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International Collaboration on Air Pollution and Pregnancy Outcomes

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Abstract

Reviews find a likely adverse effect of air pollution on perinatal outcomes, but variation of findings hinders the ability to incorporate the research into policy. The International Collaboration on Air Pollution and Pregnancy Outcomes (ICAPPO) was formed to better understand relationships between air pollution and adverse birth outcomes through standardized parallel analyses in datasets from different countries. A planning group with 10 members from 6 countries was formed to coordinate the project. Collaboration participants have datasets with air pollution values and birth outcomes. Eighteen research groups with data for approximately 20 locations in Asia, Australia, Europe, North America, and South America are participating, with most participating in an initial pilot study. Datasets generally cover the 1990s. Almost all participants have some measure of particulate matter, and most have ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Strong enthusiasm for participating and a geographically-diverse range of participants should lead to understanding uncertainties about the role of air pollution in perinatal outcomes and provide decision-makers with better tools to account for pregnancy outcomes in air pollution policies.

Keywords: Air pollution • Pregnancy outcomes • Low birth weight • Preterm birth • Particulate matter • Ozone • Carbon monoxide

Introduction

Numerous studies have investigated associations between outdoor air pollution and perinatal health outcomes, including low birth weight, preterm delivery, and infant mortality. These studies provide accumulating evidence for including perinatal outcomes in future national and international (WHO) reviews of air quality standards that previously have little considered these outcomes. Recent qualitative syntheses of these studies have concluded that there is likely an adverse effect of air pollution on pregnancy outcomes. However, there is substantial inconsistency in the methods and findings of these studies, hampering efforts to synthesize the existing evidence, in particular in the form of a meta-analysis. Differences among results include the pollutants associated with the adverse pregnancy outcome and the exposure window of concern. Inconsistencies in the findings among studies may arise from many aspects of each study's design [1].

Exposure definitions (including methods for assessment, time-periods of exposure, spatial resolution, available pollutants, and combinations of pollutants), outcome definitions, and use of potential confounders and effect modifiers often differ among studies. The differences in study design and lack of consistency across study results hinders the ability of decision-makers to incorporate the research evidence into policy and also slows the pace of scientific discovery of how air pollution impacts pregnancy outcomes. Scientific reviews of the evidence recommended additional research on this topic. A third international workshop was held in 2008 in Pasadena, USA, to propose a way forward for ICAPPO [2].

This workshop included planning for a collaborative pilot study and discussing epidemiologic methods, particularly those that can be applied in different settings, for collaborative analyses. A fourth workshop was held in 2009 in Dublin, Ireland to hone the study's aims and discuss future directions. The results of this study indicated that antibiotic use during the antepartum period significantly associated with the risk of EoNI in women with PTL or PROM who had no signs of clinical chorioamnionitis upon admission and delivered under 34 weeks of gestation. In addition, antibiotic use may contribute to adverse effects on vaginal microbiota, including the depletion of lactobacilli and the emergence of resistant strains of common bacteria. We emphasize that the benefits of antibiotic therapy when indicated are clearly significant. However, it's irresponsible use without any microbiological justification is dangerous and leads to adverse effects [3].

Mercer reported that administration of broad-spectrum antibiotics prolonged pregnancy and reduced gestational age-dependent morbidity such as Respiratory Distress Syndrome (RDS) and Necrotizing Enter Colitis (NEC). However, the frequencies of early-onset neonatal sepsis occurring ≤ 72 h of age, or grade 3 or 4 Intra Ventricular Hemorrhage (IVH) were similar between mothers receiving antibiotics and those receiving placebo. For PTL patients, antibiotics do not show short-term neonatal benefits and may be associated with long-term harm. A Cochrane review concluded that antibiotics intended only for pregnancy prolongation in PTL patients should not be administered. Intravenous GBS prophylaxis is recommended until GBS test results are available. In this study, eight women with PTL received antibiotics due to unknown GBS results on admission, and only one infant from those women developed EoNI. However, about one-third of EoNI occurred in the infants of women with PTL who received antibiotics for UTI. Women presenting with symptoms should obviously be treated to prevent more severe sequelae from urosepsis. Yonder reported that antibiotic therapy increased the risk of preterm birth in PTL patients without intra-amniotic microbes. They speculated that empirical antibiotic therapy for patients whose amniotic fluid was microbe-negative affects their intestinal bacteria and the homeostatic mechanisms required to maintain the immune system during pregnancy. As PTL is frequently complicated by UTI, it may be impractical for the obstetrician to withhold treatment from those with UTI according to the findings of Yoneda the vagina, with its microbiota, has a balanced ecosystem in which the dominant bacteria are vaginal Lactobacillus sp. that plays a protective role against ascending infection. The bacteria that reside in the female genital tract vary and are quite complex [4].

Methods

The ICAPPO was established to coordinate an international effort toward understanding how much differences in methodology contribute to variation in study findings. Most ICAPPO participants are researchers in the field of air pollution and pregnancy outcomes who already have datasets that link maternal exposure to air pollution with pregnancy outcomes; many of these participants have published previous papers on this topic, which comprise the major papers in the field. Other ICAPPO participants do not have an existing data source available but have expressed an interest in participating. While many ICAPPO participants are those actively involved in the research goals of this project, other researchers have provided significant contributions to the overall aims of the ICAPPO through their insights during the workshops. The first step for the ICAPPO was to collect information on the data attributes from each of the study locations with respect to the availability of variables, timeframe, study location, and other factors [5, 6]. Participants were asked to provide the following information: location, available air pollutants, study period, number of births included in the study (or number of study subjects), and covariates available (e.g., mother's smoking status during pregnancy, gestational age, mother's race). Mostly these datasets have been used for previously published studies, are currently being used for ongoing studies, or both. Datasets have typically been constructed from some type of air pollution exposure metric linked to data available from routinely collected administrative records (birth certificates), birth record datasets constructed for a specific study, or to data from a pregnancy or birth cohort study [7-10].

Results

Currently, the ICAPPO has information from over 20 separate research groups in North America, Europe, Australia, Latin America and Asia. The number of births that are available per dataset in each study location is generally in the

range of 50,000 to 500,000, though there are smaller and larger studies. The available datasets primarily link pregnancy outcome data to some measurement of air pollution data. Most data on pregnancy outcomes stem from birth certificates; thus, information on the birth outcomes and related covariates is primarily based on what is available from the birth certificates in each location [11]. Information on the key covariates available from each of the study locations is given. All study locations had data on gestational age, typically measured through re call of last menstrual period, and birth weight. Most birth certificate data include maternal and infant characteristics, such as education, parity, marital status, age, tobacco and alcohol use (sometimes), prenatal care, residence at birth, gestational age, birth weight, and date of birth (either exact date or year and month). Depending on the original source of the birth certificate data, some data may be aggregated. For example, the exact residence at birth or the exact date of birth may not be known in a public dataset. The availability of information on race and ethnicity varies, primarily by geographic locations; while race and ethnicity are important predictors of birth outcomes in the United States, other indices, such as immigration status or language are important factors in other countries. Many of the study locations also use one or more community level demographic or socioeconomic indicators (e.g., income levels by census tract or zip code in the USA). A few of the collaborating study locations (Los Angeles, USA; Generation R study, Netherlands; INMA cohort, Spain; Eden cohort, France; and Brisbane, Australia) also have questionnaire data available in addition to birth certificate information, which can be used to evaluate the quality and analytic usefulness of the more widely available covariates [12].

Discussion

Challenges of the ICAPPO relate to its ambitious nature. We have enthusiastic response from a wide range of geographic locations, although not all parts of the world are well represented, with participation primarily from North America and Europe. However, covering more areas of the world must be balanced with resources for adding additional collaborators. Although numerous researchers have expressed interest in participating in the study, the logistics of coordinating such a large effort are not trivial. Conducting the pilot study will allow us to evaluate the level of participation in the collaboration and the number of study locations may drop or increase as other commitments increase or new participants and study locations may be added. However, there are still challenges in addressing remaining variability in some of the key covariate data for the analysis. For example, maternal education will be used as the primary proxy for SES [13]. This is a commonly used index of SES in perinatal studies; is correlated, albeit imperfectly, with SES; and is also an important determinant of pregnancy outcomes. While most study locations have some measure of maternal education, there is variability in the construct of the measure, both in type of data used to for the measure (e.g., most have maternal education, a few locations have area level variables) and the cultural context of maternal education (e.g., the percentage of women who complete high school varies from location to location). The degree of infectiousness of a particular vaginal pathogen depends not only on the type of microorganism and its intrinsic virulence but also on the relative amounts of the various bacteria. In this study, Lactobacillus sp. were detected in the vaginal specimens of approximately 50% of women upon admission and no differences were observed in the vaginal micro biome upon admission between women whose infants subsequently developed EoNI and those whose infants did not. [14]. Results of the present study suggest that antibiotic therapy could cause the depletion of lactobacilli and the selection of drug-resistant organisms in the vaginal microbiota of a subset of women whose infants developed EoNI. In the neonatal intensive care unit, initial empiric therapy for EoNI should consist of ampicillin and aminoglycoside. Such a regimen is sufficient for the treatment of major pathogens, including GBS and gram-negative enteric bacteria. Antenatal antibiotic exposure can result in the replacement of common pathogens with opportunistic or drug-resistant pathogens; therefore, these microbiological changes may affect the antimicrobial strategies of the neonatal care team in the near future [15].

Conclusion

It should also greatly enhance our understanding of the effects of air pollution on pregnancy outcomes and motivate focused research questions in the field, such as biological mechanisms that link exposure to specific outcomes. It will also strengthen efforts in individual countries to understand and ultimately mitigate harmful effects from air pollution, by enhancing

understanding of their individual place-based study results in the context of comparable results from other study locations around the world. Finally, it will create a network of researchers working across the globe on environmental and pregnancy outcomes generally, which will leverage other opportunities to evaluate how the environment can influence birth outcomes, and ultimately lead to insights that will inform activities to prevent harmful exposures and improve the health of children worldwide.

Acknowledgement

None

Conflict of Interest

No conflict of interest

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