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Full-length Article

Mothers' childhood hardship forecasts adverse pregnancy outcomes: Role of inflammatory, lifestyle, and psychosocial pathways

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ABSTRACT

Research suggests the health consequences of economic hardship can be transmitted across generations. Some of these disparities are thought to be passed to offspring during gestation. But this hypothesis has not been tested in contemporary American samples, and the mechanisms of transmission have not been characterized. Accordingly, this study had two goals: first, to determine if women exposed to economic hardship during childhood showed higher rates of adverse birth outcomes; and second, to evaluate the contribution of inflammation, psychosocial, lifestyle, and obstetric characteristics to this phenomenon. This prospective study enrolled 744 women with singleton pregnancies (59.1% White; 16.3% Black; 18.7% Latina; 5.9% Other). Childhood economic hardship was measured by self-report. Birth outcomes included length of gestation and incidence of preterm birth; birth weight percentile and small for gestational age; length of hospital stay and admission to Special Care Nursery. Analyses revealed that mothers' childhood economic hardship was independently associated with multiple adverse birth outcomes, even following adjustment for demographics, maternal education, and obstetrical confounders. Women raised in economically disadvantaged conditions had shorter gestation length and higher preterm delivery rates. Their babies had lower birth weights, were more likely to be small for gestational age, stayed in the hospital longer, and had more Special Care Nursery admissions. Mediation analyses suggested these associations arose through multiple pathways, and highlighted roles for inflammation, education, adiposity, and obstetric complications. Collectively, these findings suggest that childhood economic hardship predisposes women to adverse birth outcomes, and highlights likely behavioral and biological mechanisms.

Abbreviations: IFN, interferon; IL, interleukin; PTB, preterm birth; SGA, small for gestational age; SCN, special care nursery.

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1. Introduction

Children from economically disadvantaged families are vulnerable to physical health problems across the lifespan (Miller et al., 2011; Hertzman and Boyce, 2010; Chen et al., 2002). Relative to more privileged youth, they show higher rates of and worse outcomes for pediatric disorders like asthma, respiratory infection, and obesity (Braveman and Barclay, 2009; Chen et al., 2002). Later in life they continue to have relatively poor outcomes, as reflected in higher rates of chronic illnesses that represent major societal burdens (e.g., diabetes, heart disease, stroke), and more premature mortality (Galobardes et al., 2008; Lynch and Smith, 2005). These disparities generally persist after accounting for socioeconomic status in adulthood (Cohen et al., 2010), suggesting that childhood hardship casts a long shadow with implications for health across the lifespan (Shonkoff et al., 2009).

Accumulating evidence suggests the adverse influence of childhood disadvantage may not be restricted to the individual's own life span, but also transmitted across generations (Kuzawa, 2012). Studies in this emerging literature have found that the socioeconomic conditions in which a parent was raised forecast the health of their offspring. For example, to the degree parents were exposed to childhood economic hardship, their adolescent offspring showed more cardiovascular risk, as reflected in higher blood pressure and low-grade inflammation (Schreier and Chen, 2010). In youth with asthma, parental economic hardship during childhood predicted worse disease control and larger cytokine responses to allergens (Chen et al., 2016b). In both of these studies, the associations were independent of the family's current socioeconomic conditions. Findings like this converge with studies reporting *trans*-generational health effects of inadequate nutrition and cigarette smoking (Bateson et al., 2004; Pembrey et al., 2014). Whether these associations are causal remains unclear. However, experimental studies in animals demonstrate the biological plausibility of a causal effect, showing that toxins and stressors can leave "molecular footprints" detectable in the grand-offspring of exposed organisms (Bale, 2015; Hanson and Gluckman, 2014; Kundakovic and Champagne, 2015).

Pregnancy may represent a particularly sensitive window for mother-to-child transmission of socioeconomic disparities in health. Disadvantage often coincides with exposure to psychological stressors and environmental toxins, and higher rates of cigarette smoking, obesity, and inadequate nutrition (Evans, 2004). These exposures can affect characteristics of the gestational milieu (Wadhwa et al., 2011; Burris et al., 2016; Hanson and Gluckman, 2014). Consistent with this premise, two recent studies observed that mothers' socioeconomic conditions during childhood presaged their subsequent pregnancy outcomes. Data from the 1958 British birth cohort showed that childhood hardship was associated with increased risk of preterm delivery and low birth weight (Harville et al., 2010). These associations were partially explained by hardship's link with lower socioeconomic position in adulthood and cigarette smoking during pregnancy. Similarly, multigenerational data from Aberdeen showed that mothers raised in families of lower social class delivered babies of lower weight, even after correcting for gestation length (Morton et al., 2014).

These provocative findings raise several questions. First, since both studies focused on women raised in mid-century Britain, it is unclear whether similar trends are occurring in contemporary America. In the decades since women in these studies gave birth (1970–1999), smoking during pregnancy has declined by almost 50% (American Lung Association, 2011) and access to prenatal care has expanded considerably. Thus, our first goal was to examine whether in modern-day America, women's childhood socioeconomic conditions forecast their subsequent pregnancy outcomes.

A second question concerns the underlying biological mechanisms. How could a woman's early-life conditions linger in the body, and influence a pregnancy initiated decades later? One plausible mechanism is excessive inflammation. Research shows that childhood socioeconomic hardship engenders a pro-inflammatory phenotype that persists into adulthood (Miller et al., 2011; Fagundes et al., 2013). The phenotype is characterized by exaggerated cytokine responses to bacterial stimuli, insensitivity to the anti-inflammatory actions of glucocorticoids, and higher circulating levels of inflammatory biomarkers (Miller et al., 2009; Loucks et al., 2010; Levine et al., 2015; Chen et al., 2016a; Phillips et al., 2009). Studies in animals show that high concentrations of inflammatory mediators can restrict fetal growth and speed up parturition (Challis et al., 2009). And in some cohorts of pregnant women, higher circulating inflammatory biomarkers forecast preterm delivery and lower birth weight (Sykes et al., 2012; Gillespie et al., 2015), possibly because they mirror immunologic conditions at the maternal-fetal interface. Based on these observations, our second goal was to determine whether inflammatory biomarkers during gestation link childhood socioeconomic conditions with adverse pregnancy outcomes.

Finally, if the evidence supports a mechanistic role for inflammation, it becomes important to elucidate how childhood conditions trigger this process, and whether steps along the pathway are modifiable. There are several plausible scenarios to consider in this regard. Across the lifespan, individuals exposed to childhood hardship tend to have worse psychosocial (e.g., less education, more distress and isolation) and lifestyle profiles (e.g., more smoking, excessive alcohol use, and adiposity) (Repetti et al., 2002). Both of these clusters of variables are associated with upregulated inflammatory activity and worse pregnancy outcomes (Irwin and Cole, 2011; Dunkel, 2011). Similarly, childhood disadvantage might increase women's risks for obstetric conditions, like hypertension and preeclampsia, whose pathophysiology involves excessive inflammation. Hence, our third goal was to identify what role psychosocial, lifestyle, and obstetric factors have along the pathway from childhood disadvantage to pregnancy outcomes.

2. Methods

Between June 2013 and May 2015, 744 women enrolled in the Measurement of Maternal Stress (MOMS) Study. Enrollment occurred at four sites: Northwestern University, University of Texas Health Science Center at San Antonio, University of Pittsburgh, and Schuylkill County, Pennsylvania, a rural site led by Children's Hospital of Philadelphia.

2.1. Recruitment and assessments

To be eligible, women had to be 18 or older and English speaking, with a singleton pregnancy at less than 21 weeks' gestation. Exclusion criteria included major fetal congenital anomalies or chromosomal abnormalities, progesterone treatment after 14 weeks, and chronic corticosteroid treatment (not including topical use or inhalers). Institutional Review Boards at each site approved the protocol, and all women gave written informed consent. Women completed study visits in the second (12–20′6 weeks' gestation) and third (32–35′6 weeks' gestation) trimesters.

2.2. Mothers' childhood disadvantage

Drawing on previous studies of childhood disadvantage (Cohen et al., 2013), we asked women a series of questions about their family's conditions during childhood. The questions focused on whether the family owned a home, obtained medical treatment