

Original Research

Association of Lower Socioeconomic Position in Pregnancy with Lower Diurnal Cortisol Production and Lower Birthweight in Male Infants

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ABSTRACT

Purpose: Low maternal socioeconomic position (SEP) has been associated with adverse neonatal outcomes, including preterm birth, low birthweight, intrauterine growth restriction, and infant mortality. A key biological mechanism that has been proposed to explain this association is hypothalamic-pituitary-adrenal (HPA) activity, yet the association between SEP and HPA activity in pregnancy has received little attention. In this study we aimed to examine the associations between SEP and 2 forms of maternal cortisol regulation—diurnal slope and waking response—across pregnancy. Furthermore, we aimed to assess whether these associations differed by the sex of the fetus.

Methods: A total of 217 pregnant women aged 18 to 40 years with singleton pregnancies participated. Women were excluded from participating if they were aged <18 or >40 years and if they were at risk for maternal or obstetric complications. Women provided information on socioeconomic characteristics of adults contributing to the participants' household to compute a Hollingshead Four Factor Index of Social Status score of SEP. Women provided salivary cortisol samples on awakening, 30 minutes after wakeup, and at bedtime, at 3 times over pregnancy and once 30 days postpartum to calculate the diurnal slope and cortisol awakening response (CAR). Using linear regression analyses, we

examined the relationships between maternal SEP and maternal diurnal slope and CAR. We explored the relationships between maternal SEP and cortisol by fetal sex using linear regression analyses. We also explored links between maternal SEP, maternal cortisol, and infant birth outcomes.

Findings: Women of lower SEP displayed smaller awakening responses and less change over the day compared with women of higher SEP. SEP was significantly associated with attenuated diurnal slope only among women carrying female fetuses, whereas for CAR, the association between SEP and attenuated CAR was significant only for women carrying male fetuses. Lower SEP was associated with decreased birthweight, and this association was partially explained by maternal HPA activity in pregnancy.

Implications: Women of low SEP displayed attenuated HPA activity across the perinatal period, and patterns varied by fetal sex and cortisol metric. Findings are in need of replication. More research is needed to understand the links between SEP, HPA activity, and neonatal health. (*Clin Ther.* 2016;38:265–274) © 2016 Elsevier HS Journals, Inc. All rights reserved.

Key words: cortisol, pregnancy, sex, socioeconomic position.

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INTRODUCTION

Socioeconomic position (SEP) reflects the social standing of an individual or group, and is often measured as a combination of education, income, and occupation.¹ Socioeconomic deprivation has been consistently associated with morbidity and mortality in nonpregnant adults.^{2–5} In pregnancy, low SEP is robustly associated with adverse pregnancy outcomes, including infant mortality, prematurity, low birthweight, and intrauterine growth restriction.^{6–9} Past studies have cited poor nutrition and access to health care as some factors explaining links between low SEP and adverse neonatal outcomes.^{10–12} A key physiologic process that has been proposed to explain the link between low SEP and poor health is the hypothalamic-pituitary-adrenal (HPA) axis.¹³ Low SEP may represent a chronic stressor that results in wear and tear on the HPA axis, resulting in HPA dysregulation and aberrant patterns of cortisol production. Low SEP has been associated with altered cortisol patterns in nonpregnant adults, with evidence for both elevated and attenuated concentrations among individuals of low SEP.¹³ In addition, some studies of nonpregnant adults suggest that the association between SEP and cortisol may differ by sex; Steptoe et al¹⁴ found that low SEP was associated with lower levels of cortisol among women but higher levels among men, and Kunz-Ebrecht et al¹⁵ also reported lower cortisol levels among low-SEP women (who also reported low job demands).

The association between SEP and HPA activity in pregnancy has not been extensively studied despite evidence from the literature demonstrating that glucocorticoid overexposure in utero is a key pathway linking prenatal adversity to adverse infant outcomes.¹⁶ Emerging evidence suggests that SEP is associated with altered diurnal patterns of HPA activity in pregnancy. Diurnal slope and cortisol awakening response (CAR) are under different regulatory control and may respond differently to environmental stress¹⁷; thus diurnal cortisol and CAR have been examined separately in past studies. Valladares et al¹⁸ reported that low social resources in pregnancy were associated with higher evening cortisol levels in the second half of pregnancy. Consistent findings were reported by Thayer and Kuzawa,¹⁹ who found that greater economic deprivation was associated with elevated evening, but not morning, cortisol levels in late pregnancy.

Corwin et al²⁰ also reported higher third trimester diurnal cortisol levels and glucocorticoid resistance (ie, an inability of cortisol to inhibit proinflammatory signaling pathways) among low-income, minority women, and Raikkonen et al²¹ reported increased placental glucocorticoid receptor expression among pregnant women with less education and lower occupational status.

The literature on the relationships between SEP and maternal cortisol is sparse but suggests an association between SEP and cortisol regulation in pregnancy. Past findings are limited to an examination of cortisol concentrations in late pregnancy only. It is therefore unclear whether the association between SEP and maternal cortisol differs during different gestational time periods. This is an important gap in the literature given the dramatic changes in HPA activity over the course of gestation,²² and the importance of trajectories of HPA activity over pregnancy in promoting positive maternal and neonatal health.^{23–26} It is also unclear from the literature whether the association between SEP and cortisol in pregnancy endures into the postpartum period. Thus, the primary aim of the current study was to examine the association between SEP and maternal cortisol over pregnancy and in the early postpartum period in a socioeconomically diverse sample.

Another aim of this study was to understand whether the association between SEP and maternal cortisol differs according to the sex of the fetus. Past studies have reported that maternal cortisol levels vary over gestation depending on the sex of the fetus; DiPietro et al²⁷ found that women carrying male fetuses had higher salivary cortisol levels relative to women carrying female fetuses before 30 weeks' gestation, at which point there was a crossover, and women carrying female fetuses displayed elevated cortisol levels. The influence of SEP in the association between maternal cortisol and fetal sex was not examined in the DiPietro study. In addition, a recent study reported that associations among SEP and methylation of the gene encoding placental 11 β -hydroxysteroid dehydrogenase (an enzyme involved in the inactivation of maternal cortisol, protecting the fetus from overexposure to maternal glucocorticoids) differed by fetal sex; Appleton et al²⁸ found that women reporting the greatest economic adversity in pregnancy had the highest placental 11 β methylation, particularly if they were carrying a male fetus. Given

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