0.77) [−1.32, 4.12]	

Table 2.

Hierarchical linear models with inflammation z-score as the outcome variable.

	M1			M2			M3			M4		
	Estimates	***SE***	***p***	***Estimates***	***SE***	***p***	***Estimates***	***SE***	***p***	***Estimates***	***SE***	***p***
Regression coefficients												
Intercept	0.03	0.07	.642	0.01	0.07	.836	0.01	0.07	.917	−0.01	0.07	.899
Ethnicity												
(Ref. White non-Hispanic)												
Hispanic	0.02	0.09	.844	0.05	0.10	.604	0.05	0.09	0.612	0.08	0.11	.449
Other non-Hispanic	−0.07	0.13	.589	−0.06	0.13	.636	−0.03	0.13	0.810	−0.02	0.13	.875
BMI	0.06	0.01	**<.001**	0.06	0.01	**<.001**	0.06	0.01	**<.001**	0.06	0.01	**<.001**
Gestational age	−0.01	0.00	**<.001**	−0.01	0.01	**<.001**	−0.01	0.00	**<.001**	−0.01	0.00	**<.001**
PSS	−0.03	0.07	.670	−0.03	0.07	.669	−0.04	0.07	.572	−0.04	0.07	.560
CESD	−0.02	0.10	.822	−0.01	0.10	.896	0.00	0.10	.991	0.01	0.10	.936
Community SSS	−0.07	0.02	**.004**	−0.08	0.02	**.002**	-	-	-	-	-	-
Nation SSS	-	-	-	-	-	-	−0.06	0.03	**.048**	−0.06	0.03	**.036**
Objective SES	-	-	-	0.04	0.05	.417	-	-	-	0.04	0.05	.490
Variance components												
Within-person variance σ^2	0.21			0.21			0.21			0.21		
Between-person variance τ_{00}	0.30			0.30			0.31			0.30		
Model summary												
Observations	576			576			576			576		
Pseudo R^2	0.233			0.235			0.219			0.221		
AIC	1085.4			1086.7			1089.8			1091.3		
BIC	1128.9			1134.6			1133.3			1139.2		
χ^2 (*p*-value)	-			0.66 (.418)			-			0.48 (.490)		

Note. Model M1 includes community SSS as the main predictor. M2 was additionally adjusted for objective SES. Likewise, model M3 includes nation SSS and M4 was additionally adjusted for objective SES. χ^2-difference test was conducted for model comparison of M1 vs. M2 and M3 vs. M4. Subjective social status was coded as rung J (1, lowest position) to rung A (10, highest position).