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Prenatal exposure to diurnal temperature variation and early childhood pneumonia

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ABSTRACT

Background: Childhood pneumonia is one of the leading single causes of mortality and morbidity in children worldwide, but its etiology still remains unclear.
Objective: We investigate the association between childhood pneumonia and exposure to diurnal temperature variation (DTV) in different timing windows.
Methods: We conducted a prospective cohort study of 2,598 children aged 3–6 years in Changsha, China. The lifetime prevalence of pneumonia was assessed by a questionnaire administered by the parents. Individual exposure to DTV during both prenatal and postnatal periods was estimated. Logic regression models was used to examine the association between childhood pneumonia and DTV exposure in terms of odds ratios (OR) and 95% confidence interval (CI).
Results: Lifetime prevalence of childhood pneumonia in preschool children in Changsha was high up to 38.6%. We found that childhood pneumonia was significantly associated with prenatal DTV exposure, with adjusted OR (95%CI) =1.19 (1.02–1.38), particularly during the second trimester. However, childhood pneumonia not associated with postnatal DTV exposure. Sensitivity analysis indicated that boys are more susceptible to the pneumonia risk of diurnal temperature variation than girls. We further observed that the prevalence of childhood pneumonia was decreased in recent years as DTV shrinked.
Conclusions: Early childhood pneumonia was associated with prenatal exposure to the diurnal temperature variation (DTV) during pregnancy, particularly in the second trimester, which suggests fetal origin of childhood pneumonia.

1. Introduction

Childhood pneumonia is one of the leading causes of mortality in children aged less than 5 years worldwide (Bhutta et al., 2013). Although mortality due to childhood pneumonia has been declining in the past decades, the morbidity from pneumonia still remains high (Podewils et al., 2004). Pneumonia increased risk of impaired lung growth and reduced vital capacity and forced expiratory volume (Shaheen et al., 1994), which can not only have a lethal effect on child's life (Igor et al., 2013), but also significantly increase the economic and social burdens on child's family and healthcare (Liu et al., 2015; Rudan et al., 2008). It is of note that in the developing countries poverty, nutritional deficit, and limited access to medical care aggravate the consequences of childhood pneumonia. Therefore, there is a critical need to investigate the main risk factors of childhood pneumonia so as to better understand its causation, etiology and pathogenesis, and thus to provide more effective preventative and treatment strategies for childhood pneumonia and its complications and sequelae.

Mounting evidence suggested that childhood pneumonia is a complex disease involving infectious and environmental factors (Kim et al., 2016; Walker et al., 2013). Although many recent epidemiologic studies paid attention to air pollution and found its significant association with childhood pneumonia (Ilabaca et al., 1999; MacIntyre et al., 2014; Smith et al., 2011), temperature as one of chief environmental factors has been shown to be another significant risk factor for the development of childhood pneumonia (Paynter et al., 2010; Xu et al., 2012, 2014b). Recently, diurnal temperature variation (DTV) has been suggested as a predictor of mortality and as an independent risk factor for human health (Braga et al., 2002; Chen et al., 2011; Wen et al., 2016), particularly for cardiovascular and respiratory diseases (Kan et al., 2007; Song et al., 2008; Zhao et al.,

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2016). Only few studies investigated the impact of outdoor daily temperature ranges on respiratory diseases hospital admission visits and its morbidity (Qiu et al., 2015; Xu et al., 2014a; Zhang et al., 2014), childhood asthma (Xu et al., 2013), and childhood respiratory tract infection (Li et al., 2014).

Early life factors influence developmental plasticity and resulting altered programming which leads to later development of a variety of complex diseases, termed the Development Origins of Health and Diseases (DOHaD) paradigm (Gluckman et al., 2008). Several studies addressed on prenatal exposure to air pollution and the development of respiratory diseases (Deng et al., 2016a; DiFranza et al., 2004; Gilliland et al., 2001), however, the effect of prenatal exposure to DTV has never been examined. It is of interest whether long-term exposure to DTV is a risk factor for childhood pneumonia independent of corresponding absolute temperature. The serious lack of knowledge and epidemiological evidence on the role of prenatal exposure to DTV in the development of childhood pneumonia prompts the need for further investigation.

In our study, we hypothesize that childhood pneumonia has fatal origins and further speculate that pneumonia is triggered by long-term exposure to diurnal temperature variation in specific trimester of pregnancy. To test this hypothesis, we investigated the association between early childhood pneumonia and DTV in different timing windows, with an objective to identify the susceptible window of exposure. We carried out the investigation in a prospective cohort study in Changsha, a part of nationwide multicentre "China-Children-Homes-Health (CCHH)"study (Deng et al., 2016b; Zhang et al., 2013).

2. Materials and method

2.1. Study population

Between September 2011 and January 2012, we conducted a survey for respiratory disease and symptoms in children in Changsha. A total of 4988 questionnaires were distributed to the children at 36 randomly chosen kindergartens throughout the city. The study was described in detail elsewhere (Deng et al., 2015a). Children were instructed to have the questionnaire completed by parents and to return it to kindergartens within one week. We received 3897 completed questionnaires with the overall response rate 78%. We excluded 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 pneumonia among children <3 years is often confused. The children without information on the health outcome were also excluded. Totally, the 2598 valid questionnaires were entered into a database.

2.2. Exposure assessment

2.2.1. Timing windows

We divided the life-time exposure into prenatal and postal timing windows. We further divided prenatal period 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 1st to 3rd months, the 4th to 6th months, and the 7th to the last month of pregnancy. The postnatal exposure was defined from first year to the past year, and we further analyzed the first and past years.

2.2.2. Diurnal temperature variation (DTV)

We selected three criteria temperatures, daily mean, maximum, and minimum temperatures (Tmean, Tmax, Tmin), to represent the ambient temperature in Changsha. The diurnal temperature variation (DTV) was defined as DTV=Tmax-Tmin. Daily temperature during 2004–2011 (including all the timing windows of the selected children) was obtained from China Meteorological Administration. Individual exposure to DTV was calculated as follows: (1) Prenatal exposure during entire pregnancy was calculated as average of the monthly mean DTV during all the months of gestation; (2) Exposure during the first, second and third trimesters were respectively calculated as the average of the monthly mean DTV during the periods from 1st to 3rd months, from 4th to 6th months, and from 7th to the last month of gestation; (3) Postnatal exposure was calculated as average of the DTV during the period from the first year to the past year of life; (4) First-year exposure was calculated as the average of monthly DTV during the first year; (5) Past-year exposure was calculated as the average of the monthly DTV during the past year.

2.3. Health outcome

The health outcome is the lifetime prevalence of doctor-diagnosed pneumonia that was defined as an affirmative answer to the question: "Has your child ever been diagnosed with pneumonia?"

2.4. Covariates

Potential confounding variables were obtained from the parent-administered questionnaires. Main covariates included personal factors (child's sex, child's age, birth season, breast-feeding, day-care attendance, occurrence of common cold during the last 12 months, maternal productive age, and parental atopy) and residential factors (housing size, building age, living area, environmental tobacco smoke (ETS), new furniture/redecoration, visiable mold and dampness, and mosquito insence used). These covariates have been identified as being related to the childhood pneumonia and may influence the effect estimates. Child's birth season was divided into spring (from March to May), summer (from June to August), autumn (from September to November), and winter (from December to next February) according to the climate characteristics in Changsha. Parental atopy was defined as a history of maternal or paternal asthma and allergic rhinitis. Outdoor air pollution has also been identified as a confounding variable for childhood pneumonia (MacIntyre et al., 2014). In our study, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and particulate matter ≤10 μm in diameter (PM_{10}) were used to represent ambient air pollution in Changsha (Deng et al., 2015a).

2.5. Statistical analysis

We used multiple logistic regression models to evaluate the association between exposure to each DTV during different trimesters and childhood pneumonia by adjusting potential confounding covariates. Associations in the regression analysis were calculated as odds ratio (OR) with 95% confidence interval (95% CI). A p value less than 0.05 was considered statistically significant. In our analysis, DTV was entered into the models as both continuous and categorical variables. For continuous model, OR was estimated by per IQR increase in exposure levels. For category model, the entire DTV distribution was divided into four intervals (<8 °C, 8.0–8.5 °C, 8.5–9.0 °C, >9 °C during the entire pregnancy, and <7 °C, 7–8 °C, 8–9 °C, >9 °C during three trimesters). The childhood pneumonia risk at each interval was estimated by setting the lowest interval as reference (OR=1). We then implemented a quadratic spline approach to fit the nonlinear associations. This spline specification allows the DTV-pneumonia relation to vary within each interval of the pneumonia distribution. To investigate the robust of the link between exposure to DTV and childhood pneumonia, we further carried out sensitivity analysis for gender difference. All statistical analyses were performed by SPSS software (version 16.0, SPSS Inc., Chicago, USA).

3. Results

Of 2598 children, 1004 (38.6%) had a history of doctor-diagnosed