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Impact of temperature and relative humidity variability on children's allergic diseases and critical time window identification

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Abstract

Background The effects of temperature and relative humidity on different types of children's allergic diseases have not been comprehensively evaluated so far. This study aims to assess the impact of temperature and relative humidity variability on children's allergic diseases and to identify the critical time window.

Methods We collected outpatient data on allergen testing in children between July 2020 and January 2022 from the Affiliated Children's Hospital of Nanjing Medical University. We defined the 1st, 10th, 90th, and 99th percentiles as extreme cold, moderate cold, moderate hot, and extreme hot for temperature, and as low, moderate high, and extreme high for relative humidity, respectively. A distributed lag nonlinear model (DLNM) combined with a binomial regression model was used to assess the possible nonlinear relationship at different periods. Subgroup analysis by gender and age was conducted.

Results We found that extreme and moderate cold temperatures were positively associated with skin allergies and total allergies (28 days: OR = 4.69, 95% CI: 2.88, 7.63; OR = 3.36, 95% CI: 2.39, 4.73) and (28 days: OR = 3.76, CI: 2.43, 5.81; OR = 2.71, 95% CI: 2.00, 3.68), respectively. Moderate and extreme hot temperatures were negatively associated with food allergies (28 days: OR = 0.13, 95% CI: 0.04, 0.41 and OR = 0.04; 95% CI: 0.01, 0.27). Low relative humidity was negatively associated with respiratory allergies, skin allergies, and total allergic diseases (28 days: OR = 0.26, 95% CI: 0.10, 0.71; OR = 0.29, 95% CI: 0.15, 0.55; and OR = 0.42, 95% CI: 0.26, 0.68). Meanwhile, extreme high relative humidity was negatively associated with respiratory allergies, and positively associated with skin allergies, food allergies, and total allergies (28 days: OR = 0.16, 95%CI: 0.07, 0.37; OR = 3.60, 95% CI: 2.52, 5.14; OR = 15.61, 95% CI: 3.23, 75.56; and OR = 2.33, 95% CI: 1.73, 3.15). A stronger relationship between temperature, relative humidity, and allergic diseases was observed in children under 5 years, specifically girls.

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Conclusions Our study provides evidence that temperature and relative humidity variability may be associated with allergic diseases, however, the directionality of the relationship differs by allergic type.

Keywords Temperature, Relative humidity, Childhood allergic diseases, Childhood allergies, Critical time window

Background

Allergic diseases are a group of hypersensitivity diseases caused by the body's immune system to normally harmless substances in the environment, including respiratory allergies, food allergies, skin allergies, etc. The prevalence of allergic diseases is increasing dramatically and it is estimated to affect 4 billion people globally by 2050s, leading to a huge economic burden and considerable consumption of healthcare resources [1]. The International Study of Asthma and Allergies in Childhood (ISAAC) has reported a rising global trend in the prevalence of pediatric allergic disorders and is estimated to be 15–20% among children worldwide [2]. Although allergic diseases in early childhood are mostly mild and self-limiting [3], they tend to develop into lifelong chronic diseases and even lead to complications such as pneumonia, sinusitis, or skin infections [4, 5]. As a result, there is growing concern about allergy disorders.

Allergies are not only genetic disorders but also may be widely influenced by the role of environmental factors. In the past decades, climate change is still one of the foremost environmental factors of our time due to human activities and rapid industrialization. The concentration of greenhouse gases continues to rise steadily due to land use change and fossil fuel combustion, resulting in a rise in global temperatures [6]. Global warming leads to glacier melting, sea level rise, and precipitation changes, further triggering changes in relative humidity [7]. Existing studies have shown that temperature and relative humidity are associated with allergic disease outcomes. Seasonal temperature variability was positively associated with outpatient visits for respiratory allergies [8]. A large slope of cooling between two adjacent days had a delayed and short-lasting effect on allergic rhinitis [3]. In addition to high and low temperatures, relative humidity had an acute adverse effect on allergic rhinitis and the presence of allergic conjunctivitis [9, 10]. Temperature changes might affect the ability of the immune system to resist infectious agents [10], and increase the release of reactive oxygen species (ROS), activation of the transcription factor nuclear factor κB (NF-κB), and subsequent release of pro-inflammatory mediators. Moreover, sudden low temperatures can cause cooling of the nasal and bronchial mucosa, which may seriously damage ciliary movement, ultimately leading to respiratory diseases [11]. Relative humidity affects mucus cilia clearance, and alterations in the mucosal layer can disrupt epithelial junctions, and damaged epithelial cells may promote allergic diseases and asthma responses by releasing inflammatory mediators [8]. Temperature and relative humidity share similar mechanisms for immune system disorders [12, 13], and the synergistic effect of temperature and relative humidity on children's immune systems remains to be elucidated.

Children are a particularly vulnerable group owing to their relatively undeveloped immune systems [14]. They tend to have higher levels of exposure to ambient temperature on account of their high surface-to-body ratio, lower thermoregulatory capacity, decreased sweating capacity, and lower cardiac output [15]. Heat waves and relative humidity are found to be associated with higher emergency room visits to children's hospitals [10], demonstrating that children are sensitive to short-term exposures. Thus, it is important to identify sensitive time windows for the effects of ambient temperature and relative humidity on allergic diseases in children.

A few studies have reported the effect of temperature or relative humidity on one type of allergic disease in children. For instance, Wang and colleagues assessed the effect of temperature variability on childhood allergic rhinitis in China and found that significant temperature decreases between consecutive days may be related to increased risk of allergic rhinitis in children [3]. Li and colleagues examined the effect of extreme temperatures on childhood respiratory allergies and found that extreme temperatures were associated with increased outpatient visits among children with respiratory allergies [16]. In the case of relative humidity, Duan and colleagues explored the effect of relative humidity on allergic rhinitis in children and found that high and low relative humidity were associated with an increased risk of rhinitis among children [9]. To our knowledge, no previous study has comprehensively investigated the effects of temperature and relative humidity exposure on multiple types of allergic diseases in children. A case-control study was designed to explore the effects of temperature and relative humidity on different types of allergic diseases. We evaluated the temperature and relative humidity exposures of children for 7, 14, 21, and 28 days to determine sensitivity time windows.

Methods

Study population

A hospital-based case-control study was conducted at the Children's Hospital of Nanjing Medical University. Children attending the outpatient clinic for routine comprehensive pediatric clinical care between July 2020 and January 2022 and diagnosed with allergic diseases were recruited in the study. Children with allergic diseases such as respiratory allergy, skin allergy, and food allergy were included in the study if they met the following criteria: (1) Nanjing resident. (2) Had allergic symptoms 28 days before allergic testing. Children with a known history of chronic diseases that may trigger allergic symptoms were excluded from the study, including autoimmune diseases such as lupus, rheumatoid arthritis, and inflammatory bowel disease; chronic obstructive pulmonary disease (COPD); chronic infections such as recurrent respiratory infections; gastroesophageal reflux disease (GERD) or inflammatory bowel diseases (IBD); and eosinophilic disorders such as eosinophilic esophagitis or eosinophilic asthma. Children diagnosed with allergic diseases (cases) were matched by gender with healthy children without allergic diseases (control), who attended the outpatient clinic for other reasons than allergic conditions. Overall, a total of 6141 children were recruited in the study, among them, 3304 were diagnosed with allergic diseases and 2837 were healthy controls without allergic diseases. This study was approved by the Ethics Committee of the Children's Hospital at Nanjing Medical University, and the data utilized were completely anonymous. Written informed consent was obtained from the children's guardians.

Exposure assessment

The meteorological data including temperature and relative humidity were obtained from the Nanjing Meteorological Bureau. All measurement data were subject to strict quality control. We calculated the daily average temperature and relative humidity at each child's home address by inverse distance weighting (IDW) modeling method with ArcGIS. Based on the time of allergen testing, this study was conducted four weeks back to investigate the acute effect of temperature and relative humidity on the outcomes, and we estimated daily average exposure before allergen testing for 7 days, 14 days, 21 days, and 28 days.

Outcome assessment

Allergic diseases were diagnosed according to the China Consensus Document on Allergy Diagnostic, which reported that allergic diseases are principally diagnosed based not only on allergen tests but also on clinical manifestations, medical history, and physical examination [17]. The most common allergic diseases explored in our study include respiratory, skin, and food allergies as shown in Table S1. Respiratory allergies are caused by proteins in the air, which are inhaled and trigger airway inflammation. In the present study, respiratory allergies were considered when allergen tests showed increased serum total IgE levels accompanied by recurrent coughing, sneezing, runny nose, nasal congestion, and other cold-like symptoms. Skin allergies were considered when the skin appeared red, swollen, itchy, and peeling symptoms and elevated serum IgE levels. Furthermore, patients were considered to have food allergies when there were elevated IgE and manifestations of nausea and vomiting, abdominal pain, diarrhea, and haematochezia after meals [18]. All diagnoses were guided by pediatricians.

Statistical analyses

Sociodemographic characteristics and exposures were compared using a t-test for continuous variables and the chi-square test for categorical variables. Distributions of sociodemographic characteristics are presented as mean (±SD) for continuous variables and proportions (n [%]) for categorical variables. Daily change curves of average temperature and relative humidity in Nanjing from May 2020 to January 2022 were plotted. Estimates of temperature and relative humidity exposure in different periods are presented as mean, standard deviation, median, 95th percentile, etc.

We employed a distributed lag nonlinear model (DLNM) combined with a binomial regression model to assess the possible nonlinear relationship between temperature and relative humidity on allergic diseases at different periods. DLNM explores a nonlinear exposure-outcome relationship at different lag periods as detailed and explained elsewhere [19]. We used a binomial regression model due to the binary nature of the outcomes included in this study (1 = presence of allergic diseases or 0 = absence of allergic diseases). In brief, first, we applied DLNM to create the cross-basis function for temperature and relative humidity separately. A natural cubic spline (ns) function, degree of freedom(df) = 3 at equal knots ranges of exposure (temperature and relative humidity) was set to account for a nonlinear linear relationship. An ns function, df = 3, at equal knots ranges of lags (0–28 days) was used to allow more flexibility. Since temperature and relative humidity were recorded for days 7, 14, 21, and 28, the cross-basis function for each parameter was computed separately. Secondly, we incorporated the cross-basis functions in the binomial linear regression model to assess the effect of temperature and relative humidity on allergic diseases while adjusting for season. The mathematical formula used in the main model was adopted as follows:

$$E(Y) = \alpha + \beta 1 * cb.Temp + \beta 2 * cb.RH + season$$

Where:

E(Y) is the binary outcome variable indicating allergic diseases (1 for presence and 0 for absence); α is the intercept; cb. Temp is the cross-basis function for temperature and cb.RH is the cross-basis function for relative

Table 1 Characteristics of the study population ($N = 6141$) in Nanjing, China, 2020–2022

	***N* (%) or mean ± SD**		
	Overall	**Non allergic diseases**	**Allergic diseases**
N	6142	2837	3305
Age(year)	3.68 ± 2.85	3.67 ± 2.64	3.69 ± 3.03
< 5	4246(69.13)	2029(71.52)	2217(67.08)
≥ 5	1896(30.87)	808(28.48)	1088(32.92)
Gender			
Male	3695(60.16)	1727(60.87)	1968(59.55)
Female	2447(39.84)	1110(39.13)	1337(40.45)
Season			
Spring	1224(19.93)	487(17.17)	737(22.30)
Summer	1453(23.66)	699(24.64)	754(22.81)
Autumn	2146(34.94)	1049(36.96)	1097(33.19)
Winter	1319(21.48)	602(21.22)	717(21.69)
Year			
2020	1621(26.39)	634(22.35)	987(29.86)
2021	4352(70.86)	2114(74.52)	2238(67.72)
2022	169(2.75)	89(3.14)	80(2.42)

humidity. These cross-basis functions were delivered from the DLNM to assess the possible nonlinear relationship between temperature and relative humidity on allergic diseases at different lag periods; β1 and β2 are the coefficients of the cross-basis functions for temperature and relative humidity, respectively. We defined the 1st, 10th, 90th, and 99th percentiles as extreme cold, moderate cold, moderate hot, and extreme hot for temperatures and as low, moderate, high, and extreme high for relative humidity, respectively as shown in Tables S2 and S3. The odds ratio (OR) and 95% confidence interval (CI) were computed by comparing the defined percentiles of temperature and relative humidity with the reference, 21℃ for temperature, and the median value of relative humidity (74%).

Considering the balance between the case and controls, a 1:4 propensity score matching was conducted for food allergies (Figure S1). Subgroup analyses were performed to assess potential modifications of gender and age (<5 years old and ≥5 years old) on the associations, and to assess the sensitivity of our findings. Because of the small sample size, food allergies were not included in the analysis. All statistical analyses were performed using R software (version 4.2.1, R Core Team 2022). Statistical significance was considered at $P \leq 0.05$ for each analysis.

Results

Study population characteristics

From July 2020 to January 2022, a total of 6142 children were recruited in our study, including 3305 children with allergic diseases and 2837 healthy children. The mean age of children with allergic diseases (cases) was 3.69±3.03 and 67.08% of them were under 5 years old. The male-to-female sex ratio was well-balanced and the majority of the participants suffered from allergic diseases in autumn (Table 1).

Distribution of exposures

Trends of daily average temperature and relative humidity in Nanjing from May 2020 to January 2022 are described in Fig. 1. The relative humidity fluctuation was relatively stable throughout the year and the average humidity was 73.78%. The average temperature peaked in

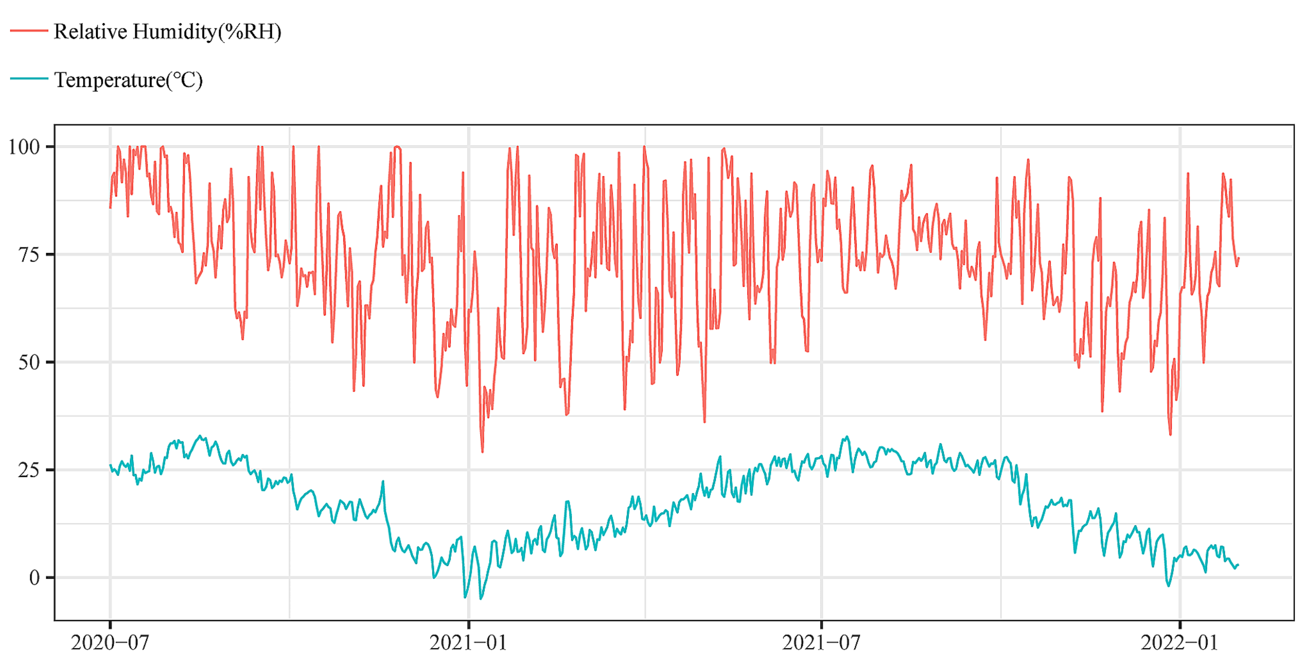

Fig. 1 The distribution of average temperature and relative humidity in Nanjing, China, 2020–2022

July and reached the nadir in January every year. Table S4 and Table S5 show the mean and median of average temperature and relative humidity within different periods before allergen testing varied little, with the average temperature stable at about 17℃ and relative humidity stable at about 73%.

The overall effect of temperature and relative humidity and allergic diseases

The three-dimensional (3-D) plots show the overall picture of the effect of temperature and relative humidity on different types of allergies at different lag periods compared with the reference at 21℃ for temperature and 74% for relative humidity from days (0–7, 0–14, 0–21, and 0–28) (Figures S2 and S3). The results show complex or nonlinear relationships between temperature and relative humidity with respiratory allergies, skin allergies, food allergies, and total allergic diseases with high risks at extreme cold and hot temperatures as well as at low relative humidity and extremely high relative humidity. The overall effect of temperature and relative humidity on allergic diseases for 7, 14, 21, and 28 days are presented in Figs. 2 and 3. We found that the direction of association between temperature and relative humidity differs by allergic type. Particularly, extreme and moderate cold and hot temperatures were associated with an increased risk of skin and total allergic diseases compared with the reference 21℃. In addition, moderate and extremely hot temperatures were significantly associated with an increased risk of food allergies in 0–14 days, after 28 days the inverse relationship was observed. Moreover, low, and moderate relative humidity were associated with decreased risk of both skin and total allergic diseases, while high and extremely high relative humidity were associated with increased risk of skin and total allergic diseases when compared with the reference 74%. On the other hand, relative humidity was negatively associated with respiratory allergies, and positively associated with food allergies, particularly at high and extremely high relative humidity.

The cumulative effect of temperature and relative humidity on allergic diseases at specific percentile and lag

We computed the cumulative effect of temperature and relative humidity on respiratory allergies, skin allergies, food allergies, and total allergies at 1st, 10th, 90th, and 99th percentiles, and at lag 7 (0,3,5,7), 14 (0,5,10, 14), 21 (0,7,14,21), and 28 (0,7,14, 28) days as shown in Table 2. The results show that extreme and moderate colds were positively associated with skin allergies and total allergies (28 days: OR=4.69, 95% CI: 2.88, 7.63; OR=3.36, 95% CI: 2.39, 4.73) and (28 days: OR=3.76, CI: 2.43, 5.81; OR=2.71, 95% CI: 2.00, 3.68), respectively. Additionally, moderately hot and extremely hot temperatures were negatively associated with food allergies (28 days: OR=0.13, 95% CI: 0.04, 0.41 and OR=0.04; 95% CI: 0.01, 0.27). In the case of relative humidity, low relative humidity was negatively associated with respiratory allergies, skin allergies, and total allergic diseases (0–28 days: OR=0.26, 95% CI: 0.10, 0.71; OR=0.29, 95% CI: 0.15, 0.55; and OR=0.42, 95% CI: 0.26, 0.68). Meanwhile, extreme relative humidity was negatively associated with respiratory allergies, and positively associated with skin allergies, food allergies, and total allergies (28 days: OR=0.16, 95%CI: 0.07, 0.37; OR=3.60, 95% CI: 2.52, 5.14; OR=15.61, 95% CI: 3.23, 75.56; and OR=2.33, 95% CI: 1.73, 3.15).

Subgroup analyses

We conducted subgroup analyses to determine the potential modification of gender and age on the association between temperature and relative humidity variability with different types of allergic diseases, and to confirm the robustness of our results. The findings showed that extreme and moderately cold temperatures were associated with an increased risk of skin allergies and total allergies and a high and extreme high relative were related to an increased risk of skin and total allergies, and the effects were more pronounced in girls than in boys (Tables 3 and Table S6). Moreover, the proportion of children under 5 years represented nearly 70% of the total sample. In age-specific analysis, a stronger relationship between low and moderately cold temperatures, as well as high and extremely high relative humidity and skin, respiratory allergies, and total allergies were observed among children under 5 years. The results of the subgroup analysis were consistent with the primary analysis, suggesting that our results are statistically robust (Tables 4 and Table S7).

Discussion

As far as we know, this is the first study to comprehensively evaluate the effects of average temperature and relative humidity on different types of children's allergic diseases. In the present study, we found that extreme and moderate cold temperatures were positively associated with skin allergies and total allergies. Moderate and extreme hot temperatures were negatively associated with food allergies. Low relative humidity was negatively associated with respiratory allergies, skin allergies, and total allergic diseases. Meanwhile, extreme high relative humidity was negatively associated with respiratory allergies, and positively associated with skin allergies, food allergies, and total allergies. These findings were more pronounced in girls and children under 5 years in subgroup analyses.

Relative humidity fluctuated relatively steadily throughout the year, while daily average temperature had

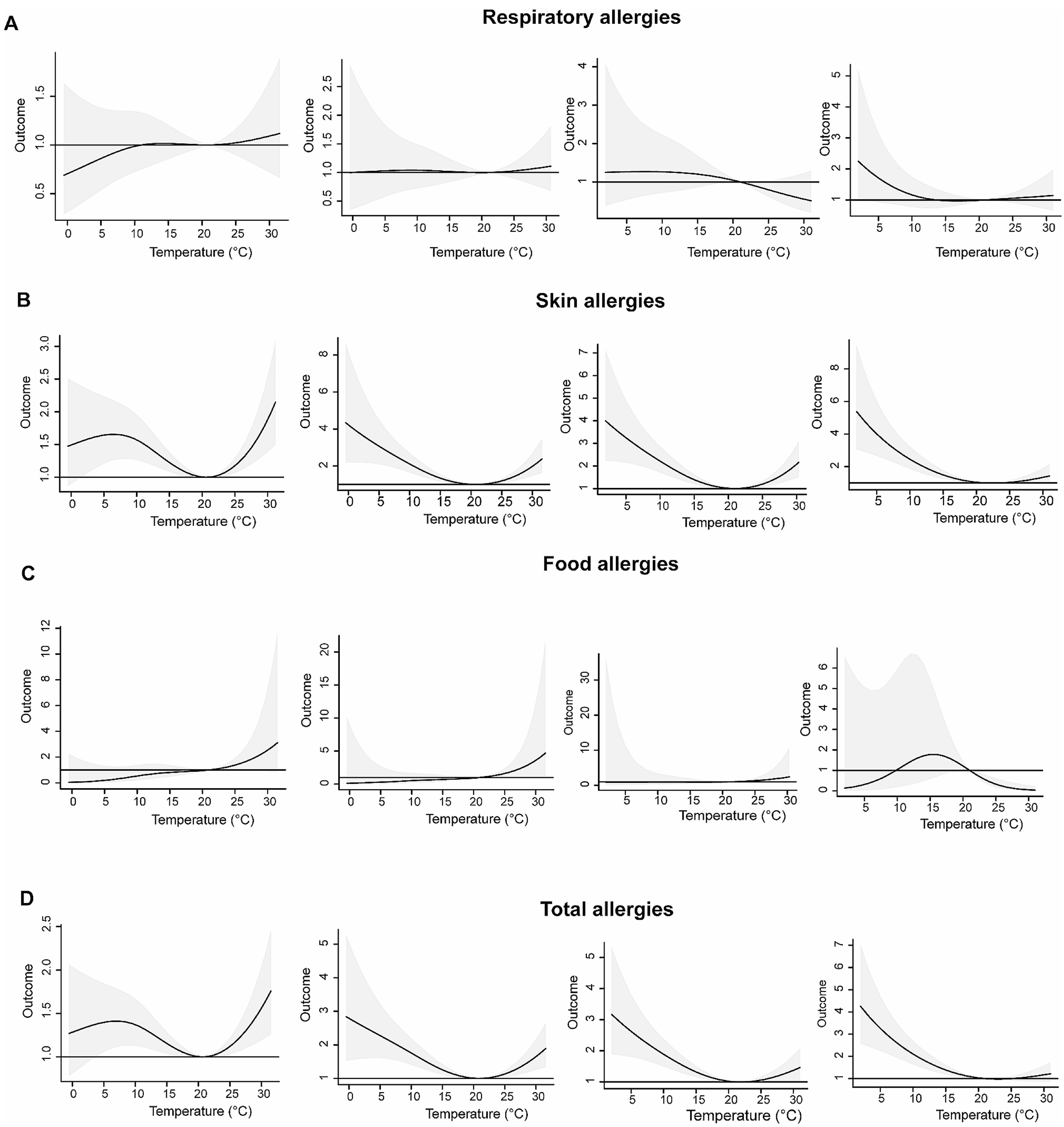

Fig. 2 The overall effect of temperature on allergic diseases among children at different times (7, 14, 21, and 28 days) (**A**) Respiratory allergies. (**B**) Skin allergies. (**C**) Food allergies. (**D**) Total allergies

distinct peaks and troughs. After calculating individual exposures, we found that the mean and median values of average temperature and relative humidity in different periods before diagnosis of allergic diseases did not change much.

Our study found that low temperatures could lead to a greater risk of allergic diseases in children, especially skin allergies. Previous studies in Hefei and Changchun both showed that low temperatures increased the risk of allergic diseases and a large drop in temperature between two adjacent days could exert adverse effects on childhood allergies [3, 8], which is consistent with our findings. Therefore, low temperature may play an important role in patients with allergic diseases, because it can cause airway hyperresponsiveness, tracheal smooth muscle contraction, and pulmonary circulation reduction [8].

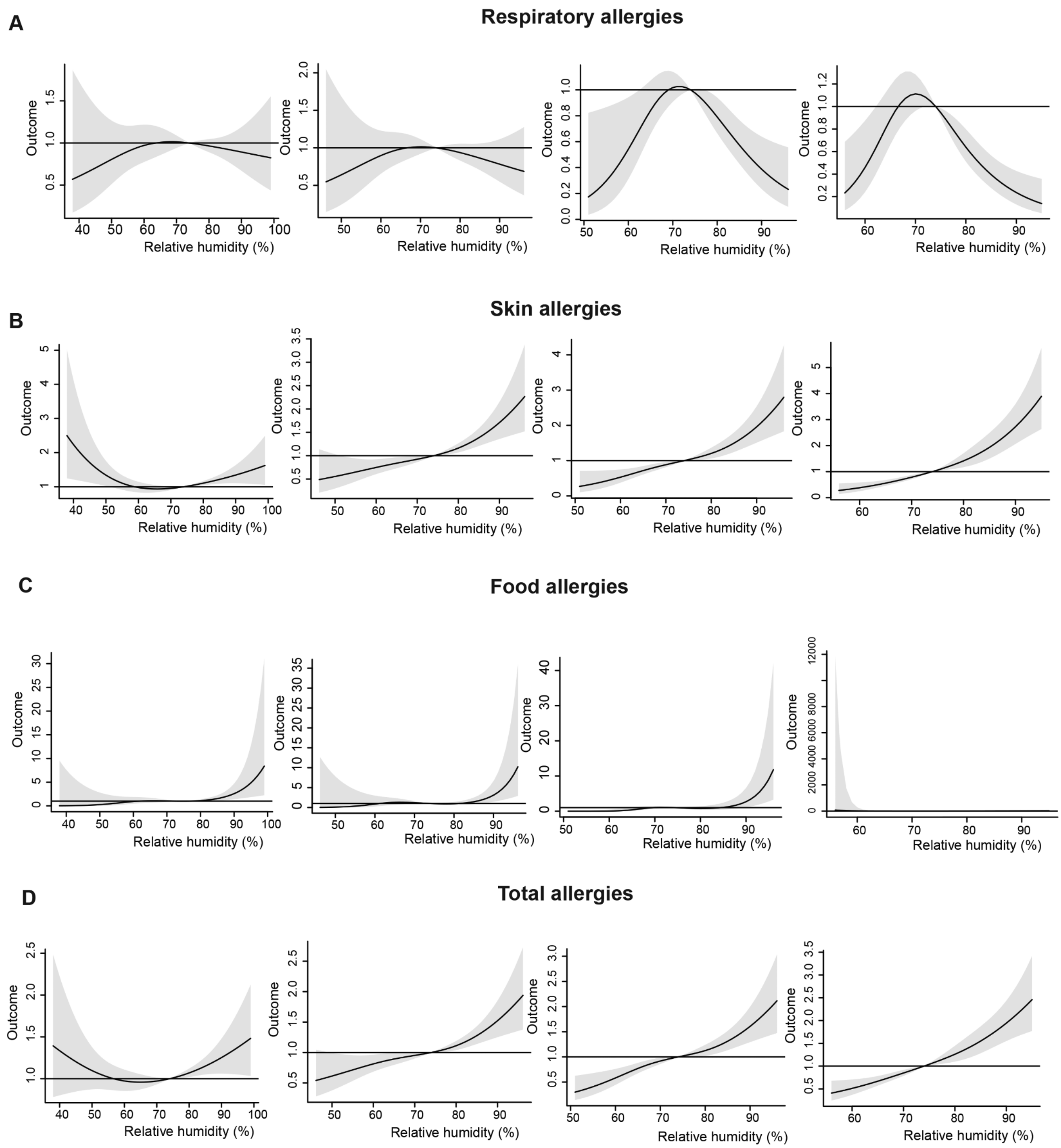

Fig. 3 The overall effect of relative humidity on allergic diseases among children at different times (7, 14, 21, and 28 days) (**A**) Respiratory allergies. (**B**) Skin allergies. (**C**) Food allergies. (**D**) Total allergies

Conversely, low relative humidity was negatively associated with respiratory and skin allergies. Meanwhile, extremely high relative humidity was negatively associated with respiratory allergies, and positively associated with skin allergies, and food allergies in children. A previous study in Hefei found that both high and low relative humidity had a greater risk of respiratory allergies [9], which is inconsistent with our findings. In our research, we found that low and high relative humidity was associated with decreased respiratory allergies. In agreement with part of our findings, a study conducted in California, US showed that low relative humidity was associated with decreased respiratory allergy [20]. The reason for the difference in regional humidity results may be that Nanjing is located in the middle and lower reaches of the Yangtze River, with abundant precipitation throughout

Table 2 Association between temperature and relative humidity with allergic diseases within different periods

	Lag (days)	Respiratory allergies *N* = 833)	Skin allergies (*N* = 2375)	Food allergies (*N* = 96)	Total allergic diseases (*N* = 3304)
		OR (95%CI)	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**
Temperature	**0–7**				
Extreme cold	0	0.77 (0.39, 1.49)	1.54(0.99, 2.40)	0.08(0.00, 1.72)	1.33(0.90, 1.97)
Moderate cold	3	0.92 (0.62, 1.36)	**1.65(1.25, 2.19)**	0.28(0.06, 1.26)	**1.41(1.10, 1.81)**
Moderate hot	5	1.05 (0.82, 1.36)	**1.46(1.21, 1.77)**	1.86(0.96, 3.60)	**1.31(1.10, 1.55)**
Extreme hot	7	1.11 (0.68, 1.81)	**2.15(1.50, 3.08)**	2.90(0.85, 9.92)	**1.72(1.25, 2.36)**
Temperature	**0–14**				
Extreme cold	0	1.02 (0.49, 2.10)	**3.59(2.18, 5.93)**	0.22(0.01, 4.01)	**2.51(1.60, 3.93)**
Moderate cold	5	1.04(0.64, 1.67)	**2.81(2.01, 3.91)**	0.35(0.06, 2.16)	**2.14(1.59, 2.90)**
Moderate hot	10	1.06(0.80, 1.40)	**1.50(1.23, 1.82)**	**2.36(1.10, 5.06**)	**1.34(1.13, 1.59)**
Extreme hot	14	1.11(0.68, 1.80)	**2.18(1.54, 3.06)**	**4.04(1.04, 15.70)**	**1.77(1.30, 2.40)**
Temperature	**0–21**				
Extreme cold	0	1.38(0.63, 3.00)	**3.73(2.22, 6.28)**	0.85(0.03, 24.06)	**2.99(1.88, 4.79)**
Moderate cold	7	1.19(0.72, 1.98)	**2.85(2.03, 4.00)**	0.91(0.13, 6.59)	**2.38(1.73, 3.27)**
Moderate hot	14	0.98(0.73, 1.33)	**1.53(1.23, 1.91)**	1.76(0.69, 4.52)	1.20(0.98, 1.48)
Extreme hot	21	0.97(0.58, 1.60)	**2.16(1.51, 3.08)**	2.40(0.53, 10.80)	**1.42(1.02, 1.98)**
Temperature	**0–28**				
Extreme cold	0	1.94(0.95, 3.95)	**4.69(2.88, 7.63)**	0.21 (0.01, 5.58)	**3.76(2.43, 5.81)**
Moderate cold	7	1.39(0.85, 2.27)	**3.36(2.39, 4.73)**	0.58(0.07, 4.97)	**2.71(2.00, 3.68)**
Moderate hot	14	1.09(0.81, 1.46)	1.15(0.92, 1.44)	**0.13(0.04, 0.41)**	1.06(0.88, 1.29)
Extreme hot	28	1.13(0.70, 1.81)	1.36(0.94, 1.97)	**0.04(0.01, 0.27)**	1.19(0.86, 1.63)
Relative humidity	**0–7**				
Low relative humidity	0	0.72 (0.36, 1.41)	**1.66(1.11, 2.47)**	0.12(0.00, 4.14)	1.19(0.85, 1.66)
Moderate relative humidity	3	0.96 (0.75, 1.21)	**1.02(0.86, 1.21)**	0.85(0.38, 1.89)	0.98(0.86, 1.132)
High relative humidity	5	0.93(0.78, 1.09)	**1.23(1.10, 1.39)**	**1.65(1.11, 2.46)**	**1.17(1.05, 1.29)**
Extreme high relative humidity	7	0.85(0.53, 1.37)	**1.53(1.08, 2.16)**	**4.91(1.86, 12.96)**	**1.40(1.05, 1.88)**
Relative humidity	**0–14**				
Low relative humidity	0	0.74(0.38,1.44)	0.56(0.30, 1.03)	0.25(0.01, 5.11)	**0.63(0.40, 0.99)**
Moderate relative humidity	5	0.94(0.73,1.21)	**0.79(0.66, 0.94)**	1.10(0.45, 2.68)	**0.85(0.74, 0.98)**
High relative humidity	10	0.90(0.76,1.05)	**1.30(1.16, 1.47)**	1.16(0.71, 1.89)	**1.22(1.10, 1.34)**
Extreme high relative humidity	14	0.71(0.41,1.23)	**2.19(1.50, 3.19)**	**8.28(2.60, 26.29)**	**1.88(1.36, 2.60)**
Relative humidity	**0–21**				
Low relative humidity	0	**0.36(0.15, 0.89)**	**0.40(0.22, 0.72)**	**0.002(0.00, 0.21)**	**0.45(0.29, 0.70)**
Moderate relative humidity	7	0.70(0.49, 1.00)	**0.63(0.50, 0.79)**	**0.13(0.02, 0.69)**	**0.69(0.57, 0.82)**
High relative humidity	14	**0.75(0.62, 0.91)**	**1.27(1.10, 1.46)**	0.75(0.38, 1.47)	**1.16(1.04, 1.30)**
Extreme high relative humidity	21	**0.26(0.12, 0.57)**	**2.59(1.76, 3.79)**	**8.45(2.64, 27.00)**	**1.99(1.44, 2.76)**
Relative humidity	**0–28**				
Low relative humidity	0	**0.26(0.10, 0.71)**	**0.29(0.15, 0.55)**	52.61(0.46, 6012.15)	**0.42(0.26, 0.68)**
Moderate relative humidity	7	0.74(0.51, 1.08)	0.48(0.37,5 0.63)	3.40(0.49, 23.44)	**0.61(0.50, 0.75)**
High relative humidity	14	**0.60(0.47, 0.76)**	**1.52(1.23, 1.88)**	3.71(0.96, 14.33)	**1.32(1.13, 1.54)**
Extreme high relative humidity	28	**0.16(0.07, 0.37)**	**3.60(2.52, 5.14)**	**15.61(3.23, 75.56)**	**2.33(1.73, 3.15)**

Note OR, odds ratio; CI, confidence interval. The 1st, 10th, 90th, and 99th percentiles refer to extreme cold, moderate cold, moderate hot, and extreme hot for temperature and as low, moderate, high, and extreme high for relative humidity, respectively. The model was adjusted for the season. The reference was 21℃ and 74% for temperature and relative humidity, respectively

the year, whereas Hefei is relatively drier due to the different sea and land locations. In addition, the difference in results may be due to the variety of respiratory allergies included in our study. Among the types of respiratory allergies analyzed in this study, bronchial asthma had the highest prevalence, followed by allergic rhinitis. Food and skin allergies are the other types of childhood allergies included in this study, as far as we investigated, there have been no studies that explored their relationship to temperature and relative humidity. This limited us to directly compare the findings with others. However, low and high relative humidity has been recorded to affect the skin and respiratory tract [12].

Table 3 Association between different allergic diseases with temperature and relative humidity exposure within different periods among female

	Lag (days)	Respiratory allergies *N* = 833)	Skin allergies (*N* = 2375)	Total allergic diseases (*N* = 3304)
		OR (95%CI)	OR (95%CI)	OR (95%CI)
Temperature	**0–7**			
Extreme cold	0	1.01(0.31, 3.34)	1.14 (0.54, 2.40)	1.34(0.69, 2.58)
Moderate cold	3	1.20(0.59, 2.41)	1.33(0.83, 2.14)	1.40(0.93, 2.11)
Moderate hot	5	1.40(0.88, 2.24)	1.10 (0.80, 1.50)	1.18(0.89, 1.57)
Extreme hot	7	1.85(0.80, 4.27)	1.25 (0.72, 2.19)	1.40(0.85, 2.32)
Temperature	**0–14**			
Extreme cold	0	1.32 (0.35, 5.01)	**3.85 (1.63, 9.10)**	**2.70(1.26, 5.79)**
Moderate cold	5	1.23 (0.50, 3.04)	**2.91 (1.64, 5.17)**	**2.23(1.35, 3.69)**
Moderate hot	10	1.26 (0.78, 2.06)	0.95 (0.68, 1.34)	1.09(0.82, 1.46)
Extreme hot	14	1.50(0.63, 3.55)	1.00 (0.56, 1.79)	1.24(0.76, 2.02)
Temperature	**0–21**			
Extreme cold	0	**5.82 (1.16, 29.26)**	**4.27 (1.65, 11.02)**	**3.78 (1.71, 8.34)**
Moderate cold	7	**3.07 (1.02, 9.230**	**3.21 (1.64, 6.27)**	**2.94(1.69, 5.12)**
Moderate hot	14	**2.10(1.11, 3.98)**	0.75 (0.49, 1.13)	1.08 (0.76, 1.53)
Extreme hot	21	**2.89 (1.12, 7.46)**	0.69 (0.37, 1.28)	1.19(0.70, 2.01)
Temperature	**0–28**			
Extreme cold	0	**4.69 (1.21, 18.16)**	**5.48 (2.33, 12.91)**	**3.46(1.71, 6.99)**
Moderate cold	7	**2.83 (1.13, 7.09)**	**3.38 (1.84, 6.23)**	**2.53(1.54, 4.14)**
Moderate hot	14	1.56 (0.86, 2.84)	**0.53 (0.34, 0.81)**	0.88(0.62, 1.25)
Extreme hot	28	2.01 (0.79, 5.10)	**0.38 (0.19, 0.76)**	0.87(0.50, 1.51)
Relative humidity	**0–7**			
Low relative humidity	0	0.23(0.04, 1.11)	1.34 (0.62, 2.86)	0.79(0.45, 1.420
Moderate relative humidity	3	0.92 (0.58, 1.46)	0.89 (0.65, 1.20)	0.90(0.72, 1.14)
High relative humidity	5	0.84 (0.61, 1.16)	**1.43 (1.16, 1.75)**	**1.22(1.04, 1.45)**
Extreme high relative humidity	7	0.87 (0.33, 2.25)	**2.07 (1.12, 3.83)**	1.64 (1.00, 2.70)
Relative humidity	**0–14**			
Low relative humidity	0	0.21 (0.03, 1.63)	**0.080 (0.02, 0.31)**	0.41(0.17, 1.02)
Moderate relative humidity	5	0.67 (0.36, 1.23)	**0.45(0.32, 0.66)**	**0.70(0.54, 0.90)**
High relative humidity	10	**0.63 (0.42, 0.93)**	**1.75 (1.39, 2.20)**	**1.40(1.18, 1.65)**
Extreme high relative humidity	14	**0.13 (0.02, 0.84)**	**6.34 (2.99, 13.44)**	**2.61 (1.54, 4.42)**
Relative humidity	**0–21**			
Low relative humidity	0	**0.03 (0.00, 0.23)**	**0.05 (0.01, 0.22)**	**0.20(0.08, 0.48)**
Moderate relative humidity	7	**0.23 (0.09, 0.58)**	**0.25 (0.15, 0.42)**	**0.48(0.34, 0.66)**
High relative humidity	14	**0.33 (0.20, 0.55)**	**1.86 (1.38, 2.51)**	**1.24(1.01, 1.53)**
Extreme high relative humidity	21	**0.002(0.00, 0.10)**	**19.43 (8.04, 46.94)**	**2.49 (1.41, 4.40)**
Relative humidity	**0–28**			
Low relative humidity	0	**0.004(0.00, 0.07)**	**0.04(0.0, 0.18)**	**0.27(0.11, 0.67)**
Moderate relative humidity	7	**0.14 (0.05, 0.37)**	**0.17(0.09, 0.31)**	**0.48(0.33, 0.70)**
High relative humidity	14	**0.39 (0.22, 0.70)**	**2.44(1.55, 3.85)**	**1.43 (1.07, 1.91)**
Extreme high relative humidity	28	**0.02 (0.00, 0.30)**	**25.71(11.48, 7.54)**	**2.93(1.73, 4.97)**

Note OR, odds ratio; CI, confidence interval. The 1st, 10th, 90th, and 99th percentiles refer to extreme cold, moderate cold, moderate hot, and extreme hot for temperature and as low, moderate, high, and extreme high for relative humidity, respectively. The model was adjusted for the season. The reference was 21℃ and 74% for temperature and relative humidity, respectively.

Low temperature and high relative humidity could lead to a greater risk of allergic diseases in children, especially skin allergies, and this finding was more pronounced in girls and children under 5 years in subgroup analyses. There were some potential biological explanations for the effects of temperature and relative humidity on childhood allergies. The physiological reason for the gender difference might be that girls' skin barriers were more fragile and sensitive than boys', which makes them more vulnerable to the stimulation of external climate change [21]. In addition, low temperatures typically affect girls more than boys due to girls having lower metabolic rates and lower skin temperatures than boys. During heat, boys tend to sweat more and blood flows rapidly around their skin compared to girls. These mechanisms effectively disperse excess heat, resulting in

Table 4 Association between different allergic diseases with temperature and relative humidity exposure within different periods among children < 5 years

	Lag (days)	Respiratory allergies *N* = 833)	Skin allergies (*N* = 2375)	Total allergic diseases (*N* = 3304)
		OR (95%CI)	OR (95%CI)	OR (95%CI)
Temperature	**0–7**			
Extreme cold	0	1.07(0.43, 2.64)	1.29(0.77, 2.18)	**1.22(0.76, 1.95)**
Moderate cold	3	1.33(0.75, 2.36)	**1.65(1.18, 2.30)**	**1.46(1.08, 1.97)**
Moderate hot	5	0.84(0.56, 1.26)	**1.37(1.09, 1.71)**	1.19(0.97, 1.47)
Extreme hot	7	0.79(0.37,1.70)	**1.99(1.29, 3.05)**	1.50(1.02, 2.22)
Temperature	**0–14**			
Extreme cold	0	1.00(0.37, 2.70)	**2.72(1.50, 4.91)**	**2.16(1.27, 3.68)**
Moderate cold	5	1.10(0.55, 2.21)	**2.57(1.74, 3.79)**	**2.13(1.49, 3.03)**
Moderate hot	10	0.74(0.47, 1.16)	**1.39(1.09, 1.77)**	**1.29(1.04, 1.61)**
Extreme hot	14	0.63(0.29, 1.37)	**1.94(1.28, 2.96)**	**1.71(1.17, 2.50)**
Temperature	**0–21**			
Extreme cold	0	1.25(0.43, 3.63)	**2.65(1.41, 4.97)**	**2.15(1.23, 3.77)**
Moderate cold	7	1.27(0.61, 2.64)	**2.48(1.61, 3.82)**	**2.11(1.43, 3.11)**
Moderate hot	14	0.67(0.41, 1.10)	**1.53(1.15, 2.03)**	1.15(0.90, 1.47)
Extreme hot	21	0.55(0.25, 1.23)	**2.13(1.36, 3.35)**	**1.36(0.91, 2.03)**
Temperature	**0–28**			
Extreme cold	0	1.34(0.50, 3.55)	**3.14(1.78, 5.53)**	**2.85(1.71, 4.75)**
Moderate cold	7	1.19(0.58, 2.42)	**2.70(1.83, 4.00)**	**2.48(1.74, 3.54)**
Moderate hot	14	0.81(0.50, 1.32)	1.03(0.79, 1.35)	0.97(0.77, 1.22)
Extreme hot	28	0.72(0.33, 1.57)	1.17(0.75, 1.85)	1.04(0.70, 1.54)
Relative humidity	**0–7**			
Low relative humidity	0	0.44(0.16, 1.19)	**1.66(1.04, 2.65)**	1.22 (0.82, 1.82)
Moderate relative humidity	3	1.00(0.71, 1.43)	1.07(0.87, 1.32)	1.03 (0.87, 1.23)
High relative humidity	5	0.80(0.62, 1.05)	**1.33(1.15, 1.55)**	**1.23 (1.09, 1.40)**
Extreme high relative humidity	7	0.72 (0.36, 1.44)	**1.85(1.25, 2.73)**	**1.64 (1.16, 2.31)**
Relative humidity	**0–14**			
Low relative humidity	0	0.90 (0.34, 2.40)	0.74(0.34, 1.62)	0.70 (0.39, 1.26)
Moderate relative humidity	5	1.25(0.86, 1.82)	**0.79(0.64, 0.98)**	0.87(0.73, 1.03)
High relative humidity	10	0.65 (0.49, 0.85)	**1.41(1.22, 1.63)**	**1.27(1.13, 1.43)**
Extreme high relative humidity	14	0.35 (0.12, 1.02)	**2.50(1.58, 3.95)**	**2.13(1.45, 3.12)**
Relative humidity	**0–21**			
Low relative humidity	0	0.63(0.17, 2.29)	**0.46(0.22, 0.98)**	0.65(0.38, 1.12)
Moderate relative humidity	7	0.89(0.51, 1.54)	**0.67(0.50, 0.90)**	**0.78(0.62, 0.97)**
High relative humidity	14	0.47(0.32, 0.68)	**1.28(1.07, 1.53)**	**1.22 (1.07, 1.40)**
Extreme high relative humidity	21	0.01(0.00, 0.16)	**3.07(1.85, 5.09)**	**2.30 (1.52, 3.47)**
Relative humidity	**0–28**			
Low relative humidity	0	0.46(0.11, 1.95)	0.53(0.23, 1.26)	0.65(0.35, 1.18)
Moderate relative humidity	7	1.02(0.58, 1.79)	**0.57(0.42, 0.77)**	**0.68(0.54, 0.85)**
High relative humidity	14	**0.31(0.19, 0.50)**	**1.75(1.39, 2.21)**	**1.46(1.23, 1.72)**
Extreme high relative humidity	28	**0.003 (0.00, 0.12)**	**4.56(2.84,7.32)**	**2.67(1.83, 3.90)**

Note OR, odds ratio; CI, confidence interval. The 1st, 10th, 90th, and 99th percentiles refer to extreme cold, moderate cold, moderate hot, and extreme hot for temperature and as low, moderate, high, and extreme high for relative humidity, respectively. The model was adjusted for the season. The reference was 21℃ and 74% for temperature and relative humidity, respectively.

slightly lower skin temperatures compared to girls [22]. Besides, we found that all results were more pronounced in children under 5 years, which might be attributed to the following factors. Biological mechanism research has shown that allergic reactions occur mainly in early childhood and exposure to even trace amounts of allergens could cause atopic individuals to produce IgE antibodies [23]. Compared with children over 5 years old, children under 5 years old had relatively immature immune system development, weak resistance to exposure stimulation, and were more prone to disease [24]. Furthermore, temperature changes affect the immune system's ability to resist infectious agents, trigger the release of inflammatory mediators, and increase IgE, ultimately leading to the development of allergic diseases [4, 25]. Moreover, younger children are more susceptible to temperature impacts due to several more factors. They are relatively underdeveloped and have fewer self-care abilities [21]. Their high surface-to-body ratio leads to increased exposure to ambient temperatures. Additionally, they have lower thermoregulatory capacity and sweating capacities, along with cardiac output [15]. Their high metabolic rate can make them more vulnerable to extreme temperatures [26]. Furthermore, younger children often spend more time engaging in outdoor physical activities, which further exposes them to heat and cold [27]. Ultimately, rising temperatures could lead to abnormalities in the human immune system, leading to allergic diseases in the population [28]. All these factors contributed to the difference in age between the correlation results in this study.

Several strengths of this study should be mentioned. Firstly, to the best of our knowledge, this is the first study to thoroughly and systematically explore the connection between temperature, relative humidity, and various types of allergic disorders in children, which may enrich the understanding of health impacts on various types of allergies. Our findings thus added new evidence to the existing literature on temperature, relative humidity, and allergic disorders in children. We also undertook stratified analysis by gender and age. Results of the pertinent research would assist in directing the avoidance of allergic disorders from the adverse effects of temperature and relative humidity. Secondly, the study included a large sample size, with a total of 3305 allergic disease cases. Lastly, we used DLNM to calculate individual exposure to average temperature and relative humidity before allergen testing for 7 days, 14 days, 21 days, and 28 days. The acute and relatively long-term impacts of temperature and humidity on allergies were also covered at these times, which could further prompt relevant departments to prevent the occurrence of allergic diseases in advance within the corresponding period.

The limitations of this study should also be acknowledged. The study was conducted in one city, which limited the extrapolation of our findings to other regions. Moreover, it was a retrospective case-control study that could not straightly prove a causal relationship between temperature and relative humidity and allergic diseases. Some biases due to exposure misclassification might be inevitable. So, it could only provide evidence for possible associations between them, and a stronger causal association needed to be verified in subsequent cohort studies.

In general, our research provided a clue that temperature and relative humidity could affect different types of childhood allergic diseases within different periods. These findings could help environmental and climate authorities, community health authorities, public health departments, and child guardians to prevent allergic diseases as early as possible.

Conclusions

Our study demonstrated that low temperature and high relative humidity had greater risk implications for the occurrence of allergic diseases in children. However, the directionality of the relationship differs by allergic type. Specifically, extreme and moderate cold temperatures were positively associated with skin allergies, and moderate and extreme hot temperatures were negatively associated with food allergies. Low relative humidity was negatively associated with respiratory allergies and skin allergies, and extreme high relative humidity was negatively associated with respiratory allergies, and positively associated with skin allergies and food allergies. A stronger relationship between temperature and relative humidity and allergic diseases was more pronounced in children under 5 years, particularly girls. By taking into account the effect of temperature and relative humidity on allergic diseases in children, health practitioners can improve the quality of care for children with allergic diseases by taking a holistic approach. This approach considers environmental factors alongside medical interventions to optimize outcomes and enhance the overall well-being of children with allergic diseases. Simultaneously, guardians, meteorological administrations, and public health administrations should collaborate to take effective measures.

Supplementary Information

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Supplementary Material 1

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Author contributions

S.Y: Conception, study design, data acquisition, analysis, and interpretation, and draft the original manuscript. F.M.B: Conception, study design, data analysis, and interpretation, and draft the original manuscript Z.Z: Conception, study design, data acquisition, analysis, and interpretation, and draft the original manuscript. S.M.M and H.Q: Conception, study design, data analysis, and interpretation, and revised the manuscript. L.G and X.W: Conception, study design, interpretation of data, revised manuscript, and supervision. All authors read and approved the final version of the manuscript.

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Data availability

The datasets used in this study are available from the corresponding authors upon reasonable request.

Declarations

Ethical approval

This study was approved by the Ethics Committee of the Children's Hospital at Nanjing Medical University, and the data utilized were completely anonymous.

Consent to participate
Written informed consent was obtained from the children's guardians.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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