born to mothers with overall distress (OR: 1.60 [95% confidence interval (CI): 1.32–1.93]), depression (OR: 1.46 [95% CI: 1.20–1.77]), and anxiety (OR: 1.39 [95% CI: 1.15–1.67]) during pregnancy. Similar positive associations were observed among children of mothers with a history of asthma and atopy compared with those without such a history and among children of non-smokers versus smokers. No associations were observed between paternal psychological distress during pregnancy or maternal and paternal psychological distress after delivery and childhood wheezing or physician-diagnosed asthma.

CONCLUSIONS. This study found that children of mothers experiencing psychological distress during pregnancy had increased odds of wheezing in the first 6 years of life. This finding was independent of paternal psychological distress or psychological distress in either parent after delivery, suggesting an intrauterine programming effect on fetal lung development and resulting respiratory morbidity.

REVIEWER COMMENTS. Few studies have explored the association of maternal psychological distress on childhood wheezing and none previously in a population of this size. As the authors noted, there is a potential for bias given that children included were more often from parents with a higher educational level and less psychological distress during pregnancy than those lost to follow-up. Nevertheless, the mechanisms that may connect maternal psychological distress with childhood wheezing are currently unknown, and the potential of an intrauterine biological mechanism based on the results of this study highlight the need for further research measuring stress markers, changes in the immune system, and possible epigenetic mechanisms that contribute to intrauterine programming for atopic disease outcomes.

Effects of Prenatal Community Violence and Ambient Air Pollution on Childhood Wheeze in an Urban Population

PURPOSE OF THE STUDY. Prenatal exposures to maternal stress and physical toxins can affect children’s respiratory development and health. This study sought to examine the effects of prenatal psychosocial stressors (exposure to community violence [ECV]) and physical (traffic-related air pollution) stressors on childhood wheeze concurrently in an urban population.

STUDY POPULATION. The study enrolled 989 women (≥18 years old) in mid- to late pregnancy (28.4 ± 7.9 weeks) receiving care at Brigham & Women’s Hospital in Boston, Massachusetts, between August 2002 and December 2009. Of these, 708 mother–child pairs completed the study and were included in the analyses.

METHODS. In this cohort study, mothers completed a multi-item survey to assess prenatal ECV, and results were summarized into a continuous scale. Prenatal exposure to black carbon was estimated based on residence during pregnancy by using land-use regression modeling; exposure to particulate matter of diameter <2.5 μm (PM2.5) was estimated by using land-use regression modeling incorporating satellite data. Mothers reported child wheeze at 3-month intervals up to age 24 months, with ≥2 episodes constituting repeated wheeze. The independent effects of ECV and air pollutants on repeated wheeze were analyzed by using multivariate logistic regression. Interactions between ECV and air pollutants were examined in stratified analyses.

RESULTS. Most mothers were of an ethnic minority (55% Hispanic and 29% black) and low socioeconomic status (62% with ≤12 years of education). Eighty-seven (12%) children wheezed repeatedly. In the multivariate models, ECV (odds ratio [OR]: 1.95 [95% confidence interval (CI): 1.13–3.36]) was independently associated with wheeze, adjusting for gender, race/ethnicity, maternal education, birth season, maternal atopy, and cockroach antigen. Black carbon (OR: 1.84 [95% CI: 1.08–3.12]) and PM2.5 (OR: 2.02 [95% CI: 1.20–3.40]) produced similar associations. In stratified analyses, a statistically significant association was shown between high prenatal ECV and increased repeated wheeze in the low black carbon and low PM2.5 groups, suggesting an interaction between ECV and air pollution.

CONCLUSIONS. The findings suggest that increased ECV and higher exposure to air pollutants in the prenatal period independently contribute to repeated wheeze in these urban children. In addition, the stratified analyses suggest that place-based psychosocial stressors may affect the mother such that physical pollutants adversely affect the fetus, even at relatively lower levels.

REVIEWER COMMENTS. Childhood wheezing respiratory illness causes significant morbidity, particularly in urban communities of lower socioeconomic status, and characterizing its risk factors remains important. This study contributes to known associations with community violence and ambient pollution by providing additional evidence that they exert independent effects on wheeze and novel evidence that they may interact such that their effects are synergistic. Future larger scale studies are necessary to clarify these interactions, as well as to confirm that these relationships hold in the long term.
Asthma During Pregnancy and Clinical Outcomes in Offspring: A National Cohort Study


PURPOSE OF THE STUDY. The goal of this study was to determine the associations between asthma during pregnancy and the offspring’s risk of a wide variety of childhood diseases.

STUDY POPULATION. Birth data between 1996 and 2002 were prospectively collected from the Danish National Birth Cohort; 66712 mother–child pairs were eligible and completed the study. Mothers had given birth to live singletons, most were aged >27 years, they had a medium to high socioeconomic status, were in average to very good health, were multiparous, and ~25% of the women reported smoking. A total of 4145 (6.2%) had a diagnosis of self-reported asthma during their pregnancy.

METHODS. Computer-assisted interviews at ~12 and 30 weeks’ gestation and at 6 months’ postpartum were used to gather information about maternal asthma. Information on the children’s diseases was obtained from the Danish National Hospital Register. Cox and logistic regression models were used to analyze the associations between asthma during pregnancy and the risk of offspring disease, as well as controlling for potential confounders.

RESULTS. Offspring were followed up for mean of 6.2 years (range: 3.6–8.9 years). Positive associations included an increased risk of infectious and parasitic diseases (hazard ratio [HR]: 1.34 [95% confidence interval (CI): 1.23–1.46]) and diseases of the nervous system (HR: 1.43 [95% CI: 1.18–1.73]), ear (HR: 1.33 [95% CI: 1.19–1.48]), respiratory system (HR 1.43 [95% CI: 1.34–1.52]), and skin (HR: 1.39 [95% CI: 1.20–1.60]). Potential associations not confirmed by analysis included endocrine and metabolic disorders (HR: 1.26 [95% CI: 1.02–1.55]), digestive system diseases (HR: 1.17 [95% CI: 1.04–1.32]), and congenital malformations (odds ratio: 1.13 [95% CI: 1.01–1.26]). There was no noted increased risk between maternal asthma and neoplasm, mental disorders, or diseases of the blood and immune system, circulatory system, musculoskeletal system, and genitourinary system.

CONCLUSIONS. The observed associations may be secondary to maternal hypoxia restricting fetal oxygenation, increase in cytokine exposure, or dysregulation of the hypothalamic-pituitary-adrenal axis. Results suggest the importance of monitoring and evaluating for maternal asthma during pregnancy and continuing to carefully follow up the offspring postnatally.

REVIEWER COMMENTS. This study assessed maternal asthma and its long-term consequences on the offspring. A large patient cohort with prospectively collected data and the inclusion of medically verified diagnoses significantly strengthened the results. Asthma severity information was not assessed by spirometry or the use of asthma controller medications, nor did the study examine the number of maternal asthma exacerbations during the prenatal and perinatal periods. The association between maternal asthma and childhood diseases emphasizes the importance of monitoring the infant postnatally, as well as through childhood, for these diseases.

Seasonality of Asthma: A Retrospective Population Study


PURPOSE OF THE STUDY. The goal of this study was to evaluate whether seasonal variations in asthma (with the highest incidence in September) can be documented in a large cohort of children in primary care and to determine the impact of age, gender, and urban/rural living.

STUDY POPULATION. A historical population of children aged 2 to 15 years in Israel’s Clalit Health Services registry, seen from 2005 to 2009, were included in this study. A total of 919,873 children were identified.

METHODS. Electronic record reviews were conducted. The key study outcomes were the diagnosis of asthma exacerbations and asthma medication prescriptions, analyzed according to week of diagnosis. Statistical models were built to assess relative strength of secular trends, seasonality, and age group.

RESULTS. The authors documented that 8.9% of children were asthmatic, and 62% were boys. The age groups were as follows: 49% aged 2 to 5 years, 24% aged 6 to 9 years, and 27% aged 10 to 16 years. There was a 2.01-fold increase in pediatric asthma exacerbations and a 2.28-fold increase in prescriptions of asthma bronchodilator medications during September compared with August. The association between the opening of school and the incidence of asthma-related visits to the primary care physician was greatest in children aged 2 to 5 years (odds ratio: 2.15) and 6 to 11 years (1.90-fold). Adolescents had a lesser peak (1.81-fold). There was a second rise in late fall, with fluctuations throughout winter, and a trough in summer.
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