

## The Effects of the Interaction between Prenatal Stress and Diet on Maternal Insulin Resistance and Inflammatory Profile

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**Abstract :** Maternal nutrition and stress are independently recognized as among the most important factors that influence prenatal biology, with implications for fetal development and poor pregnancy outcomes. While there is substantial evidence from non-pregnancy human and animal studies that a complex, bi-directional relationship exists between nutrition and stress, to the author's best knowledge, their interaction in the context of pregnancy has been significantly understudied. The aim of this study is to assess the interaction between maternal psychological stress and diet quality across pregnancy and its effects on biomarkers of prenatal insulin resistance and inflammation. This is a prospective longitudinal study of N=235 women carrying a healthy, singleton pregnancy, recruited from prenatal clinics of the University of California, Irvine Medical Center. Participants completed a 4-day ambulatory assessment in early, middle and late pregnancy, which included multiple daily electronic diary entries using Ecological Momentary Assessment (EMA) technology on a dedicated study smartphone. The EMA diaries gathered moment-level data on maternal perceived stress, negative mood, positive mood and quality of social interactions. The numerical scores for these variables were averaged across each study time-point and converted to Z-scores. A single composite variable for 'STRESS' was computed as follows: (Negative mood+Perceived stress)-(Positive mood+Social interaction quality). Dietary intakes were assessed by three 24-hour dietary recalls conducted within two weeks of each 4-day assessment. Daily nutrient and food group intakes were averaged across each study time-point. The Alternative Healthy Eating Index adapted for pregnancy (AHEI-P) was computed for early, middle and late pregnancy as a validated summary measure of diet quality. At the end of each 4-day ambulatory assessment, women provided a fasting blood sample, which was assayed for levels of glucose, insulin, Interleukin (IL)-6 and Tumor Necrosis Factor (TNF)- $\alpha$ . Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was computed. Pearson's correlation was used to explore the relationship between maternal STRESS and AHEI-P within and between each study time-point. Linear regression was employed to test the association of the stress-diet interaction (STRESS\*AHEI-P) with the biological markers HOMA-IR, IL-6 and TNF- $\alpha$  at each study time-point, adjusting for key covariates (pre-pregnancy body mass index, maternal education level, race/ethnicity). Maternal STRESS and AHEI-P were significantly inversely correlated in early ( $r=-0.164$ ,  $p=0.018$ ) and mid-pregnancy ( $r=-0.160$ ,  $p=0.019$ ), and AHEI-P from earlier gestational time-points correlated with later STRESS (early AHEI-P x mid STRESS:  $r=-0.168$ ,  $p=0.017$ ; mid AHEI-P x late STRESS:  $r=-0.142$ ,  $p=0.041$ ). In regression models, the interaction term was not associated with HOMA-IR or IL-6 at any gestational time-point. The stress-diet interaction term was significantly associated with TNF- $\alpha$  according to the following patterns: early AHEI-P\*early STRESS vs early TNF- $\alpha$  ( $p=0.005$ ); early AHEI-P\*early STRESS vs mid TNF- $\alpha$  ( $p=0.002$ ); early AHEI-P\*mid STRESS vs mid TNF- $\alpha$  ( $p=0.005$ ); mid AHEI-P\*mid STRESS vs mid TNF- $\alpha$  ( $p=0.070$ ); mid AHEI-P\*late STRESS vs late TNF- $\alpha$  ( $p=0.011$ ). Poor diet quality is significantly related to higher psychosocial stress levels in pregnant women across gestation, which may promote inflammation via TNF- $\alpha$ . Future prenatal studies should consider the combined effects of maternal stress and diet when evaluating either one of these factors on pregnancy or infant outcomes.

**Keywords :** diet quality, inflammation, insulin resistance, nutrition, pregnancy, stress, tumor necrosis factor-alpha

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