Environmental Research 150 (2016) 119–127

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Exposure to outdoor air pollution during trimesters of pregnancy and childhood asthma, allergic rhinitis, and eczema

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ARTICLE INFO

Article history:
Received 13 November 2015
Received in revised form
26 May 2016
Accepted 28 May 2016

Keywords:
Allergy
Traffic-related air pollution
Fetal origins
Prenatal exposure
Multi- pollutant and trimester model

ABSTRACT

Background: Mounting evidence suggests that exposure to ambient air pollution is associated with the development of childhood allergic diseases, but the effect of prenatal exposure to air pollution on the risk of childhood asthma and allergy is unclear.
Objectives: We evaluated the association between maternal exposure to outdoor air pollution during different trimesters of pregnancy and incidence of asthma, allergic rhinitis, and eczema in 2598 preschool children aged 3–6 years in China.
Methods: Children's lifetime incidence of allergic diseases was obtained using questionnaire. Individual exposure to outdoor air pollutants during trimesters of pregnancy was estimated by an inverse distance weighted (IDW) method based on the measured concentrations at monitoring stations. We used multiple logistic regression method to estimate the odds ratio (OR) of asthma, allergic rhinitis, and eczema for per interquartile range (IQR) increase in the exposure to air pollutant in each trimester, which was adjusted for the effect of other air pollutants and its effect in other trimesters by a multi-pollutant/trimester model.
Results: Incidence of asthma (6.8%), allergic rhinitis (7.3%), and eczema (28.6%) in children was associated with maternal exposure to traffic-related pollutant NO_2 during entire pregnancy with OR (95% confidence interval [CI]) respectively 1.63 (0.99–2.70), 1.69 (1.03–2.77), and 1.37 (1.04–1.80). After adjustment for other pollutants and trimesters, we found the association was significant only in specific trimester: the first trimester for eczema (1.54, 1.14–2.09), the second trimester for asthma (1.72, 1.02–2.97), and the third trimester for allergic rhinitis (1.77, 1.09–2.89). Sensitivity analysis indicated that the trimester sensitive to the development of allergic diseases was stable.
Conclusion: Maternal exposure to traffic-related air pollutant NO_2 during pregnancy, especially in specific trimesters, is associated with an increased risk of developing asthma, rhinitis, and eczema in children. Our results support the hypothesis that childhood allergic diseases originate in fetal life and are triggered by traffic-related air pollution in sensitive trimesters.

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1. Introduction

Asthma and allergy are the most common diseases and major health issues in children worldwide because they lead to a heavy economic burden and poor quality of life (Asher, 2006; Eder et al., 2006). During past decades, most developing countries such as China witnessed a rapid increase in the prevalence of childhood asthma and allergies that deserves more attention (Ait-Khaled et al., 2007; Zhang et al., 2013). Although it is largely accepted that gene-environment interactions contribute to the development of asthma and allergies, the changing environment is likely responsible for the rapid increase in the prevalence (London, 2007).

Mounting evidence suggests that long-term exposure to ambient air pollution is associated with the development of asthma and allergies in children (Guarnieri and Balmes, 2014; Kim et al., 2013), and a distinct need is then to find out the key component of air pollution and the critical exposure window so as to develop more effective measures of prevention and intervention. Many recent epidemiological studies in developed countries have

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http://dx.doi.org/10.1016/j.envres.2016.05.050
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demonstrated that the traffic-related air pollution has been linked with childhood asthma and allergies (Brauer et al., 2002; Brunekreef and Sunyer, 2003; Gauderman et al., 2005; Gehring et al., 2010; Jerrett et al., 2008; Morgenstern et al., 2007). With the rapid urbanization and economic development during the past decade, China has recently witnessed a substantial increase in the amount of motor vehicles in larger cities that causes heavy traffic-related air pollution. However, there is a lack of studies in China whether the strikingly increased traffic-related air pollution is associated with the rapid increase of childhood asthma and allergies.

Early-life exposure to air pollution has recently been considered as an important determinant in the later development of allergic diseases in children (Warner, 2004). According to Barker hypothesis (Barker and Osmond, 1986), prenatal and early postnatal exposures influence developmental plasticity and result in altered programming which leads to development of a broad spectrum of diseases in childhood and adulthood (Gluckman et al., 2008). Emerging evidences show that exposure to air pollution during pregnancy is associated with elevated risk of adverse birth outcomes (Fleisch et al., 2015; Lakshmanan et al., 2015; de Medeiros et al., 2009; Srám et al., 2005) that have long-term health implications, including increased susceptibility to diseases in the later life (Kajekar, 2007). Some recent studies highlighted that exposure to air pollution during pregnancy is a potential stimulus for the early programming of asthma and allergy (Clark et al., 2010; Kozyrskyj et al., 2011; Sbihi et al., 2015), and our recent work also indicated that prenatal exposure to air pollution was significantly associated with asthma and allergic diseases in preschool children in China (Deng et al., 2015a, 2016, 2015b). Furthermore, some studies found that early childhood allergic diseases were associated with trimester-specific exposure during pregnancy (Aguilera et al., 2013; Esplugues et al., 2011; Hsu et al., 2015; Huang et al., 2015). Despite the importance of early-life exposure in the development of allergy, information on the effect of air pollution exposure, particularly during pregnancy, on allergic diseases early in life has rarely been assessed. The scarce epidemiological evidence on the effect of prenatal exposure to air pollution on the risk of childhood asthma and allergic diseases warrants further investigation.

In this study, we endorse the hypothesis on the fetal origins of childhood allergic diseases and further speculate that disease originates in specific trimester of pregnancy and is triggered by traffic-related air pollution. To test the hypothesis, the objective of our present work is to investigate the association between maternal exposure to air pollution during trimesters of pregnancy and lifetime incidence of asthma, allergic rhinitis, and eczema in preschool children. We carried out the investigation in a prospective cohort study in Changsha, a part of nationwide multicenter "China-Children-Homes-Health (CCHH)" study (Zhang et al., 2013).

2. Materials and methods

2.1. Study population

Between September 2011 and January 2012, we conducted a survey for childhood asthma and allergies in the kindergartens in Changsha, the capital city of Hunan Province in south–central China, having a population of 7.22 million and covering an area of 1909 km^2. The study protocol was approved by the Ethics Committee of the Central South University and also by the health department of each kindergarten. We used a self-administered Chinese questionnaire that combined the standard questionnaire designed by the International Study of Asthma and Allergies in Childhood (ISAAC) (Asher et al., 2006) and a Swedish questionnaire about dampness in buildings and health (DBH) (Bornehag et al., 2004) to collect information on health status, possible exposures to chemical substances in the immediate environment, and lifestyles of the children and their family members. A total of 4988 questionnaires were randomly distributed to the children at 36 participating kindergartens. Children were instructed to have the questionnaire completed by parents and to return it to kindergartens within one week.

We received 3897 completed questionnaires and the overall response rate was 78%. We first excluded 745 children from kindergartens having a response rate lower than 50%, as these excluded kindergartens were mostly distributed in the suburban areas where the children are mainly from the far rural areas and their parents are mainly rural migrant workers, and thus the children's exposure during pregnancy cannot be estimated by using the urban data. Then, we also excluded 162 children with low birth weight (<2.5 kg) and preterm birth (<37 weeks of gestation), and 10 children with multiple births, as these conditions may confound the association between air pollution and asthma (Brauer et al., 2008). We further excluded 80 children aged younger than 3 and older than 6, i.e. the children aged 3–6 were chosen in our study because there are few children >6 years in kindergartens and diagnosis of asthma among children <3 years is often confused. The 302 children without information on the health outcomes were finally excluded. Totally, the 2598 responses of valid questionnaires were used.

2.2. Exposure assessment

2.2.1. Exposure time window

We divided the entire pregnancy into three trimesters. The entire pregnancy was defined as the period from the first month to the last month of pregnancy. The first, second and third trimesters were respectively the periods from the first to third month, the fourth to sixth month, and the seventh to the last month of pregnancy.

2.2.2. Exposure to ambient air pollutants

We selected three pollutants, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and particulate matter ≤ 10 μm in diameter (PM_{10}) to represent ambient air pollution in Changsha where SO_2 was used as an indicator of industry–related air pollution, NO_2 as traffic–related air pollution, and PM_{10} as a surrogate of complex mixture of air pollutants (Kan et al., 2012). Daily 24–hour average concentrations of PM_{10}, SO_2 and NO_2 were obtained from 7 municipal air quality monitoring stations during 2005–2008 that included the period of maternal pregnancy for all the children aged 3–6 in the present study. Measurements at the monitoring stations followed the standard methods set by the State Environmental Protection Agency of China: PM_{10} by a tapered element oscillating microbalance (TEOM1400, Rupprecht & Patashnick, USA), SO_2 by ultraviolet fluorescent method (ML/EC9850, Ecotech, Australia) and NO_2 by the chemiluminescent method (ML/EC9841B, Ecotech, Australia). The detailed information on the monitoring stations and surveyed kindergartens was provided in our previous study (Deng et al., 2015a).

Individual exposure to air pollution was estimated by an inverse distance weighted (IDW) method described elsewhere (Deng et al., 2015a). Briefly, maternal exposure during pregnancy was calculated in terms of air pollutant concentrations at the kindergarten, because parents usually enrolled their children in the kindergarten nearest to their homes and worked near homes. At first, the average daily concentration at each kindergarten was calculated by the obtained daily concentrations from the nearest 4 monitoring stations. Then, the monthly mean concentrations of air pollutants at each kindergarten were computed as the averages

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