Association of prenatal and early childhood stress with reduced lung function in 7-year-olds

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Abstract

Background: No prior study has examined associations between prenatal and early-life stress on childhood lung function or identified critical windows of exposure.

Objective: To prospectively examine associations between prenatal and early-life stress and childhood lung function.

Methods: Stress was indexed by a maternal negative life events (NLEs) score ascertained during pregnancy and between 1 and 2 years post partum. Spirometry was performed when children were a mean (SD) of 6.99 (0.89) years old. Associations of prenatal and early postnatal stress with spirometry z-scores were examined in 199 children using linear regression. Effect modification by child sex was explored.

Results: Most mothers were minorities (65% Hispanic, 21% African American), had 12 years or less of education (67%), and did not smoke prenatally (78%). The highest level of prenatal stress (≥5 NLEs) was associated with lower levels of forced expiratory volume in 1 second (FEV1) (z score = −0.53, P = .03), forced vital capacity (FVC) (z score = −0.49, P = .04), and forced expiratory flow between 25% and 75% (FEF25%–75%) (z score = −0.68, P = .01) after covariate adjustment; effects were similar for postnatal stress considered separately. In sex-stratified analyses, high postnatal stress (≥5 NLEs) was associated with lower FEV1 (z score = −0.76, P = .01), FVC (z score = −0.77, P = .01), and FEF25%–75% (z score = −0.67, P = .02) in boys but not girls, although the interaction term was not significant (P for interaction >.10).

Conclusion: These are the first prospective data that link perinatal stress with reduced child lung function. High levels of stress in the prenatal and postnatal periods were associated with symmetric reductions in FEV1 and FVC consistent with impaired lung growth. Given that lung function growth patterns are established by 7 years of age, these findings have lifelong implications.

Introduction

An important step toward identifying children at risk for chronic respiratory disease is characterizing exposures and mechanisms that lead to and maintain early predisposition. Lung function at birth and lung function growth patterns established by 7 years of age determine early adulthood pulmonary function. Impaired adult maximal attained lung function is a major risk factor for the development of chronic obstructive pulmonary disease (COPD), the projected fourth leading cause of death by 2020. Longitudinal studies have associated early life factors, including active and passive smoking prenatally and during childhood, birth weight, gestational age, and asthma, with reduced lung function during the life course. However, these factors account for a relatively small proportion of the risk, suggesting that as yet unidentified risk factors exist. Further delineation of factors that contribute to lung function development that may be amenable to intervention is thus important.
Developmental origins of lung structure and function, beginning in utero, involve the coordinated maturation of the immune, neural, and endocrine systems. Environmental toxins, such as psychological stress, that disrupt these interrelated systems in critical developmental periods can alter the course of lung morphogenesis and maturation, resulting in long-term changes in the respiratory system. Infants remain vulnerable because these systems are highly reactive and labile in response to environmental stressors, particularly in the first 2 years when rapid lung development continues.

Although studies link stress to age-related deterioration in pulmonary function, the few studies that have examined effects on childhood lung function present mixed results. Urban Boston children exposed to higher levels of interpersonal violence over childhood had symmetric reductions in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁) by 6 to 7 years of age. A study of adolescents in California found associations between family conflict and reductions in FEV₁ among boys but not girls. A study in the United Kingdom found no association between racism and adolescent lung function. Prior study has examined associations between stress starting prenatally and childhood lung function or assessed the relative effect of prenatal or postnatal stress exposure to better delineate critical windows. Leveraging an ethnically mixed prospective pregnancy cohort study, we examined the relative importance of exposure to prenatal and/or postnatal stress in association with children's lung function by 7 years of age. Specifically, we first examined effects of prenatal and postnatal stress in independent models, then mutually adjusted for prenatal and postnatal stress to examine their relative importance. We also explored effect modification by child's sex.

Methods

Study Participants

Participants were from the Asthma Coalition on Community, Environment, and Social Stress project, a pregnancy cohort designed to examine the effects of perinatal stress and other environmental factors on childhood respiratory disorders. Between August 2002 and January 2007, 500 English- or Spanish-speaking pregnant women (mean [SD] of 28.4 [7.9] weeks' gestation) receiving care at Brigham & Women's Hospital, Boston Medical Center, and affiliated community health centers were enrolled. Research assistants approached women receiving prenatal care on select clinic days; 78% of those approached who were eligible agreed to enroll. There were no significant differences in race/ethnicity, educational level, and income between women enrolled and those who declined; 455 gave birth to a live born infant and continued follow-up. Lung function was measured at baseline and/or in the third trimester were classified as prenatal smokers; postnatal smoke exposure was based on maternal report of smoking and/or whether others smoked in the home at each postpartum interview. Maternal-reported clinician-diagnosed asthma was ascertained through interviews at approximately 3-month intervals for the first 24 months of life and then annually thereafter up to the time of spirometry. Mothers were asked, “Has a doctor or nurse ever said that your child had asthma?”

Covariates

Potential confounders and pathway variables were considered. Questionnaires ascertained maternal age, educational level, race/ethnicity, asthma history (ever having clinician-diagnosed asthma), as well as child's sex, season of birth, and birth weight. Child's gestational age was based on reported last menstrual period or obstetric estimates based on a second-trimester ultrasonogram if dates differed by more than 10 days on medical record review. Sex-specific birth weight for gestational age z scores were calculated based on US reference data. Mothers who reported smoking at baseline and/or in the third trimester were classified as prenatal smokers; postnatal smoke exposure was based on maternal report of smoking and/or whether others smoked in the home at each postpartum interview. Maternal-reported clinician-diagnosed asthma was ascertained through interviews at approximately 3-month intervals for the first 24 months of life and then annually thereafter up to the time of spirometry. Mothers were asked, “Has a doctor or nurse ever said that your child had asthma?”

Statistical Analysis

We considered stress exposure categorized in 2 different ways. In the primary initial analysis, the NLEs score was categorized a priori as 0, 1 to 2, 3 to 4, or 5 or higher to assess exposure-response associations. Univariate and multivariable linear regressions were run to examine associations between prenatal and postnatal maternal stress and children's pulmonary function measures, including FEV₁, FVC, FEF₂₅₋₇₅%, and FEV₁/FVC z scores. We first examined effects of prenatal and postnatal NLEs in separate models. In addition to the covariates accounted for in deriving the spirometry measure z scores (age, sex, height, race/ethnicity), we adjusted for potential confounders linked to stress and lung function, including maternal educational level and child's asthma diagnosis. We next adjusted for variables potentially on the pathway between stress and lung function, including sex-specific birth weight for gestational age z score and maternal tobacco
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