HEALTH EFFECTS INSTITUTE

STATEMENT

Synopsis of Research Report 189

Ambient Air Pollution and Adverse Pregnancy Outcomes in Wuhan, China

BACKGROUND

Several recent studies have suggested that maternal exposures to air pollution and temperature extremes might contribute to low birth weight (LBW), preterm birth (PTB), and other outcomes that can adversely affect infant health. At the time the current study began, most other studies had been conducted in the United States or Europe. Dr. Zhengmin Qian proposed to extend work he had done on ambient particulate air pollution and daily mortality in Wuhan, China (Qian et al. 2010), as part of the HEI-sponsored Public Health and Air Pollution in Asia program, to study adverse birth outcomes. Wuhan is the capital city of Hubei province, has a large population of about 6.4 million within the urban study area, experiences temperture extremes, and generally has higher air pollution levels than those observed in the United States and Europe, thus providing a good opportunity to explore questions about air pollution and health.

APPROACH

Qian and colleagues planned a cohort and nested case–control design with four specific aims, examining whether increased exposures to air pollutants ($PM_{2.5}$, PM_{10}, SO_2, NO_2, O_3, and CO) during vulnerable pregnancy periods were associated with increased rates of PTB, LBW (< 2500 g), or intrauterine growth retardation (IUGR, defined as having a birth weight below the 10th percentile of singleton live births in Wuhan) after adjusting for major risk factors and whether the associations were confounded by copollutant exposures, affected by residual confounding, or modified by temperature extremes, socioeconomic status (SES), or secondhand smoke (SHS) exposure.

The cohort study included 95,911 births that occurred from June 10, 2011, to June 9, 2013, and met typical prespecified inclusion criteria used in other birth outcome studies. The case–control study included 3146 cases (PTB, LBW, or both, but not IUGR) and 4263 controls (matched to the cases by birth month) for whom investigators were able to complete home visits and questionnaires.

What This Study Adds

- The investigators created one of the largest administrative cohorts in a major Chinese city with which to examine their hypotheses about the effects of exposures to $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3 and other key covariates on preterm birth, low birth weight, and intrauterine growth retardation.
- In cohort and case–control studies, the investigators found weak evidence of effects of exposure to air pollution during the entire pregnancy on preterm birth and low birth weight. The effects were similar, in some cases, to those found in other studies. They found limited evidence of air pollution effects on intrauterine growth retardation and found analyses of vulnerable exposure windows to be inconclusive.
- In the HEI Review Committee's view, given a number of challenges, including unresolved differences between the findings of the cohort and case–control studies, the results should be considered suggestive rather than conclusive, and should be interpreted carefully together.
- Given the opportunities created by this data set, the Committee encourages further exploration and analysis by the investigators going forward.

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Zhengmin Qian at Saint Louis University College for Public Health and Social Justice, St. Louis, Missouri, and colleagues. The complete report, *Ambient Air Pollution and Adverse Pregnancy Outcomes in Wuhan, China* (© 2016 Health Effects Institute), can be obtained from HEI or our Web site (see next page).

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The investigators obtained air pollution and daily weather data for August 2010 to June 2013 from nine monitoring stations representing background air pollution sites in seven Wuhan inner-city districts. Only two of these stations provided $PM_{2.5}$ data. For the cohort study, the investigators assigned exposures to mothers according to the daily mean concentrations from the monitor nearest the residential community in which the mother lived at the time of the birth. For the case–control study, they assigned exposures based on the inverse distance weighted average of daily mean concentrations from the three nearest monitors, for all but $PM_{2.5}$ for which the method was not specified.

They also collected data on various factors that might confound or modify the impact of the pollutants on the adverse outcomes, including data collected in the cohort from mothers at the time of delivery and, in the case–control study, from questionnaires administered to mothers. In the case–control study, covariates representing SES (as indicated by the mother's educational attainment and household income) and SHS exposures were of particular interest.

The primary statistical analyses of the pollutant associations with PTB, LBW, and IUGR were conducted using logistic regression models. In the cohort study, exposures during the pregnancy period of interest (full term, trimesters, and selected months) were included as continuous variables. In the case–control study, the exposures were modeled as binary variables (i.e., above or below the median pollutant concentrations). Numerous sensitivity analyses were conducted.

RESULTS AND INTERPRETATION

Although originally planning a nested case–control study, the investigators encountered challenges that led them to analyze the cohort and case–control studies using different ways of assigning exposures and characterizing them in their statistical models. These decisions precluded direct comparisons between the sets of results, making it difficult to answer the questions about residual confounding that nested case–control studies are designed to answer. The odds ratios from the two study designs using different exposures also have different interpretations.

Still, one can ask whether the sets of findings were qualitatively consistent with each other or with those of similar studies. There were some similarities. Both studies suggested that increased $PM_{2.5}$, PM_{10}, CO, and O_3 exposures over the full pregnancy were associated with small increases in the odds of PTB (the case–control study also showed an association with NO_2) and that increased $PM_{2.5}$ exposures were associated with significantly increased odds of LBW. However, most of the other pollutants had no effect on LBW, except CO in the cohort study and O_3 in the case–control study, both of which increased the odds of LBW. The exposures over the entire pregnancy were generally associated with decreased odds of IUGR. Adjustments for potential confounders were greatest for the delivery covariates.

The investigators found no systematic association of any of these outcomes with particular trimesters or months, another result that differed from those of some other studies. They found little evidence that their main results were confounded or modified by the presence of copollutants, although with the exception of O_3, most of the pollutants were highly correlated, making it difficult to disentangle the effects of individual pollutants.

Could the two sets of data be analyzed in a more comparable way, as in a standard nested case–control study? At the Committee's request, the investigators reanalyzed the case–control data using the same exposures and models as in the cohort study. The results were strikingly different from those using the inverse distance weighted exposures, modeled as binary variables — the pollutants had either no effect or an apparent beneficial effect on PTB and LBW. The Committee was not convinced by the explanations offered for these differences, leaving the reasons for them unresolved.

CONCLUSIONS

This study set out to answer important questions about the effects of air pollution exposure on three measures of adverse birth outcomes — LBW, PTB, and IUGR — in a large cohort of mothers and newborns in Wuhan, China. Given the cohort size, high pollution levels and temperatures, and detailed covariate data, the investigators were well poised to address these questions. They sought to pattern their work on other studies of birth outcomes, were very responsive to Committee questions, and provided many additional analyses and explanations.

In the Committee's view, however, the study was unable to address with confidence several of its specific aims. Most important, the differences in results when the case–control data were analyzed with different exposure metrics remain unexplained, raising concerns about the ability to draw conclusions from subsequent analyses assessing residual confounding and effect modification by temperature extremes, SES, and SHS exposure. Consequently, any individual findings from the cohort and case–control studies should be considered suggestive rather than conclusive, and should be interpreted carefully together.

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