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Exposure to ambient bioaerosols is associated with allergic skin diseases in Greater Taipei residents☆

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ABSTRACT

Allergic skin diseases may result from various types of chemical and biological allergens. This study investigated the association between ambient bioaerosol exposure and allergic skin diseases by using the exposure data obtained from land use regression models and interpolated data. Data on daily average outpatient visits for atopic dermatitis (ICD-9-CM 691.8) and contact dermatitis and other eczema (ICD-9-CM 692.9) between November 2011 and August 2012 were obtained from the National Health Insurance Research Database. A generalized estimating equation was used to analyze the associations between the skin diseases and ambient bioaerosol levels. The results indicated that during the study period, contact dermatitis and other eczema were more prevalent than atopic dermatitis in the study area. Most cases were observed in districts of Taipei City and 3 major districts of New Taipei City, namely Xinzhuang, Banqiao, and Xindian. In univariate analysis, most bioaerosols were positively associated with both skin diseases. After adjustment for air pollution and sociodemographic factors, exposure to total fungal spores was significantly associated with atopic dermatitis in males (relative risk [RR] = 1.12; 95% confidence interval [CI] = 1.05–1.19). Contact dermatitis and other eczema had significant relationships with *Cladosporium* in males (RR = 1.07; 95% CI = 1.02–1.14) and with *Aspergillus*/*Penicillium* in females (RR = 1.04; 95% CI = 1.02–1.07). Meteorological parameters, namely wind speed, temperature, and rainfall, were also significantly associated with skin diseases. Our findings reveal that exposure to ambient bioaerosols is a significant and independent risk factor for allergic skin diseases.

1. Introduction

Skin allergy is a common disease that can deteriorate quality of life, work efficiency, and academic performance (Civelek et al., 2011; Kieć-Swierczyńska et al., 2008; Magnavita et al., 2011). Common skin diseases, such as atopic and contact dermatitis, are prevalent worldwide in both children and adults (Simon and Kernland Lang, 2011). Approximately 6.7% of Taiwanese children experience atopic dermatitis, for which various risk factors have been reported (Wang et al., 2007, 2016). Previous studies have found that apart from a genotypic background (Chang et al., 2012), these skin diseases are associated with factors such as socioeconomic status, lifestyle, and dietary intake. These factors are positively and significantly correlated to case number and symptom severity (Apfelbacher et al., 2011; Karadag et al., 2007). The other crucial determinants are environmental factors, of which temperature, relative humidity, indoor environmental conditions, and everyday chemical and biological agents can induce skin symptoms (Lee et al., 2007; Sybilski et al., 2015; Wang et al., 2007).

Among the environmental factors, bioaerosols have been widely reported as risk factors for many diseases such as asthma, allergic rhinitis, and infections as well as skin allergies (Atkinson et al., 2006; Burge and Rogers, 2000; Harley et al., 2009; Macher, 1999). Most atopic patients have a positive skin reaction to bioaerosols, such as fungal, dust mite, and pet allergens, in the skin prick test (Codispoti et al., 2015; Mimura et al., 2014; Reponen et al., 2012). These allergens can activate the immune system and induce the skin reaction process, thus presenting common symptoms on patient skin, such as redness, swelling, itching, and skin dryness

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(Fischer et al., 1999; Simon and Kernland Lang, 2011).

Personal exposure assessment of bioaerosols is commonly conducted in indoor and occupational environments because of the availability of sampling equipment and electricity. In addition, environmental conditions in these environments are more stable than those in ambient environments (Garcia et al., 2013; Kallawicha et al., 2015a; Madsen et al., 2009; Wang et al., 2015). In a large-scale area, researchers typically use the data from one or a few fixed-site monitoring stations to estimate personal exposure (Atkinson et al., 2006; Chao and Lee, 2013; Chen et al., 2011, 2014a; Lierl and Hornung, 2003). To more accurately characterize the spatiotemporal distribution of ambient bioaerosols, we have successfully developed land use regression (LUR) models to estimate the levels of several bioaerosols in the Greater Taipei area in previous studies (Kallawicha et al., 2015b, 2015c). These models explained approximately 45%–60% of variation in ambient fungal spore distributions, and the results were comparable with other air pollution studies that applied LUR models to estimate ambient pollutants (Adam-Poupart et al., 2014; Chen et al., 2010; Kashima et al., 2009; Rivera et al., 2012; Saraswat et al., 2013). However, the LUR models of other ambient bioaerosols (i.e., endotoxins and total bacteria) were less ideal (Kallawicha et al., 2015b).

In this present study, we investigated the association of skin diseases with ambient bioaerosol exposure. We focused on the outpatient visits of "atopic dermatitis" and "contact dermatitis and other eczema" of the residents of Greater Taipei. The exposure levels were derived from the LUR models and bioaerosol monitoring results of previous studies (Kallawicha et al., 2015b, 2015c).

2. Materials and methods

2.1. Health care facility visit data

Health care data were obtained from the National Health Insurance Research Database (NHIRD) through the Health and Welfare Data Science Center, Ministry of Health and Welfare, Taiwan. The National Health Insurance program covers more than 99.9% of Taiwan residents and has contracts with more than 97% of health care providers nationwide (Lee et al., 2010; Lu and Hsiao, 2003; National Health Insurance Administration, 2014). To protect patient privacy, information related to patient identity or care provider is scrambled before inclusion in the NHIRD and is further scrambled before being released to researchers. Therefore, informed consent did not need to be obtained from the study patients. Because patient addresses are unavailable in the NHIRD, we considered the location of the visited facilities as the exposure location of the patients. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes were used to identify the health outcomes of interest. The health outcomes were the number of outpatient visits for allergic skin diseases, including atopic dermatitis (ICD-9-CM 691.8), and contact dermatitis and other eczema (ICD-9-CM 692.9), at each district in the Greater Taipei area during the study period. The Greater Taipei area map is shown in Supplement Material, Fig. S1.

2.2. Bioaerosol exposure data

The exposure levels were derived from previously collected data (Kallawicha et al., 2015b, 2015c). Briefly, ambient air samples were collected from 44 representative sites across the Greater Taipei area. Four sampling campaigns were conducted between November 2011 and August 2012, with each campaign lasting 1–2 weeks. LUR models for bioaerosols were developed and cross-validated. Potential bioaerosol determinants (i.e., land utilization and social and environmental parameters) were included during model construction. We used validated LUR models to estimate the exposure levels of total fungal spores and major fungal taxa in each district of the Greater Taipei area. The LUR models were validated using the leave-one-out cross validation method with cross-validation R^2 ($CV\text{-}R^2$) ranging from 0.38 to 0.57. Various studies used the LUR with similar $CV\text{-}R^2$ to estimate air pollutant levels (Adam-Poupart et al., 2014; Chen et al., 2010a; Kashima et al., 2009; Rivera et al., 2012; Saraswat et al., 2013). Because of the relatively low $CV\text{-}R^2$ of the LUR models for bacterial aerosols (total bacteria $CV\text{-}R^2 = 0.11$ and endotoxin $CV\text{-}R^2 = 0.31$), we used the spatial interpolation technique (ordinary kriging) from a geographic information system to estimate the bacterial and endotoxin concentrations in each district during the study period (Kallawicha et al., 2015b, 2015c).

2.3. Environmental data

Meteorological data, namely temperature (°C), rainfall (mm), relative humidity (%), and wind speed (m/s), were obtained from 49 monitoring stations of Taiwan's Central Weather Bureau. From 18 monitoring stations of Taiwan's Environmental Protection Administration, we obtained atmospheric pollutant data, including particulate matter with aerodynamic diameters of $\leq$10 and $\leq$ 2.5 μm (PM_{10} and $PM_{2.5}$, respectively), carbon monoxide (CO), ozone (O_3), nitrogen oxides (NO_x, NO, NO_2), and sulfur dioxide (SO_2). Because the monitoring stations were not evenly distributed in every district, the ordinary kriging technique was used to interpolate the data, and the average of each environmental parameter was calculated for each Greater Taipei district.

2.4. Sociodemographic data

Sociodemographic data included the size and density (person/km^2) of the population, the percentage of the population (age >15 years) with a higher education, the percentage of aboriginals, the percentage of elderly population (age >65 years), number of hospitals, density of hospitals (number of hospitals/km^2), number of physicians per 100,000 people, and the urbanization level of each district (Liu et al., 2006).

2.5. Statistical analysis

We used a paired *t*-test to examine the difference between the average numbers of male and female outpatient visits. The effect of bioaerosol exposure on skin diseases was assessed by using multivariate Poisson models with generalized estimating equations. The numbers of outpatient visits to the health care facilities in each district of the Greater Taipei area were used as the dependent variables. The independent variables included bioaerosol levels, meteorological parameters, and air pollutant concentrations. Because of the limitation of data accessibility and availability, only the average outpatient visit numbers for each district during each seasonal sampling campaign were obtained. To avoid the effects of weekends or holidays, we only included normal working days when counting outpatient visits. Each potential predictor variable was analyzed in the univariate model. To approximate normality, ambient bioaerosol concentrations were transformed using the base-10 logarithm in the regression analysis. The variables with a p value $\leq$ 0.2 were included in further multivariate analysis. Social demographic factors and air pollutants with a p value < 0.05 were adjusted in the final model. Relative risks (RRs) were calculated for significant bioaerosols and meteorological parameters (p < 0.05). Bioaerosol RRs were calculated on the basis of a 10-fold increase. Statistical analyses and data processing were performed using Microsoft Excel 2007 and PROC GENMOD in SAS (v. 9.2, SAS

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