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Greater temperature variation within a day associated with increased emergency hospital admissions for asthma☆,☆☆

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HIGHLIGHTS

- We examined the association between diurnal temperature range (DTR) and asthma.
- We observed greater DTR associated with increased emergency asthma hospitalizations.
- The effect of DTR was independent of daily mean/minimum temperature and air pollution.
- DTR exhibited significantly greater effect in cool season, in males and children.
- Great DTR was an environmental risk factor for asthma exacerbation.

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ABSTRACT

Asthma is one of the most common chronic conditions affecting both children and adults. Examining the health effects of environmental triggers such as temperature variation may have implications for maintenance of asthma control and prevention. We hypothesized that large diurnal temperature range (DTR) might be a source of additional environmental stress and therefore a risk factor for asthma exacerbation. Daily meteorological data, air pollution concentrations and emergency hospital admissions for asthma from 2004 to 2011 in Hong Kong were collected. Poisson regression models were used to fit the relationship between daily DTR and asthma, after adjusting for the time trend, seasonality, mean temperature, humidity, and levels of outdoor air pollution. Acute adverse effect of DTR on asthma was observed. An increment of 1 °C in DTR over lag0 to lag4 days was associated with a 2.49% (95% CI: 1.86%, 3.14%) increase in daily emergency asthma hospitalizations. The association between DTR and asthma was robust on the adjustment for daily absolute temperature and air pollution. DTR exhibited significantly greater effect in cool season. Males and female children appeared to be more vulnerable to DTR. Results supported that greater temperature variation within a day was an environmental risk factor for asthma exacerbation.

1. Introduction

Asthma is one of the most common chronic conditions affecting both children and adults. It is characterized by airway hyper-responsiveness to physiologic or environmental triggers. This hyper-responsiveness results in pronounced constriction of airway muscles, inflammation, swelling, mucus production, and subsequent respiratory distress (Subbarao et al., 2009). Risk factors for incident asthma among children included male sex, atopic sensitization, parental history of asthma, early-life stressors and infections, obesity, and exposure to indoor allergens, tobacco smoke and outdoor pollutants. Risk factors for adult-onset asthma included female sex, airway hyper-responsiveness, lifestyle factors, and work-related exposures (King et al., 2004). Although a family history of asthma is common, it is neither sufficient nor necessary for the development of asthma. The substantial increase in the incidence of asthma over the past few decades and the geographic variation in both base prevalence rates and the magnitude of the increases support that environmental factors play a large role in the current asthma epidemic (Subbarao et al., 2009).

Although the etiology of asthma has not been fully elucidated, there is evidence that the environmental risk factors such as prenatal cigarette smoking (Neuman et al., 2012), air pollution (Lee et al., 2006; Ko et al.,

Abbreviations: DTR, diurnal temperature range; ERR, excess relative risk; ICD-9, international statistical classification of diseases, 9th revision; lag_n, lag/previous n days; PACF, partial autocorrelation function; PM_{10}, particles with an aerodynamic diameter less than 10 micron; NO_2, nitrogen dioxide; O_3, ozone.

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2007; Mar and Koenig, 2009), climate factors (Chen et al., 2006; D'Amato et al., 2010; Harju et al., 2010; Xu et al., 2013a), may increase the risk of asthma attacks. The diurnal temperature range (DTR), defined as the difference between maximal and minimal temperatures within one day, is a meteorological indicator which may be related to a variety of health outcomes (Chen et al., 2007; Liang et al., 2008; Cao et al., 2009; Tam et al., 2009; Lim et al., 2012). It is of interest whether the temperature variation within one day, i.e. DTR, is the risk factor for asthma independent of the corresponding absolute temperature. Only a few studies examined the associations between outdoor short-term temperature changes and asthma morbidity (Lim et al., 2012; Wasilevich et al., 2012; Xu et al., 2013b), and the results were conflicting with each other and inconclusive. The study conducted in four metropolitan areas in Korea (Lim et al., 2012) and the study conducted in Brisbane, Australia (Xu et al., 2013b) supported a positive association between DTR and asthma, while the other study conducted in Detroit, Michigan suggested a negligible association between short-term temperature change and emergency department visits for asthma among children (Wasilevich et al., 2012).

To examine the health effects of environmental triggers such as temperature variation may have implications for patient education and maintenance of asthma control and prevention. In this study, we hypothesized that large diurnal temperature change might be a source of additional environmental stress and therefore a risk factor for asthma exacerbation. We aimed to examine the associations between DTR and asthma, and to test the effect differences by season, age group and gender to identify the vulnerable subgroups.

2. Materials and methods

2.1. Data collection

A daily count of emergency hospital admissions for asthma (ICD-9: 493) as the principal diagnosis from year 2004 to 2011 was obtained from the Hospital Authority Corporate Data Warehouse. Hospital Authority is the statutory body running all public hospitals in Hong Kong. The records of admission were taken from the publicly funded hospitals providing 24 hour accident and emergency services and covering 90% of hospital beds in Hong Kong for local residents (Wong et al., 1999). The patient data included age, gender, date of admission, source of admissions, and principal diagnosis on discharge. We abstracted the overall daily asthma admissions, asthma admissions by gender and by two age groups (age <15, and ≥ 15 years old) as the health outcomes. It is the Hospital policy that all patients under 15 years of age are admitted to the pediatric wards (Wong et al., 2001). Daily admissions for influenza (ICD-9:487) were used to identify influenza epidemics, which were then treated as a potential confounder in the data analysis (Thach et al., 2010). Ethics approval and consent from individual subjects were not required by our institute as we just used aggregated data but not any individualized data in this study.

We collected the meteorological information including the daily maximum, minimum, mean temperature and relative humidity for the same period from the Hong Kong Observatory. DTR was calculated by the maximum temperature minus the minimum temperature within the same day.

As air pollutants (including particles with an aerodynamic diameter less than 10 micron, PM_{10}; nitrogen dioxide, NO_2; and ozone, O_3) are associated with emergency asthma hospitalizations in Hong Kong (Lee et al., 2006; Ko et al., 2007), we also collected the air pollution data from the Environmental Protection Department and included them in the regression models for adjustment. Hourly concentrations of PM_{10}, NO_2 and O_3 monitored in 10 general stations were used to generate daily mean air pollution concentrations in Hong Kong (Qiu et al., 2013).

2.2. Statistical modeling

This was a longitudinal time series study. Generalized additive Poisson regression models were used to fit the relationship between the daily DTR and the emergency asthma hospitalizations. We used the smoothing spline, *s(.)*, to filter out seasonal patterns and long-term trends in daily hospitalizations, as well as the daily mean temperature and relative humidity (Peng et al., 2006). We also included an adjustment for the day of the week and dichotomous variables such as public holidays and influenza epidemic.

To reduce the problems associated with multiple testing and model selection strategies, we followed previous studies to select a priori model specifications including the degree of freedom (*df*) for the time trend and other meteorological variables (Dominici et al., 2006; Peng et al., 2006; Qiu et al., 2013). We used a *df* of 8 per year for the time trend, a *df* of 6 for the mean temperature of the current day ($Temp_0$) and the previous 3 days' moving average ($Temp_{1-3}$) and a *df* of 3 for the current day relative humidity ($Humid_0$). We included the day of the week (*DOW*) and public holidays (*Holiday*) in the model as dummy variables (Schwartz et al., 1996). To adjust for the confounding effect of an influenza epidemic on emergency hospital admissions, we entered a dummy variable for the weeks with a number of influenza hospital admissions exceeding the 75 percentile in a year into the core model (Wong et al., 2002).

Briefly, we set up a core model to remove the long term trends, seasonal variations, and adjust for time varying confounders as follows:

$$\begin{aligned} log(E(Y)) = {} & \alpha + s(t, df = 8/year \times no.\ of\ years) \\ & + s(Temp_0, df = 6) + s(Temp_{1-3}, df = 6) \\ & + s(Humid_0, df = 3) + \beta_1 DOW + \beta_2 Holiday \\ & + \beta_3\ influenza \end{aligned} \tag{1}$$

Here *E(Y)* means the expected daily emergency asthma hospital admission counts on day t; *s(.)* is the smoothing spline function for nonlinear variables. We examined the residuals of the core model to check whether there were discernable patterns and autocorrelation by means of residual plot and partial autocorrelation function (PACF) plot. The PACF of residuals of the core model (1) was less than 0.1 for all lags, showing no serial autocorrelations in the residuals and sufficient confounder control (Wong et al., 2008). No discernible patterns and no autocorrelation in the residuals are the criteria for an adequate core model setup which is intended to remove all potential confounders in the daily variations of health outcome. The linear effects of DTR were then estimated for the same day and up to four days before the outcome (single-lag effect from lag_0 to lag_4). The overall cumulative effects of DTR due to the exposure over the period of lag0 through lag4 were estimated by constrained distributed lag models and denoted as 'dlm_{04}' (Gasparrini et al., 2010). Exposure–response relationship between DTR and asthma hospitalizations was graphically examined by distributed lag model as well (Gasparrini et al., 2010; Xu et al., 2013b). Sensitivity analyses were conducted to test such association by further adjusting for the confounding effects from air pollution. Sensitivity analysis was also conducted to test whether the DTR effect is stable by replacing the mean temperature with the minimum temperature in core model (1) or by including the adjustment for the temperature with longer lags up to two weeks.

In addition to the whole period analysis, we examined the effect of DTR for the warm season (from May to October) and the cool season (November to April) separately, using half the *df* of 4 per year for the time trend (Kan et al., 2008). Effect differences by gender under different age groups were also examined by using the subgroups of asthma hospitalizations as the health outcomes (Kan et al., 2008). We tested the statistical significance of differences by season, gender or age group by calculating $(\beta_1 - \beta_2)/\sqrt{SE_1{}^2 + SE_2{}^2}$, where β_1 and β_2 are the estimates for the two categories (e.g., warm and cool season, or females