HEI

STATEMENT

Synopsis of Research Report 219

HEALTH EFFECTS INSTITUTE

Air Pollution and Children's Asthma: Prenatal and Postnatal Assessment of an Array of Air Pollutants

BACKGROUND

Exposure to fine particulate matter and other air pollutants is associated with a myriad of health effects, including increased risk of asthma, a chronic disease that affects 262 million people worldwide and is the most common chronic disease in children. Asthma leads to reduced quality of life, emergency room visits, hospitalizations, and missed school and work days. It is also associated with high health care costs. Asthma prevalence among children and adolescents in high income countries has increased in recent decades. A better understanding of the risk factors that contribute to asthma and how they can be modified is needed. In particular, there is little information about the role of exposure to individual and combined air pollutants in relation to childhood asthma risk and on exposure windows during pregnancy and early childhood that are related to the development of asthma. Additionally, the biological mechanisms of the association between air pollution exposure and asthma are not well understood.

Dr. Pedersen at the University of Copenhagen and colleagues sought to investigate early-life air pollution exposures from multiple sources and in different exposure windows in relation to asthma, lung function, and various biomarkers of inflammation using data from four longitudinal birth cohort studies in Denmark. The team proposed to investigate exposures to an array of air pollutants, including the criteria pollutants — particulate matter, ozone, sulfur dioxide, nitrogen dioxide — and combinations of those pollutants. This study was funded through HEI's Request for Applications 16-1: Walter A. Rosenblith New Investigator Award.

What This Study Adds

- This study investigated children's asthma in four Danish cohorts and focused on exposure to an array of air pollutants, including fine particulate matter, ozone, sulfur dioxide, nitrogen dioxide, and combinations of those pollutants.
- Air pollutant exposures were generally associated with increased risk of developing childhood asthma but were less consistently associated with asthma-related immune mediators and with lung function.
- The study found that both prenatal and postnatal periods are important windows of exposure for asthma development.
- The study underscores the importance of health outcome assessment methods in better understanding asthma risk factors and prevalence.

APPROACH

Pedersen and colleagues linked different data sources to create a nationwide cohort and additionally used three existing population-based cohort studies of children born in Denmark between 1998 and 2016 to investigate associations between exposure to ambient air pollution and childhood asthma. They included one large, nationwide administrative cohort of about one million children and three smaller cohorts with detailed individual information on covariates such as maternal smoking during pregnancy, maternal and paternal asthma, presence of indoor sources of air pollutants, and socioeconomic status. The incorporation of smaller and larger cohorts with varying levels of information leveraged the merits of both approaches.

The investigators assessed four outcomes related to childhood asthma: (1) risk of developing asthma based on doctor diagnosis and medical records (asthma incidence), (2) total proportion of children with asthma based on parental-reported asthma and asthma-related symptoms at age seven (asthma prevalence), (3) biomarkers of inflammation that are suspected to be in the biological pathway for asthma development, DNA methylation, and gene expression, and (4) lung function in children at age six by assessing airway obstruction, which is one of the main tests for diagnosing asthma.

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Marie Pedersen at the University of Copenhagen, Denmark, and colleagues. The complete report, *Birth Cohort Studies of Long-Term Exposure to Ambient Air Pollution in Early Life and Development of Asthma in Children and Adolescents from Denmark*, © 2024 Health Effects Institute, can be downloaded from *www.healtheffects.org/publications*.

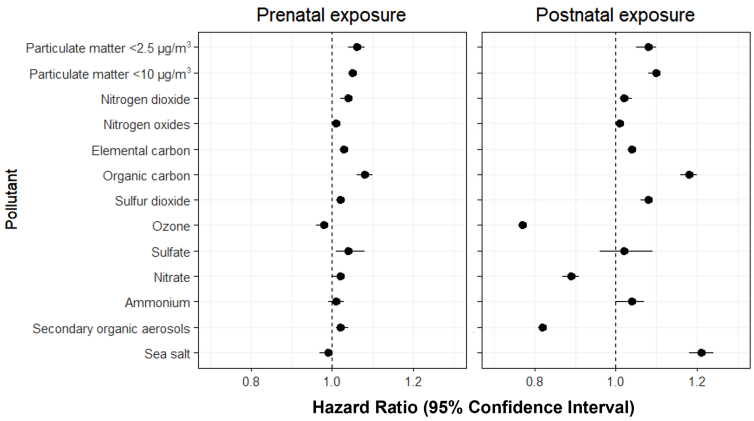
The investigators used a sophisticated chemical transport model system that integrates three separate models to estimate regional, urban, and street level ambient air pollution concentrations. Concentrations of 13 pollutants were estimated, including particulate matter and nitrogen dioxide. They estimated prenatal and postnatal mean exposures during pregnancy and the first year of life for each residential address, while accounting for residential mobility. Additionally, they estimated mean long-term exposure from birth to the age of follow up for analyses that investigated asthma prevalence at age 7 and lung function at age 6.

Pedersen and colleagues used various statistical models to estimate associations between ambient air pollution exposure and the four asthma outcomes. Additionally, they performed analyses using two-pollutant models with fine particulate matter and nitrogen dioxide for asthma incidence and lung function. They adjusted for many individual and area-level covariates and assessed robustness of the associations of air pollution and asthma incidence using various sensitivity analyses.

KEY RESULTS

In the nationwide cohort, 6.1% of about one million children born between 1998 and 2016 were diagnosed with asthma over the course of the study period (asthma incidence). Children in this study were exposed to average concentrations of 10.5 μg/m^3 for fine particulate matter and 17.5 μg/m^3 for nitrogen dioxide during the prenatal period. For most air pollutants, prenatal exposures were moderately to highly correlated with postnatal exposures.

Prenatal exposure to all air pollutants except for ozone and sea salt and postnatal exposure to most air pollutants except for ozone, nitrate, and sea salt were associated with increased risk of developing asthma (**Statement Figure**).



Statement Figure. Associations between prenatal and postnatal exposure to ambient air pollutants and risk of asthma development among children in the Danish Nationwide Cohort.

Associations for postnatal exposures were consistent after adjustment for prenatal exposures. In two-pollutant models, Pedersen and colleagues observed that prenatal exposure to fine particulate matter was more consistently associated with asthma incidence than was prenatal exposure to nitrogen dioxide.

In the smaller cohorts, 4.4% of children had asthma at age 7 (asthma prevalence). Additionally in the smaller cohorts, prenatal and postnatal exposures to some air pollutants were associated with reduced lung function at age 6. For example, a 2%–3% reduction in lung function was associated with prenatal exposure to fine particulate matter and ammonium. Additionally, prenatal exposures to particulate matter and nitrogen dioxide were associated with altered profiles of biomarkers of immune mediators, but not with DNA methylation or gene expression. These altered profiles included biomarkers related to asthma, anti-inflammatory immune responses, and pro-inflammatory immune responses, presenting a unique immune signature.

INTERPRETATION AND CONCLUSIONS

This study represents an important contribution to our knowledge about exposure to ambient air pollutants in relation to childhood asthma and immune mediators. The study's findings suggest that both prenatal and postnatal ambient air pollution exposures affect asthma development. These findings were observed at fine particulate matter and nitrogen dioxide levels below the current (25 and 40 μg/m^3) and even the proposed (10 and 20 μg/m^3) annual European Union air quality standards. Additionally, the study found that asthma outcome assessment methods are critical in better understanding asthma risk factors and prevalence.

The study observed less consistent results for associations of air pollution exposures with asthma-related immune mediators and with lung function. However, the report presents an important step toward the better understanding of air pollution exposure in relation to asthma development, including specific risk factors and critical windows of exposure.

Continued development of two-pollutant and multipollutant models would further advance our understanding of asthma risk and development. Ultimately, this study has documented that prenatal and postnatal exposures to ambient air pollutants, such as particulate matter and nitrogen dioxide, are associated with increased risk of childhood asthma in Denmark.

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