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Preconceptional and perinatal exposure to traffic-related air pollution and eczema in preschool children

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ABSTRACT

Background: Evidence linking prenatal exposure to outdoor air pollution with eczema in early childhood is scare, and the role of components of air pollution and exposure timing remains unclear.
Objectives: We investigated the association between exposure to air pollution during preconceptional and perinatal period and the risk of eczema in preschool children.
Methods: We conducted a prospective cohort study of 2598 children aged 3–6 years in Changsha, China. The prevalence of eczema was assessed by a standardized health questionnaire administered by the parents. Individual exposures to nitrogen dioxide (NO_2), sulfur dioxide (SO_2) and particulate matter with an aerodynamic diameter $\leq 10\,\mu m$ (PM_{10}) during the 4th-6th and 1st-3rd month before pregnancy, entire pregnancy, and three trimesters were estimated by an inverse distance weighted (IDW) method based on concentrations measured at monitoring stations. Association between childhood eczema and exposure to air pollution was examined by logistic regression models in terms of odds ratio (OR) and 95% confidence interval (CI) for an interquartile range (IQR) increase in exposure.
Results: Life-time prevalence of eczema in preschool children in Changsha was 28.6%. Childhood eczema was associated with traffic-related air pollutant NO_2 during 3 months before pregnancy and entire pregnancy with adjusted ORs = 1.19 (95% CI: 1.04–1.37) and 1.21 (95% CI: 1.03–1.42) respectively. The highest risk of eczema was observed for the 1st trimester exposure to NO_2 [OR = 1.26 (95% CI: 1.09–1.46)]. However, no association was detected for SO_2 and PM_{10} exposure during any window. High-level exposure to NO_2 during the whole time period significantly increased the effect of NO_2 in all windows on eczema risk as compared with low-level exposure. Sensitivity analysis indicated that the association between both preconceptional and perinatal exposure to NO_2 and childhood eczema was consistent and robust, and this association was modified by some personal, parental hereditary and indoor environmental factors.
Conclusion: Our findings support the hypothesis that early childhood eczema is associated with exposure to traffic-related air pollutant during both preconceptional and perinatal period, especially at a high level of exposure.

1. Introduction

Eczema is the most common inflammatory skin disease in childhood which affects as many as 15%–30% children worldwide [41,62]. Eczema has been on the increase over the past decades [56] along with a faster increasing rate in developing countries [63], such as China [64]. Moreover, early manifestation of eczema has been observed to be associated with an increased risk of asthma and allergic rhinitis later in life [57], and is thus regarded as one of the first steps in the atopic march [31]. Because of its high prevalence and progression into respiratory allergies, childhood eczema could pose a significant burden on healthcare resources and patients' quality of life [15,25]. Therefore, the major need lies

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in exploring the key causal or pathogenic factors and critical time windows to establish more effective strategies for the prevention and management.

Although the occurrence of eczema is associated with genetic factors [36], recently rapid rising incidence rate is likely to be related with environmental factors [60]. Air pollution as one of chief environmental risk factors has been shown to be associated with the development or aggravation of eczema [2]. Previous studies demonstrated that a variety of air pollutants such as particulate matter, volatile organic compounds (VOCs) and traffic-related air pollution could exacerbate eczema symptoms in patients [2,40], but little evidence have been addressed on the association between long-term exposure to air pollution and the development of eczema [2]. Furthermore, exposure to air pollution particularly at a high level may induce oxidative stress in the skin, leading to skin barrier dysfunction or immune dysregulation, which probably conforms to the "outside-inside" hypothesis regarding on the cause of development of atopic dramatis (AD) [2]. 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 [34]. However, there is a lack of studies in China to explore whether the strikingly increased traffic-related air pollution is associated with the rapid increase of childhood eczema.

Prenatal exposure to air pollution has recently been suggested to be an important determinant in the later development of allergic diseases in children [17,19,21,61], which is frequently surmised to be of greater significance than later exposure due to the susceptibility of target organs and systems during developmental periods of life [54]. Infants could be indirectly affected by air pollution before birth either because it crosses the protective barrier of the placenta or because it has a systemic effect on the health of the mother [18]. Maternal exposure to air pollution during pregnancy may alter the immune competence in offspring and thus increase the risk of child's developing health conditions later in life, including asthma and allergies [6]. Furthermore, this impact may be also linked with both paternal and maternal exposure before pregnancy. Air pollution exposure before and during pregnancy may affect placental functional morphology and can be at the origin of disturbances in the functional balance between immune response mechanisms in the newborn [58], and this epigenetic effect has been assessed mostly for maternal exposure especially during pregnancy but rarely for paternal exposure on childhood allergic diseases. However, a recent study suggested the existence of epigenetic windows of susceptibility to environmental insults during sperm development, which highlighted that preconceptional exposure might be related with the development of childhood allergies or susceptibility through a paternal line [55]. Hence, whether effects observed after birth, especially in early childhood, actually reflects the lingering effects of exposures before birth deserves to be investigated. However, only a few recent studies have assessed the effect of prenatal exposure to air pollution on childhood eczema [23,30,32,44] and their findings are inconsistent. Recently, a stronger association has been proved between early childhood eczema and the first trimester exposure to traffic-related pollution during pregnancy [30]. However, limited previous studies only focused on pregnancy exposure, but little information is known about its impact before pregnancy. Therefore, it is of significance to investigate the effect of exposure to ambient air pollution during both preconceptional and perinatal periods on the risk of eczema in early childhood, so as to effectively reduce the onset of eczema and other allergic diseases.

In this study, we endorse the hypothesis on the fetal origins of childhood eczema and further speculate that eczema originates in specific trimester of pregnancy and even critical time before pregnancy, which is triggered by ambient air pollution. To test the hypothesis, we investigated the association between early childhood eczema and air pollution exposure during preconceptional period including 4th-6th and 1st-3rd month before pregnancy, entire pregnancy and different trimesters, with an objective to identify the key components of air pollution and susceptible time window in the development of eczema. We carried out the investigation in a prospective cohort study in Changsha, a part of nationwide multi-center "China-Children-Homes-Health (CCHH)" study [20,64].

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 Chinese version of the standard questionnaire designed by the International Study of Asthma and Allergies in Childhood (ISAAC) [4] and a Swedish questionnaire about dampness in building and health (DBH) [9] to collect information on health status, possible exposures to chemical substances in the immediate, 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 preconceptional and perinatal periods cannot be estimated by using urban data [20]. 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 allergic diseases [12]. 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 and <3 years in kindergartens. The 302 children without information about covariates were finally excluded. Therefore, the 2598 responses of valid questionnaires were used.

2.2. Exposure assessment

2.2.1. Exposure time window

We divided the preconceptional period into two time windows which were defined as the 4th–6th and 1st–3rd month before pregnancy. Furthermore, the entire pregnancy was divided 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