

Impacts of meteorological and environmental factors on allergic rhinitis in children

Shan He¹ · Zhe Mou² · Li Peng² · Jie Chen¹

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Abstract Meteorological and environmental factors influence the pathogenesis of allergic rhinitis (AR). An understanding of the risk factors will facilitate the development of diagnostic and preventative tools for AR children and improve their quality of life. However, research on the impact of these factors on subjective symptoms in AR children remains scarce. This study explored the relationships between subjective symptoms in pollen and dust mite positive AR children, and meteorological and environmental factors. Using a linear mixed effect model, we analyzed the correlations between monthly data on the subjective symptoms of 351 AR children (from the Shanghai Children's Medical Center) and meteorological and environmental factors during 2013. The monthly meteorological and environmental data were provided by the Shanghai Meteorological Service and Shanghai Environmental Protection Bureau. Temperature and humidity were negatively correlated with the subjective symptom score, with a 0.04 point increase observed for every 1 °C decrease in temperature ($P < 0.0001$) or 10 % decline in humidity ($P = 0.0412$). The particulate matter (PM) 10 and PM2.5 concentrations were positively correlated with the subjective symptom score, with a 10 $\mu\text{g}/\text{m}^3$ increase in PM10 and PM2.5 yielding a 0.02 ($P = 0.0235$) and 0.03 ($P = 0.0281$) increase in the subjective symptom score, respectively. In conclusion, meteorological and environmental factors were

correlated with subjective symptoms in AR children. Low temperatures, lower humidity, and high PM10 and PM2.5 concentrations aggravated subjective symptoms in AR children.

Keywords Allergic rhinitis · Meteorological factors · Environmental factors · Children

Introduction

Allergic rhinitis (AR) is a multifactorial and heterogeneous disease caused by interactions between genetic and environmental factors. In recent decades, the incidence of AR has soared worldwide (von Mutius et al. 2006; Zhang and Zhang 2014). This increase is due to both patients' enhanced awareness of the need to seek medical help and greater exposure to known and unknown risk factors. Lately, there has been an increased focus on the effects of meteorological and environmental factors in the pathogenesis of allergic diseases. Variations in meteorological factors impact on AR patients; however, AR attacks are seldom induced by changes in a single meteorological factor. Rather, they are a result of interactions among multiple meteorological factors. In addition, the concentrations of allergens, such as pollen and dust mites, among others, are usually influenced by meteorological factors, such as the mean temperature, relative humidity, and diurnal temperature range. For example, these all impact the pollination period and pollen counts of plants (Silverberg et al. 2015). China is a vast country with large differences in environmental and climatic conditions.

In recent years, both suspended particulate matter (PM) and the density of allergens have increased with industrial development and environmental pollution. Air pollution severely affects human health, particularly children's growth and

✉ Jie Chen
chenj20052015@sina.com

¹ Department of Otorhinolaryngology, Shanghai Children's Medical Center, affiliated with Shanghai Jiaotong University School of Medicine, Shanghai 200127, China

² Shanghai Key Laboratory of Children's Environment and Health, Meteorological Bureau of Shanghai Pudong New Area, Shanghai 200135, China

development, sleep, and quality of life, resulting in heavy social and economic burdens (Nathan 2007). Many epidemiological studies have discussed the association between exposure to air pollution and the occurrence of allergic diseases in individuals. The studies have found PM, ozone (O₃), and nitrogen oxides (NO_x) to be the most common air pollutants (Gehring et al. 2010; Kim et al. 2011; Miyake et al. 2010). Epidemiological and toxicological studies both show a causal relationship between air pollution and increased AR incidence (Azalim et al. 2014; Medek et al. 2012; Porebski et al. 2014).

Meteorological factors and environmental pollution can influence the development of AR in everyday life (Azalim et al. 2014; Gehring et al. 2010; Kim et al. 2011; Medek et al. 2012; Miyake et al. 2010; Nicolussi et al. 2014; Porebski et al. 2014); therefore, recognition of these risk factors facilitates a deeper understanding of the pathogenic mechanisms of AR, decreases its epidemiological and socioeconomic impacts, provides accurate reference information for the diagnosis and prevention of AR in children, and improves their quality of life. However, studies into the impact of meteorological and environmental factors on the subjective symptoms of AR in children have been scarce. Although subjective symptoms of AR in children are less objective than laboratory indices, variations in the subjective symptoms influence parental decisions to seek medical help or allow interventional treatments. We analyzed the correlations between subjective symptoms of AR in children (allergic to pollen and dust mites), and meteorological and environmental factors, such as pollution levels. Our study aimed to provide important reference information about AR disease in children, as well as implications for the prevention of AR in children and an early warning of symptom occurrence.

Materials and methods

Study design

This was a model analysis based on a cross-sectional study and meteorological database that was conducted between January 2012 and December 2013, at the Children's Medical Center, affiliated with the Shanghai Jiaotong University School of Medicine. The Ethics Committee of the Shanghai Children's Medical Center approved this study. We selected 400 children who were settled in Shanghai as study subjects from children who were previously diagnosed with allergic rhinitis. In December 2012, we enrolled the children's parents and provided related information and education. All the children's parents underwent standardized questionnaire surveys. And each child received diary cards for a 12-month analysis of the subjective AR symptoms scale. The children's parents were well informed of the study objectives and significance, and they all understood and supported our study. In total, 400

children were enrolled in the study, and written informed consents were obtained from their guardians prior to the study.

Uniform AR diagnostic criteria (Bousquet et al. 2008), as well as the standardized allergen (serum-specific IgE or skin prick) tests, standardized questionnaires, and diary cards of subjective scale of AR symptoms, were used. All doctors and nurses working on the study received uniform training.

Patients

To be included in the study, the children had: (1) two or more of the following four symptoms: sneezing, runny nose, itchy nose, or nasal obstruction for more than 1 h every day; (2) received anterior rhinoscopy and had a positive serum specific IgE or skin prick test for dust mites or mixed tree pollen (having not taken medications, such as antihistamine or glucocorticoids, that can affect the results of skin prick tests, for 1 week before the tests); and (3) aged between 3 and 16 years.

Children with diseases such as nasal infections, polyps, or tumors, and those with mental health problems, were excluded from the study.

Questionnaires

A uniform query mode and filling criteria were adopted in the questionnaires. The following information was collected: general information about the children, including age, sex, height, weight, pregnancy duration, birth status (single or twin), and primiparity (yes or no); the parents' allergy history; and information about the home, including passive smoking habits in the home environment, air-conditioned space (yes or no), pets (cat or dog) in the home (yes or no), and whether housing renovations took place in the year before the study until the end of the follow-up period. Full-term birth was defined as birth after a pregnancy of at least 36 weeks; passive smoking was defined as current exposure to a smoking environment; and parents' allergy history was defined as either parent having any history of AR, allergic conjunctivitis, asthma, or eczema. The same doctor surveyed all the enrolled children and their parents, all the doctors involved in the study had epidemiological knowledge and received strict training.

Rhinitis diary cards

We adopted a self-modified scoring scale based on the international standardized scale (Bousquet et al. 2007) and issued a diary card of the subjective AR symptoms scale to each child. They then recorded the six symptoms (itchy nose, sneezing, running nose, stuffynose, itchy eye, and morning cough) every night. Assisted by the parents, the degrees of their symptoms were also assessed, with "0" considered as asymptomatic, "1" as mildly symptomatic, "2" as multi-symptomatic, "3" as significantly symptomatic, and "4" as intolerable and

requiring medical help (Fig. 1). Thus, the daily total score range was between 0 and 24 points, and higher scores indicated more significant AR symptoms. The daily total score of all six symptoms was used in the correlation analysis (see “Statistical analyses”, below). The completion of the diaries was checked by telephone every 10 days during the 1-year follow-up period. The same doctor checked every diary card and he urged the parents to complete the daily cards if they were incompletely filled. The patients and their parents attended the clinic on a monthly basis. Two people input the qualified data, to avoid and correct typos.

Meteorological and environmental data

The Shanghai Meteorological Service provided meteorological data for the period from January 1, 2013, to December 31, 2013. According to the literature (Azalim et al. 2014; Gehring et al. 2010; Kim et al. 2011; Medek et al. 2012; Miyake et al. 2010; Nicolussi et al. 2014; Porebski et al. 2014), the following indices could have a potential influence on allergic diseases and were used as analytical factors: the daily mean temperature, daily average relative humidity, and diurnal temperature range (Diurnal temperature range = Maximum temperature – Minimum temperature). Atmospheric elements were selected from data provided by both the Shanghai Environmental Protection bureau (SO₂, NO, NO₂, NO_x, PM2.5, and PM10) and the Shanghai Urban Environment and Meteorology Center (daily mean O₃ maximum, based on 8 h recordings); the data were collected from six observation sites across the city: Xujiahui, Baoshan, Chongming, Dongtan, Pudong, and Jinshan. This data was then used to provide the mean values of six meteorological stations, upon which the analysis was based.

Statistical analyses

Data are reported as mean ± standard deviation, unless otherwise specified. Spearman's correlation analyses were used to analyze the correlations between the children's symptom scores and their general information, and between PM2.5 and PM10. A linear mixed effect model was also adopted for the analysis (Li et al. 2015); this is a statistical method for processing the data with multi-layer structures. Because individual factors such as age, gender, and smoking status collected during baseline survey could influence the subject's symptoms. Therefore, during the analysis these individual

factors were regarded as fixed effects. According to individual random effects, the influence of meteorological and environmental factors on subjective symptoms was analyzed. Considering the correlation between PM2.5 and PM10, these pollutants were entered into the model. And γ_{00} was calculated as the intercept. A linear mixed effect spatial model was established to assess any differences among individual participants:

$$\begin{aligned} y_{ij} &= \beta_{0j} + e_{ij} \\ \beta_{0j} &= \gamma_{00} + \mu_{0j} \\ \gamma_{ij} &= \gamma_{00} + \mu_{0j} + e_{ij} \end{aligned}$$

In this, γ_{ij} indicates the records of daily subjective symptoms, with i representing the subjective symptoms scores on day i , and j representing the individual, j ; β_{0j} indicates the index intercept of each individual; μ_{0j} indicates the random effect of the index intercept of each individual; e_{ij} indicates the random effect; and γ_{00} indicates the total intercept of the model.

In order to improve the calculation speed and explanation of the model, the variates were centralized and the statistics analyzed using SAS 9.1 software (SAS Institute Inc., USA). The significance level (α) was 0.05.

Results

Baseline data of the follow-up population

Due to the long follow-up period of 1-year and parents' refusals or resettlements during the period, qualified questionnaires were only obtained from 351 (87.8 %) of the 400 children originally enrolled. The mean age of the 351 children was 6.5 ± 2.4 years (range 3–16 years). The results of the allergen test indicated that 257 (73.2 %) children suffered from a dust mite allergy and 94 (26.8 %) suffered from a mixed tree pollen allergy (Table 1).

Impacts of temperature and humidity on the subjective AR symptoms scores

The average monthly scores of the subjective AR symptoms indicated a maximum score of 9.2 points in December and a minimum score of 7.7 points in August and September (Fig. 2). In December and January, when the temperature was the lowest, the humidity was also lower compared to

Fig. 1 Symptom scores from the diary card used for the subjective scale of allergic rhinitis symptoms

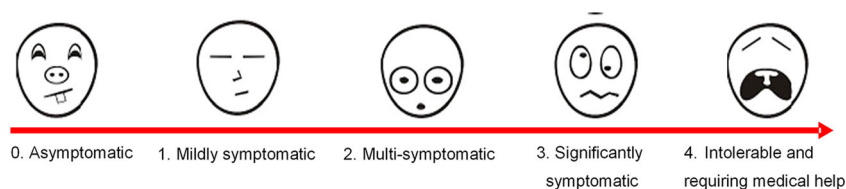


Table 1 Baseline data of the children for which qualified questionnaire were obtained during the 1-year follow-up period

	Dust mite allergy (n11e257)	Pollen allergy (n1194)	Total (nota351)
Male (<i>n</i> (%))	167 (65.0)	52 (55.3)	219 (62.4)
Full-term birth (<i>n</i> (%))	234 (91.1)	83 (88.3)	317 (90.3)
Single birth (<i>n</i> (%))	254 (98.8)	93 (98.9)	347 (98.9)
Primiparity (<i>n</i> (%))	232 (90.3)	85 (90.4)	317 (90.3)
Age (<i>n</i> ± SD)	7.3 ± 2.6	6.0 ± 1.9	6.5 ± 2.4
Height (cm; <i>n</i> ± SD)	118.5 ± 3.1	123.1 ± 4.4	120.7 ± 4.3
Weight (kg ± SD)	22.6 ± 2.6	24.9 ± 3.8	24.0 ± 3.0
Family history of allergy (<i>n</i> (%))	71 (27.6)	28 (29.8)	99 (28.2)
Passive smoking in house (<i>n</i> (%))	128 (49.8)	32 (34.0)	160 (45.6)
Air-conditioner in house (<i>n</i> (%))	241 (93.8)	83 (88.3)	324 (92.3)
Pets in house (<i>n</i> (%))	38 (14.8)	9 (9.6)	47 (13.4)
Housing renovations (<i>n</i> (%))	7 (2.7)	2 (2.1)	9 (2.6)
Annual mean symptom scores (mean ± SD)	8.5 ± 0.1	8.5 ± 0.1	8.5 ± 0.1

other months in the calendar (69.4 % and 73.6 %, respectively), and the subjective symptom scores of the dust mite allergy group were high (9.2 and 8.9 points). Between February and August, when the temperature was increasing, the subjective symptom scores of dust mite allergy group showed a decreasing trend, with some fluctuations; in particular decreases in the AR symptom scores occurred with the peaks in relative humidity that occurred in February and May (79 and 77.8 %).

In June and July, with high temperature and humidity levels the AR symptom scores reached a peak (8.7 and 8.9 points, respectively). Between September and December, when the temperature was gradually decreasing, while the humidity plateaued, the subjective symptom scores, initially dramatically, then gradually, increased. In the pollen allergy group, the subjective symptom scores peaked (at 9 and 8.8 points) in December and January, when both the temperature and humidity levels were lower. They also gradually decreased when

the humidity levels were relatively high during the period February–August.

Between March and May, the AR subjective symptom scores were higher in the pollen allergy group than in the dust mite allergy group. From August to December, the subjective symptom scores in both allergy groups increased gradually; however, the rate of increase in the pollen allergy group was higher than in the dust mite allergy group in September and October. In November there was a small decrease in the overall AR subjective score, before it rose again in December.

After the completion of two factor-ANOVA without replication (Table 2), it was found that temperature could affect AR scores ($p < 0.001$), and humidity had no effect on AR score ($p = 0.951$). This result was contradictory with the previous result from linear mixed-effects model analysis. The result showed that there was a negative correlation between humidity and AR score. The results of two-factor analysis of

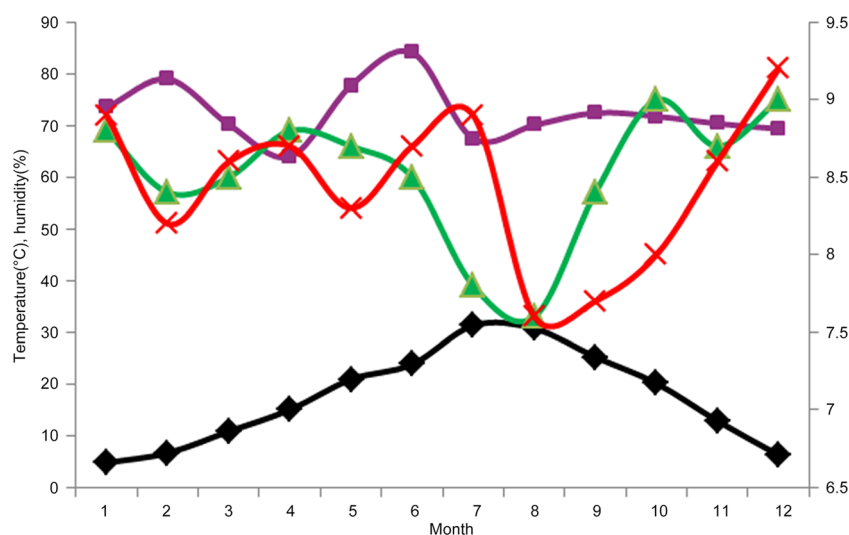
Fig. 2 The mean subjective AR symptom scores in dust mites group (crosses; red line), mean subjective AR symptom scores in pollen group (triangles; green line), monthly mean temperatures (rhombuses; black line) and humidity (squares; purple line) during 2013

Table 2 Mean subjective AR symptoms scores at different temperature and humidity intervals

Mean AR score	Temperature range						
Relative humidity	T < 5	5 < T ≤ 10	10 < T ≤ 15	15 < T ≤ 20	20 < T ≤ 25	25 < T ≤ 30	30 < T
RH ≤ 50	8.9	8.8	8.7	8.5	9.1	7.2	
50 < RH ≤ 60	9.2	8.3	8.8	8.9	8.5	7.4	8.1
RH > 60	8.7	8.7	8.7	8.7	8.3	7.9	7.9

Notes: 8.7 < subjective AR symptoms scores ≤ 9.2 (red); 8.2 < subjective AR symptoms scores ≤ 8.7 (orange); 7.7 < subjective AR symptoms scores ≤ 8.2 (green); 7.2 < subjective AR symptoms scores ≤ 7.7 (yellow)

variance are slightly different with the result from model analysis. Maybe the factors (such as individual factor, temperature factor and so on) were not controlled in two-factor analysis of variance. However, the mixed effect model investigated the humidity effect under the control of the influence of other factors, which might indicate that the influence of humidity on symptoms was weaker than the influence of temperature on symptoms. This could only be found when other factors were controlled. This allowed us to conduct an exploratory study on the children's subjective symptoms at different humidity and temperature values. We found that subjective AR symptom scores over 8.2 points often appeared when the mean temperature was below 25 °C, while subjective AR symptom scores over 8.7 points occurred when the mean humidity was below 60 % (Table 2). Thus, during the follow-up period, it appears there were negative correlations between the children's subjective AR symptoms, and both temperature and humidity; that is, both lower temperatures and humidity levels were associated with more significant subjective symptoms (Table 2; Fig. 2).

Impacts of PM2.5 and PM10 on subjective AR symptom scores

Both PM2.5 and PM10 decreased in concentration from winter (where they were highest) to summer, then increased again into autumn (although, they remained less than the winter concentrations, Fig. 3). The two parameters both peaked in January (at 66.5 and 79.3 µg/m³ for PM2.5 and PM10, respectively), corresponding to this the subjective AR symptom scores of the dust mite allergy and pollen allergy groups were at their highest levels (8.9 and 8.8 points, respectively). There were strong declines in the concentrations of both atmospheric parameters in February (to 42.1 µg/m³ for PM2.5, and 47.2 µg/m³ for PM10), and the subjective AR symptom scores also decreased for both allergy groups (8.2 and 8.4 points, respectively). Between March and September, both PM2.5 and PM10 concentrations continued to decline, but at

a slower rate. Between March and August, the AR subjective symptom scores in the pollen allergy group decreased with the decline in PM concentrations. While, although there was an overall decreasing trend in the dust mite allergy group, the scores between May and July gradually increased, and then declined precipitously in August. Between September and December, as the concentrations of PM2.5 and PM10 increased, the overall trends of the AR subjective scores in the two allergy groups also increased. The correlation analyses between the monthly subjective AR symptom scores and monthly concentrations of both PM10 and PM2.5 showed that the PM10 and PM2.5 concentrations were significantly and positively correlated with the scores of the subjective AR symptoms in dust mites group. ($r = 0.43$, $P = 0.0329$) (Fig. 3).

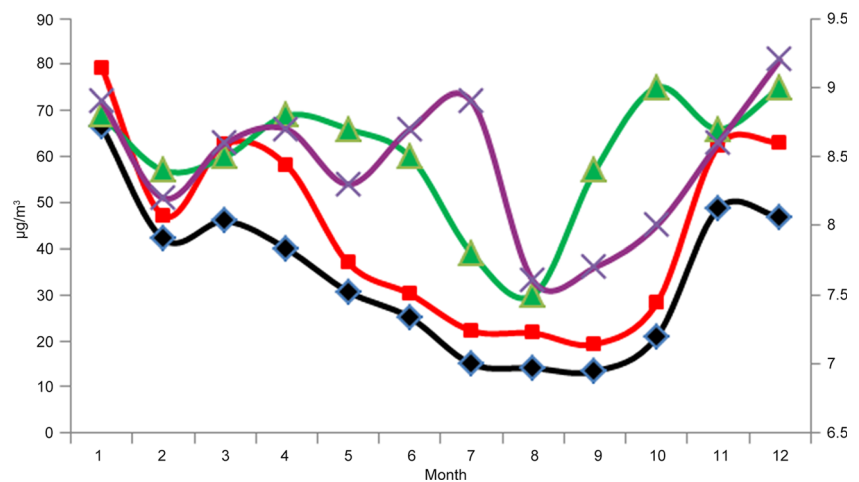
Identification of differences among individuals

The fit of the linear mixed effect spatial model indicated that $\sigma^2_{\mu 0} = 4.5$, $P < 0.01$; this suggests that: (1) there were differences among individual participants and (2) although the interclass differences were significant, intraclass differences were still large (the intraclass correlation coefficient (ICC) was 0.59 and $P = 0.0275$, showing that 59 % of the results were caused by individual differences). Since large type I errors can be caused by small ICCs, a multilevel model was considered suitable to analyze these data. Before the model was established, bias induced by the medications taken by the AR children when their symptoms were severe was controlled.

Variates that induced the individual differences

The variates of sex, body mass index (BMI), pregnancy duration, birth status, birth order, parents' history of allergy, passive smoking in the home environment, air-conditioner presence, and presence of pets (cat or dog) in the home, at two levels were added into the model. Only passive smoking in the

Fig. 3 The mean subjective AR symptom scores in dust mites group (crosses; purple line), mean subjective AR symptom scores in pollen group (triangles; green line), and monthly mean PM2.5 (rhombuses; black line) and PM10 (squares; red line) concentrations, during 2013



home environment had a significant impact on the AR subjective symptom scores of the children ($P = 0.0257$), while the others variates had no impact ($P > 0.05$). Therefore, we considered passive smoking in the home environment as the major variate that influenced the individual difference in the analysis below.

The impacts of meteorological and environmental factors on subjective symptoms

While controlling for the individual differences (passive smoking in the home environment), we introduced meteorological factors (temperature and humidity) into the linear mixed effect model; both temperature and humidity were negatively correlated with the AR subjective symptom scores, with a mean increase of 0.04 points in the scores corresponding to a decline of both 1 °C in temperature ($P < 0.0001$) and 10 % in humidity ($P = 0.0412$) (Table 3). The impacts of passive smoking in the home environment on the subjective AR symptom scores were not statistically significant, after the temperature and humidity data were added into the model ($P = 0.1179$; Table 3). However, the impacts of passive smoking in the home environment were still controlled in the model.

Since PM10 and PM2.5 were strongly correlated ($r = 0.97$), they were both included in the model, respectively. An increase of 10 $\mu\text{g}/\text{m}^3$ in PM10 and PM2.5 resulted in a mean increase of 0.02 and 0.03 points, respectively, in the AR subjective symptom scores of the children ($P = 0.0246$ and

$P = 0.0293$, respectively). According to the mixed model with NO , NO_2 , NO_x , or O_3 added, none of these parameters significantly impacted the AR subjective symptom scores (Table 4).

Discussion

Our study analyzed the correlations between meteorological and environmental factors and the symptoms of AR, in patients allergic to dust mites and mixed tree pollen, in 2013. Temperature and relative humidity were both closely and negatively correlated to the symptoms of the AR children during disease onset. Our model indicates that a mean increase of 0.04 points in the subjective AR symptom scores corresponds to a 1 °C decrease in temperature and a 10 % decrease in humidity. We infer that there may be two reasons for the observed effects of temperature and humidity: (1) the decreases in temperature and humidity lower the response threshold of nasal mucosa to allergic reactions, so increasing the chances of AR onset (Assanasen et al. 1999); and (2) weather variations like dryness caused by the temperature drop result in physical stimuli to the nasal cavity (Kim and Jang 2013), which can also induce quasi-AR symptoms. Therefore, children allergic to pollen and dust mites should be maximally protected from the damage caused by these weather variations, or a cold.

Meteorological and environmental variations cause structural changes and can activate inhaled allergens regionally, which may result in adverse effects on AR (Puc 2012).

Table 3 Impacts of temperature and humidity on the subjective AR symptom scores in the linear mixed effect model

Variates	Estimated value	Standard error	t	P
Intercept	8.0122	0.6427	12.47	<0.0001
Passive smoking in the home environment	1.744	1.059	1.65	0.1179
Mean temperature	-0.04083	0.002668	-15.3	<0.0001
Mean humidity	-0.00424	0.002077	-2.04	0.0412

Table 4 Impacts of PM10, PM2.5, NO, NO2, NO_x, and O₃ on the subjective AR symptom scores in the linear mixed effect model

Pollutant	Variates	Estimated value	Standard error	t	P
PM10	Intercept	8.014	0.6406	12.51	<0.0001
	Passive smoking in the home environment	1.7428	1.0411	1.58	0.1342
	Mean temperature	-0.03868	0.003251	-11.90	<0.0001
	Mean humidity	-0.00328	0.002392	-1.37	0.1706
	PM10	0.002169	0.000965	2.25	0.0246
PM2.5	Intercept	8.0146	0.6406	12.51	<0.0001
	Passive smoking in the home environment	1.7428	1.0411	1.58	0.1342
	Mean temperature	-0.03836	0.00335	-11.45	<0.0001
	Mean humidity	-0.00431	0.002282	-1.89	0.0590
	PM2.5	0.002708	0.001242	2.18	0.0293
NO	Intercept	8.008	0.6405	12.5	<0.0001
	Passive smoking in the home environment	1.6841	1.0469	1.72	0.1198
	Mean temperature	-0.0424	0.002826	-15.00	<0.0001
	Mean humidity	-0.0035	0.002261	-1.55	0.1217
	NO	-0.00087	0.002364	-0.37	0.7127
NO ₂	Intercept	8.0085	0.6408	12.50	<0.0001
	Passive smoking in the home environment	1.6951	1.0328	1.59	0.1201
	Mean temperature	-0.04214	0.00283	-14.89	<0.0001
	Mean humidity	-0.00392	0.002278	-1.72	0.0855
	NO ₂	-0.00135	0.001096	-1.23	0.2173
NO _x	Intercept	8.0083	0.6408	12.50	<0.0001
	Passive smoking in the home environment	1.6921	1.0543	1.58	0.1165
	Mean temperature	-0.04226	0.002826	-14.95	<0.0001
	Mean humidity	-0.00383	0.002279	-1.68	0.0927
	NO _x	-0.00084	0.000809	-1.04	0.3002
O ₃	Intercept	8.0142	0.6408	12.51	<0.0001
	Passive smoking in the home environment	1.7452	1.0564	1.63	0.1138
	Mean temperature	-0.04336	0.003214	-13.49	<0.0001
	Mean humidity	-0.00279	0.002186	-1.28	0.2021
	O ₃	0.000517	0.000928	0.56	0.5777

Concentrations of inhaled allergens, such as dust mites and mixed tree pollen, are usually influenced by meteorological factors; for example, temperature and relative humidity can both affect the pollination period and pollen counts of plants. Studies have shown that there are two obvious peak distribution periods of airborne pollen in the central urban areas of Shanghai, one in the spring (March–May) and the other in the fall (September–October) (Liu et al. 2010). Meanwhile, the actual temperature during the two seasons can increase pollen production and concentrations, and enhance the antigenicity of pollen (Beggs 2010). The impact of the allergens themselves on the subjective symptoms were not excluded in the present study; therefore, the subjective AR symptom scores increased rapidly when the pollen allergen levels were high in spring. The optimum conditions for dust mites are 20–30 °C and 80 % relative humidity (Korsgaard and Harving 2005). In our study, 73.2 % of children were allergic to dust mites. The

mid-to-late June period is the plum rain season, during which the relative humidity is high and both the indoor and outdoor temperatures are suitable for dust mite propagation; therefore, the subjective AR symptom scores during this period were higher. This is contradictory to our finding that lower humidity may increase AR symptoms, but we think this is because dust mite propagation is a more powerful influence on AR symptoms. Weather variations result in the onset of allergic respiratory diseases, such as AR and asthma, via inhaled pollen allergens, and are one of the major factors that impair public health (Beggs 2004). Changes in meteorological factors will alter the production, distribution and allergen potential of the inhaled allergens. These variations, as well as changes in allergen exposure in the population, will affect the distribution of allergic diseases and the severity of allergic reactions.

Amounting evidence has proved the adverse effects of environmental pollution on human health, and, in particular, the

health of the respiratory tract (Azalim et al. 2014; Gehring et al. 2010; Kim et al. 2011; Porebski et al. 2014). Rapid civilization and increased energy consumption greatly increase both the types and concentrations of air pollutants. Currently, the important major air pollutants are PM, O₃, and NO_x (Gehring et al. 2010; Kim et al. 2011; Miyake et al. 2010). In addition, there are also indoor pollutants, mainly sourced from tobacco smoke (Laumbach and Kipen 2012). PM is a mixture of solid and liquid matter suspended in the air, including pollen (Jenerowicz et al. 2012). Currently, the PM that causes people concern mainly comprises PM_{2.5} and PM₁₀; these two pollutants are produced during oil fuel combustion processes in industrial production and motor vehicles. PM₁₀ can be absorbed by the human body and deposited at sites such as the respiratory tracts and pulmonary alveoli, resulting in disease. Small in size and area and strong in their activity, PM_{2.5} can easily carry toxic and harmful substances, stay in the air for a long time and travel long distances, causing harm to human health and diminishing air quality (Fanning et al. 2009). Moreover, PM_{2.5} can also enhance the allergen potential of IgE-mediated allergens, and the Th2 immune response, resulting in a series of immunological and clinical changes (Rutkowski et al. 2014).

Air pollution induced by PM in the air is a cause of concern worldwide. A multicenter, large-sample investigation of Chinese air data between 2006 and 2010 showed that PM_{2.5} and PM₁₀ both generally increase in the spring, fall and winter, and decrease in the summer (Yao and Lu 2014). Shanghai is under the influence of the subtropical oceanic monsoon climate. At the beginning of summer, monsoons bring clear air to Shanghai and greatly decrease the concentration of air pollutants (including PM); this may be associated with the gradual decrease in the subjective symptom scores of AR children during summer time (July to August).

The peak periods of the AR subjective symptom scores in the mites group for the whole year occurred in January, April, and December, and they coincide with the peak periods of PM. In the period between June and October, the PM concentrations were low; corresponding to this period, the, subjective AR symptom scores increased in the dust mite allergy group in June and July, and in the pollen allergy group in September and October. Animal studies have shown that the IgE-mediated allergic reactions towards proteins are enhanced under the combined effect of PM and other pollutants, because air pollutants can affect immune function by altering the epithelial structures of animals and aggravating allergic reactions (Thompson et al. 2005). Moreover, the synergy of allergens and pollutants can greatly increase the severity of allergic reactions; this effect is not just a result of simple superposition (Takizawa 2011). In addition, other studies have shown that PM enhances the allergenicity of inhaled allergens in the respiratory tract, raises the sensitivity of IgE towards allergens, and increases the susceptibility to respiratory tract infections

(Sierra-Vargas and Teran 2012). It is believed that these effects are caused by up-regulated Th2 functions (Wang and Chau 2013). Over the years, traffic-related discharges of air pollutants has increased, with the increased number of motor vehicles, and has become the major cause of air pollution in urban areas (Gehring et al. 2010; Miyake et al. 2010; Porebski et al. 2014). The discharge of air pollutant mixtures facilitates the propagation of allergic diseases. Exposure to PM from vehicle exhaust emissions activates the antigen-specific IgE and increases histamine, resulting in increased incidence of allergic diseases, elevated mRNA levels of interleukin (IL)-4, IL-5, IL-6, and IL-10, and declined levels of interferon- γ (Sasaki et al. 2009). These studies all indicate that exposure to PM reduces the function of Th1.

In this study, we have found that passive smoking in the home environment is the main variate that causes individual differences in AR. Thus, tobacco smoke is the most important indoor air pollutant. Unlike adults, children have limited options for avoiding exposure to secondhand smoke and are unable to prevent it. The correlation between passive smoking and AR spontaneous symptoms is probably due to allergic sensitization to perennial indoor allergens, upon exposure to tobacco smoke, which results in aggravating the AR symptoms (Saulyte et al. 2014). Feng et al. (2011) reported that passive smoking reduces the bioactivity of NK cells and Th1 cytokines, such as interferon- γ , and decreases the anti-infection ability of the respiratory tract.

Since children's respiratory and immune systems are immature, their ratio of air intake to body surface area is greater than those of the adults (Moya et al. 2004); this increases their exposure to air pollutants and, therefore, results in greater susceptibility to air pollution. Thus, more attention should be paid to children, when considering the effects of environmental pollution on human health. The results of this study are based on children's subjective symptoms, instead of the objective results of IgE and other cytokine levels, which is a limitation of the study. Therefore, more in-depth studies of the risks and mechanisms of children's exposure to environmental pollutants, and their effects on allergic diseases, are required to develop a novel approach for the prevention and control of allergic diseases in children. In addition, it is necessary to study the impact of the interactions between allergens and meteorological and environmental factors.

Although we did not observe significant effects of O₃, NO_x, and SO₂ on the subjective AR symptom scores, we cannot exclude their possible synergy with other environmental pollutants that may aggravate allergic symptoms. The individual roles of environmental pollutants are uncertain, and these pollutant levels are only a marker of environmental pollutant discharges.

Our study focused on a single location and adopted a predictive method, based on subjective symptom scores, in AR children, during disease onset. Our follow-up and

meteorological and environmental data were obtained from different regions/sites in Shanghai. Therefore, while our results indicate the impact of meteorological and environmental factors on subjective AR symptoms in Shanghai, their value for children in other regions needs further verification. We used relative humidity values as the humidity measure in this study; however, absolute humidity, which is the measure of the water vapor in the atmosphere, may have been more appropriate. Unfortunately, we did not have data available for absolute humidity. We also did not exclude patients who had a cold, because it was uncommon in this population not to have a cold over the long 1-year time period. Studies with longer-term meteorological data and larger sample sizes of children with AR are required, to improve the stability and accuracy of subjective symptom prediction in children with AR, during disease onset. Such studies would also provide more precise reference information for the diagnosis and prevention of AR in children.

Conclusions

We established a linear mixed effect model to analyze the relationships between the subjective symptoms of children allergic to dust mites and tree pollen, and both meteorological and environmental factors. High temperatures and humidity levels, and low PM concentrations exhibit a protective role for AR, while low temperatures and humidity levels and high PM concentrations aggravate the subjective symptoms of AR in patients. In the future, these factors could be used as a basis for an AR pre-warning system, to guide preventative treatment options during the early disease onset period in children. Such an approach would effectively reduce the frequency and severity of AR onsets, and improve the management and prevention of AR children's symptom variations, caused by ambient air quality changes.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of the Shanghai Children's Medical Center and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all children's guardians included in the study.

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