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Prenatal particulate matter exposure and wheeze in Mexican children: effect modification by prenatal psychosocial stress

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ABSTRACT

Background: Air pollution exposure in childhood is associated with greater incidence and exacerbation of asthma, particularly in children whose parents report high levels of psychological stress. However, this interaction has not been completely elucidated in pregnancy.
Objective: To examine whether the association between prenatal exposure to particulate matter no larger than 2.5 μm in diameter ($PM_{2.5}$) and wheeze in children is modified by prenatal stress.
Methods: Mexican women were recruited during pregnancy (N = 552). Residential prenatal daily exposure to $PM_{2.5}$ was estimated using a satellite-based spatiotemporally resolved prediction model and averaged over trimesters. Maternal stress was indexed by maternal negative life events (NLE) score (range 0–11) ascertained during mid to late pregnancy. NLE scores were dichotomized at the median as low (NLE score $\leq$ 3) and high (NLE score $>$ 3) stress. Reports of ever wheeze and wheeze in the past 12 months (current wheeze) for children were obtained using the International Study of Asthma and Allergies in Childhood survey at 48 months. The association between prenatal $PM_{2.5}$ and wheeze was analyzed using a modified Poisson regression and stratified by low vs high stress.
Results: Greater $PM_{2.5}$ exposure during the first trimester was associated with increased risk of current wheeze among children with mothers reporting high prenatal stress (relative risk 1.35, 95% confidence interval 1.00–1.83, per interquartile range increase 3.8 $\mu g/m^3$) but not among those reporting low stress (relative risk 0.84, 95% confidence interval 0.61–1.16, per interquartile range increase 3.8 $\mu g/m^3$; *P* for interaction = .04).
Conclusion: Increased prenatal stress enhanced the association between $PM_{2.5}$ exposure in early pregnancy, and child wheeze at 48 months of age. It is important to consider chemical and nonchemical stressors together to more comprehensively characterize children's environmental risk.

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Introduction

Emerging evidence has linked exposure to ambient air pollution during the prenatal period to increased respiratory morbidity later in childhood.[1,2] In addition, increased prenatal maternal stress and stress correlates (eg, maternal anxiety) have been independently associated with early asthma phenotypes in many prospective epidemiologic studies.[3–8] Other data have suggested that lower socioeconomic status populations are more susceptible to the health effects of air pollution, potentially because of concomitant increased psychosocial stress.[9,10]

Epidemiologic studies have begun to document synergistic effects between stress and ambient air pollution exposure in early childhood on the incidence and exacerbation of asthma and decrements in lung function.[11–16] For example, in a 3-year follow-up study of children enrolled at 5 to 9 years of age in Southern California, annual residential exposure to oxides of nitrogen was associated with greater asthma incidence in children whose parents also reported higher perceived stress.[12] In this same study, exposure to nitric oxide, nitrogen dioxide (NO_2), and total oxides of nitrogen estimated at children's residences and schools also was associated with greater decrements in lung function among children whose parents reported high perceived stress compared with parents who reported low stress.[11] Our group previously reported that higher lifetime exposure to ambient NO_2, estimated using land use regression, in urban children followed to approximately 7 years of age was associated with increased risk of asthma diagnosis only among children also exposed to higher levels of community violence in the neighborhood.[13] Our team also reported that prenatal exposure to black carbon and particulate matter no larger than 2.5 μm in diameter ($PM_{2.5}$) was associated with increased odds of repeated wheeze at 2 years of age with an additive effect of concurrent prenatal community violence exposure.[15] Data on the potential synergistic effects of increased ambient particulate air pollution exposure and psychosocial stress starting in utero on children's respiratory health remain sparse.

Moreover, fetal lung development occurs through a complex orchestration of sequential biologic events and there might be periods when the fetus is more sensitive to pro-oxidant exposures. Recent epidemiologic evidence has shown that exposure to ambient air pollution at different periods in pregnancy is associated with respiratory outcomes in childhood.[2,17,18] Our group showed that $PM_{2.5}$ exposure during the second trimester was associated with asthma at 6 years of age in children in Boston, Massachusetts.[2] A study in China reported varying periods of importance for outdoor prenatal exposure to NO_2 and allergic or respiratory outcomes, with first-trimester exposure associated with eczema, second-trimester exposure associated with asthma, and third-trimester exposure linked with allergic rhinitis.[18] In a study in Spain, second-trimester NO_2 exposure estimated using land use regression was associated with decreased lung function at 4.5 years of age and increased risk of low lung function (<80% of predicted forced expiratory volume in 1 second).[17] Therefore, there is reason to expect that the particular timing of exposure during the prenatal period might be of importance. We leveraged existing data from an established population-based prenatally enrolled longitudinal cohort in Mexico City, Mexico to examine the association between prenatal $PM_{2.5}$ averaged over trimesters and report of wheeze in children followed to 48 months of age. We examined whether these associations were modified by prenatal psychosocial stress.

Methods

Study Population

Pregnant women who were receiving health services and prenatal care through the Mexican Social Security System (Instituto Mexicano del Seguro Social) were recruited into the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) study from July 2007 through February 2011. Women were eligible to participate if they were at less than 20 weeks of gestation, at least 18 years old, planned to stay in Mexico City for the next 3 years, had telephone access, and reported no medical history of heart or kidney disease, no daily alcohol consumption, and no use of any steroid or antiepilepsy medications. After birth, 815 mother-child dyads had at least 1 follow-up visit and 552 had completed the visit at 48 months of age and had all the necessary covariates for these analyses. Procedures were approved by institutional review boards at the Harvard School of Public Health (Boston, Massachusetts), the Icahn School of Medicine at Mount Sinai (New York, New York), and the Mexican National Institute of Public Health (Mexico City, Mexico). Women provided written informed consent.

Prenatal $PM_{2.5}$ Levels

Our group developed a hybrid satellite-based method to estimate daily $PM_{2.5}$ levels across Mexico City for 2004 through 2014. Daily exposures to $PM_{2.5}$ were estimated for each participant during pregnancy using a novel spatiotemporal model that incorporates moderate resolution imaging spectroradiometric satellite-derived aerosol optical depth measurements from the multi-angle implementation of atmospheric correction at a 1- $\times$ 1-km spatial resolution.[19] These remote sensing data are calibrated with data from 12 municipal ground-level monitors of $PM_{2.5}$, roadway density, and meteorologic data (temperature, relative humidity, planetary boundary layer, and daily precipitation) to yield estimates of daily residential $PM_{2.5}$ levels for each participant. Mixed-effect models with spatial and temporal predictors and day-specific random effects were used to account for temporal variations in the relation between $PM_{2.5}$ and aerosol optical depth. For days without aerosol optical depth data, the model was fit with a seasonal smooth function of latitude and longitude and time-varying average incorporating local monitoring. Model performance was assessed using monitor-level leave-1-out cross-validation with an R^2 of 0.724. For more in-depth model details, please refer to Just et al.[19]

Each woman's daily exposure to $PM_{2.5}$ across the pregnancy was estimated based on the gestational age and residential address during the pregnancy. Because ultrasounds were not routinely performed as standard of care, gestational age at birth was estimated based on the mother's report of her last menstrual period and by a standardized physical examination.[20] If the physical examination assessment of gestational age differed by more than 3 weeks from the gestational age based on the last menstrual period, then the physical examination was used instead of the gestational age determined by the last menstrual period. We calculated the average $PM_{2.5}$ over clinically defined trimesters (first trimester 1–13 weeks, second trimester 14–27 weeks, third trimester 28 weeks to delivery).

Measurements of Psychosocial Stress

The validated Spanish version of the Crisis in Family Systems–Revised (CRISYS)[21] survey was administered by a trained psychologist during the second or third trimester of pregnancy and during the 48-month follow-up postnatal visit. The CRISYS questionnaire assesses life events across 11 domains: financial, legal, career, relationship, home safety, neighborhood safety, medical issues (self and others), home, prejudice, and authority. Participants rated life events occurring in the past 6 months as positive, negative, or neutral. Previous research has shown increased vulnerability across multiple domains.[3,8,22] Therefore, domains with at least 1 negative life event were summed into a negative life event