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RESEARCH ARTICLE

Short-term effects of meteorological factors on childhood atopic dermatitis in Lanzhou, China

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Abstract
Atopic dermatitis (AD) is one of the leading burdens of skin disease in children globally. Meteorological factors are involved in the onset and development of AD. Several studies have examined the effects of meteorological factors on AD, but their results are inconsistent, and the understanding of the link between AD and meteorological factors remains inadequate. In this study, a total of 19,702 children aged 0 to 14 visited the outpatient clinic for AD from 2015 to 2019 in Lanzhou, China. A distributed lag nonlinear model (DLNM) applies to evaluate effects of meteorological factors on childhood AD in Lanzhou, China, and further explored age and gender differences. It was found that extremely high or low temperatures, extremely high diurnal temperature range (DTR), extremely low relative humidity (RH), and extremely high wind speed (WS) increased the risk of outpatient visits for childhood AD. Effects of extremely high DTR and extremely high WS were more intense, with maximum cumulative risks of 2.248 (95% CI 1.798, 2.811) and 3.834 (95% CI 3.086, 4.759) at lag 0–21, respectively. Furthermore, the combination of low temperature and low RH can also contribute to the higher risk of childhood AD. For extreme temperatures, children aged 7–14 years were more vulnerable. For extremely low RH, extremely high DTR and WS, boys and children aged 0–3 years were more vulnerable. Public health departments should strengthen publicity and education about how meteorological factors affect childhood AD and develop sex- and age-specific preventative measures.

Keywords Atopic dermatitis · Meteorological factors · Children · Outpatient visits · Distributed lag nonlinear model

Introduction

Atopic dermatitis (AD) is a chronic relapsing inflammatory skin disease, which is highly prevalent in children and affects approximately 20% of children worldwide (Garritsen et al. 2015). Its main clinical manifestation includes intense itch, dry skin, and eczematous dermatitis. It usually affects the flexed side of the limbs, the head, and the face (Weidinger and Novak 2016). AD, though, a non-fatal disease, is one of the greatest burdens of disease among children. It makes the life quality of children and their guardians decreased significantly because of the clinical symptoms of intense itching and a long disease course of remission and relapse. Children with AD, typically experience sleep disturbances, anxiety, poor concentration, and intellectual inferiority (Ramirez et al. 2019; Cheng et al. 2021; Jackson-Cowan et al. 2021). Parents of children with AD are at higher risk for other medical conditions, such as mental health problems and chronic pain diseases (Vittrup et al. 2022). Caring for sick children leads to workday absence of parents (Cheng and Silverberg 2021), which, in turn, increase the disease burden of childhood AD. As mentioned above high incidence and heavy disease burden, there is a call for an urgent solution to public health.

The etiology of AD is complex and still poorly understood, genetic predisposition, although immune imbalance, and skin barrier disruption are generally involved (Langan et al. 2020; Yang et al. 2020). Natural environmental factors invariably affect symptoms of AD and are being studied more thoroughly. Early in 2006, Norwegian

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scholar Byremo G has proposed moving children with AD moved from a region with a temperate climate to a region with a subtropical climate and stayed for four weeks. This action reduced the skin colonization of *Staphylococcus aureus* and improved Scoring Severity of AD (SCORAD) improved, and enhanced Life Quality Index (LQI) (Byremo et al. 2006). This observation provides a strong evidence that the exposure to natural exposure environment is involved in AD pathophysiology. Meteorological factors, as an essential part of the natural exposure environment, have shown stronger effects on childhood AD than air pollutants (Hu et al. 2020). The association between meteorological factors and AD has been widely studied by domestic and foreign scholars. Nevertheless, those research findings are not always consistent to each other. Studies conducted in southern Italy, Nigeria, and the USA showed symptoms or outpatient visits of AD are positively correlated with outdoor temperature (Onunu et al. 2007; Fleischer 2019; Patella et al. 2020). Studies from the Western Europe, Spain, and Shanghai showed negative correlations between symptoms or outpatient visits of AD and outdoor temperature (Weiland et al. 2004; Suárez-Varela et al. 2008; Hu et al. 2022). Multiple studies revealed a positive correlation between severity of AD symptoms and DTR (Kim et al. 2017; Patella et al. 2020). In terms of humidity and wind speed, most of the studies demonstrated that high humidity is conducive to the alleviation of AD symptoms (Silverberg et al. 2013; Kim et al. 2017; Ibekwe and Ukonu 2019). But, there are also studies showing that high humidity is an aggravating factor of AD (Onunu et al. 2007; Suárez-Varela et al. 2008). Fewer studies have conducted on the role of wind speed in AD. A time series study showed that the wind speed is negatively associated with clinic visits of childhood AD in Shanghai (Hu et al. 2020). However, another study from Chengdu found no relation between clinic visits of AD and wind speed (Li et al. 2018).

The link between AD and meteorological factors has not been fully understood due to inconsistent results among studies. Whether the effects of meteorological factors varied by child age and gender of children are far less investigated. Meteorological factors can influence childhood AD by interacting with other meteorological factors, and interactive effects should be considered. However, few studies have explored interactive effects. This study aims to quantify the effects of meteorological factors on childhood AD outpatient visits by employing the distributed lag nonlinear model (DLNM), and further explore interactive effects between meteorological factors using a generalized additive model(GAM). This study will help to develop more targeted prevention strategies, reduce symptom onset or relapse via avoiding or reducing trigger factors, and eventually improve the life quality of children with AD.

Materials and methods

Study area

Lanzhou, at 102° 36´ E–104° 35´ E longitude and 35° 34´ N–37° 00´ N latitude, is located in the center of Gansu Province, Northwest China (Fig. 1). Lanzhou has a temperate continental climate, with long, cold winters and short summers. It has wide DTR, weak wind speed, and low rainfall. The mean annual temperature and humidity were 10.3 °C and 53%, respectively. The city area is approximately 1631.6 km^2.

Data collection

Daily AD cases of children were obtained from three large general hospitals in Lanzhou from January 1, 2015, to December 31, 2019. Lanzhou locates in a long and narrow valley extending east–west as well as in-between the north and south mountains. These three hospitals are located at the intersection of east and west and surrounded by thickly populated regions. With high-quality medical equipment and

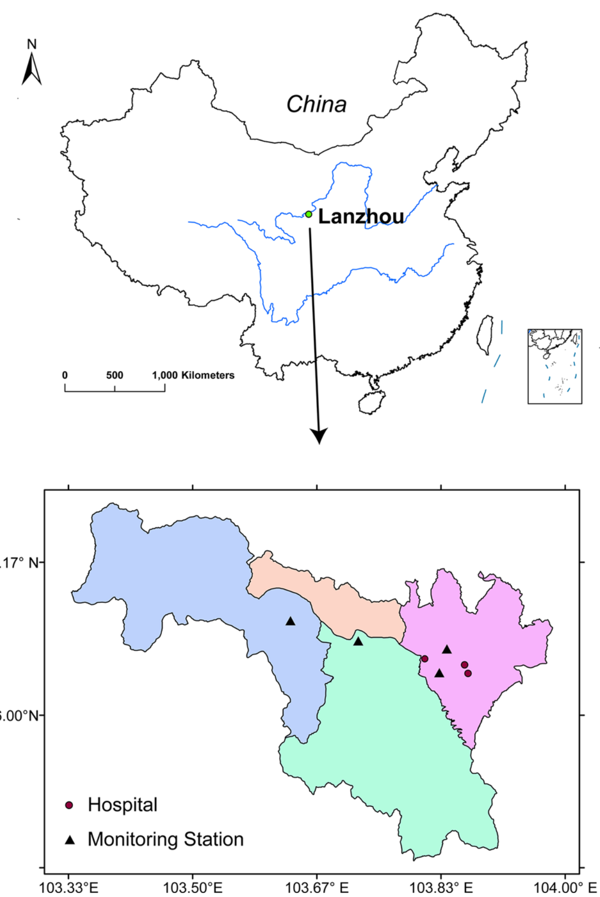

Fig. 1 Location of study area (Lanzhou) in China

service, the hospitals are providing accessible medical care. Approximately 80% of local residents and their children choose to seek medical care at these three hospitals (Ma et al. 2016, 2017; Dong et al. 2021b). Thus, children in the current study are a good representative of the general population. The collected data included the visit date, identification number, gender, age, and diagnosis. According to the International Classification of Diseases (ICD-10), the ICD code for AD is L20. The clinical diagnostics were given by experienced clinicians according to the criteria of Williams. Daily meteorological data during the study period were collected from the China Meteorological Data Network (http://data.cma.cn). The collected data include the daily minimum/maximum/mean temperature (°C), relative humidity (RH, %), atmospheric pressure (AP, hPa), and wind speed (WS, m/s). Daily average concentrations of particulate matter ≤ 10 μm (PM_{10}), sulfur dioxide (SO_2), and nitrogen dioxide (NO_2) were collected from the Lanzhou Environmental Protection Bureau.

Data analysis

Because data on of air pollutants and meteorological factors are not normally distributed, Spearman correlation analysis is used to assess the correlation between two variables. Highly correlated variables (Spearman correlation coefficient ≥ 0.7) (Mukaka 2012) were not incorporated into the model simultaneously to avoid multicollinearity. Because the number of daily outpatient visits for childhood AD is a small probability event for the total population of Lanzhou, and follows a Poisson distribution, we used meteorological factors as the independent variable and the daily number of outpatient visits of childhood AD as the dependent variable. After controlling for the long-term trend, holiday effect, and weekend effect, we used the Poisson regression model combined with a distributed lag non-linear model to explore whether meteorological factors have non-linear and lagged effect on childhood AD. The basic model is as follows:

$$\begin{aligned} \boldsymbol{Yt} \sim \mathbf{Poisson}(\mu_t)\mathbf{Log}[\mathbf{E}(\mathbf{Y}_t)] = \alpha + \boldsymbol{cb}(\text{meterological variable, lag}, \boldsymbol{df}) \\ + \boldsymbol{ns}(\mathbf{x_i}, \boldsymbol{df}) + \boldsymbol{ns}(\mathbf{PM10}, \boldsymbol{df}) + \boldsymbol{ns}(\mathbf{SO2}, \boldsymbol{df}) \\ + \boldsymbol{ns}(\mathbf{NO2}, \boldsymbol{df}) + \boldsymbol{ns}(\mathbf{time}, \boldsymbol{df}) \\ + \mathbf{as.factor}(\mathbf{dow}) + \mathbf{as.factor}(\mathbf{ph}) \end{aligned}$$

In this formula, t is the observation day. *Yt* is the number of outpatient visits for childhood AD on day t, α is the intercept, *cb* is a cross-basis function, and *ns* is a natural spline used to control long-term trend. To ensure the model stability, we performed separate models for each of the meteorological factors. Each model includes the target variable and x_i, x_i refers to the remaining meteorological factors that could lead to potential confounding effects. X_i was selected based on the following aspects. First, Spearman correlation coefficients between xi and the target variable were less than 0.70. Secondly, our model is stable after inclusion of x_i. After carefully screening, xi refers to RH in temperature model, temperature and RH in DTR model, temperature in RH model, temperature and RH in WS model. *df* is degree of freedom. Day of the week (dow) and public holiday (ph) were used as dummy variables. *dfs* of xi, time and air pollutants were set at 7/year, 4 and 4 based on the previous studies and AIC (Hao et al. 2020; Huang et al. 2020; Dong et al. 2021a). According to the lowest AIC value (Table S1), *dfs* of the target meteorological factor and the lag were determined to be 4. To fully capture the potential lag effects on meteorological variables, we extend a sufficiently long maximum lag day (21 days) based on minimal AIC values (Table S2) and two previous studies exploring associations between meteorological factors and childhood AD in Shanghai, China (Hu et al. 2020, 2022).

We used a GAM to examine the association between childhood AD cases and the interaction effects of meteorological factors. The equation reads:

$$\mathrm{Log}[\mathrm{E}(\mathrm{Yt})] = \beta + s_1(k, x) + s_2(z) + \mathrm{strata}$$

In this formula, β is the intercept, $s_1()$ is the spline function presented interaction effects of meteorological factors, k and x represent any two of three meteorological factors (temperature, RH, and WS), z refers to the remaining meteorological factor.

The 5th and 95th percentile values of meteorological factors were defined as extremely high and extremely low values, respectively. The median values of meteorological factors were used as reference values, we calculated the relative risk (RR) and 95% confidence interval (CI) to evaluate effects of meteorological factors. The single-day lag effect refers to the relationship between the number of childhood AD cases on day t and the level of meteorological factors t days ago. The cumulative effect refers to the relationship between the number of childhood AD cases on day t and the moving average value of meteorological factors on day t and the previous day. That is, for single-day lag effects, lag 0 represents the current-day, and lag 1 represents the previous-day level of meteorological factors, respectively. For cumulative effect, lag 0–1 means the 2-day moving average level of current day and the previous day level of meteorological factors.

Subgroup analysis was based on gender (boy and girl) and age (0–3 years old, 4–6 years old, and 7–14 years old). Sensitivity analyses were performed by changing the maximum lag days (18, 19, 20, and 21), *dfs* for meteorological factors (3, 4, 5, and 6) and *dfs* for time (5, 6, 7, and 8).

Results

Data description

In total, 19,702 children visited the outpatient clinic because of AD from 2015 to 2019. There were 11,208 boys and 8494 girls with a boy-to-girl ratio of 1.32:1. On average, 11 children with AD attended the outpatient clinic per day. Children aged 0–3 years had the largest number of outpatient visits among different age subgroups and accounted for 62.43%. The average values of meteorological factors and air pollutants can be seen in Table 1. Figure 2 is a time-series plot of daily cases of outpatient visits for childhood AD, daily mean temperature, RH, DTR, WS, and AP in Lanzhou from 2015 to 2019.

Correlation analysis

Table 2 presented Spearman correlation analysis between meteorological factors and pollutants. Strong correlation between daily average temperature and daily average AP/daily minimum/maximum temperature were estimated. Thus, daily minimum temperature, daily maximum temperature, and AP were not included in the model. A negative correlation between RH, AP, SO_2, NO_2, PM_{10}, and daily mean temperature was established, with Spearman correlation coefficients were − 0.028, − 0.710, − 0.676, − 0.293, and − 0.396, respectively. The daily mean temperature was positively related to DTR and WS. Its correlation coefficients were 0.233 and 0.259, respectively. RH was positively correlated with air pressure and negatively correlated with DTR, WS, SO_2, NO_2, and PM_{10}, Their correlation coefficients were 0.137, − 0.403, − 0.191, − 0.251, − 0.173, and − 0.379, respectively. AP was negatively correlated with wind speed and positively correlated with SO_2, NO_2, and PM_{10}. Their correlation coefficients were − 0.251, 0.372, 0.181, and 0.181, respectively. WS was negatively correlated with SO_2, NO_2, and PM_{10}, correlation coefficients were − 0.358, − 0.416, and − 0.246, respectively. We observed positive correlations between air pollutants.

Effects of meteorological factors on childhood AD

Figure 3 showed three-dimensional surface plots about the impacts of meteorological factors on the number of outpatient visits for childhood AD at different lag days; nonlinear associations between meteorological factors and the risk of outpatient visits for childhood AD were observed. The highest RR of outpatient visits was observed at lag 0 when the daily mean temperature was at 31 °C, and the value of RR was 1.097 (95% CI 1.061, 1.135). The highest risk with a value of 1.182 (95% CI 1.108, 1.261) was observed when DTR was 25 °C at lag 21. The highest risk with a

Table 1 Summary statistics of childhood AD cases, meteorological variables, and air pollution variables in Lanzhou from 2015 to 2019

Variables	Mean	SD	Min	P_{25}	P_{50}	P_{75}	Max
Daily children AD cases							
Total	12.00	11.00	1.00	4.00	8.00	14.00	64.00
Boys	7.00	6.00	1.00	3.00	5.00	8.00	42.00
Girls	5.00	5.00	1.00	2.00	4.00	7.00	32.00
0–3 years	7.00	6.00	1.00	3.00	5.00	9.00	40.00
4–6 years	3.00	3.00	1.00	1.00	2.00	3.00	19.00
7–14 years	4.00	4.00	1.00	1.00	2.00	5.00	29.00
Meteorological factors							
Mean temperature (°C)	11.41	9.88	–12.30	30.40	2.29	12.73	20.02
DTR (°C)	11.55	4.26	0.90	8.50	11.65	14.50	24.80
Relative humidity (%)	50.80	14.85	11.71	39.62	51.00	61.51	96.09
Atmospheric pressure (hPa)	848.66	5.78	833.00	844.34	848.57	852.75	866.43
Mean wind speed (m/s)	1.26	0.40	0.20	1.00	1.18	1.50	3.13
Air pollutants							
PM_{10} (ug/m^3)	114.42	87.52	16.00	69.00	97.46	134.56	1484.54
SO_2 (ug/m^3)	19.64	13.35	3.54	9.93	15.05	26.00	81.87
NO_2 (ug/m^3)	48.64	17.96	12.58	36.98	46.64	56.00	146.60

Mean, SD, Min, Max, P_{25}, P_{50}, P_{75} represented the mean, standard deviation, minimum, maximum, the 25th percentile, median, and 75th percentile variables, respectively

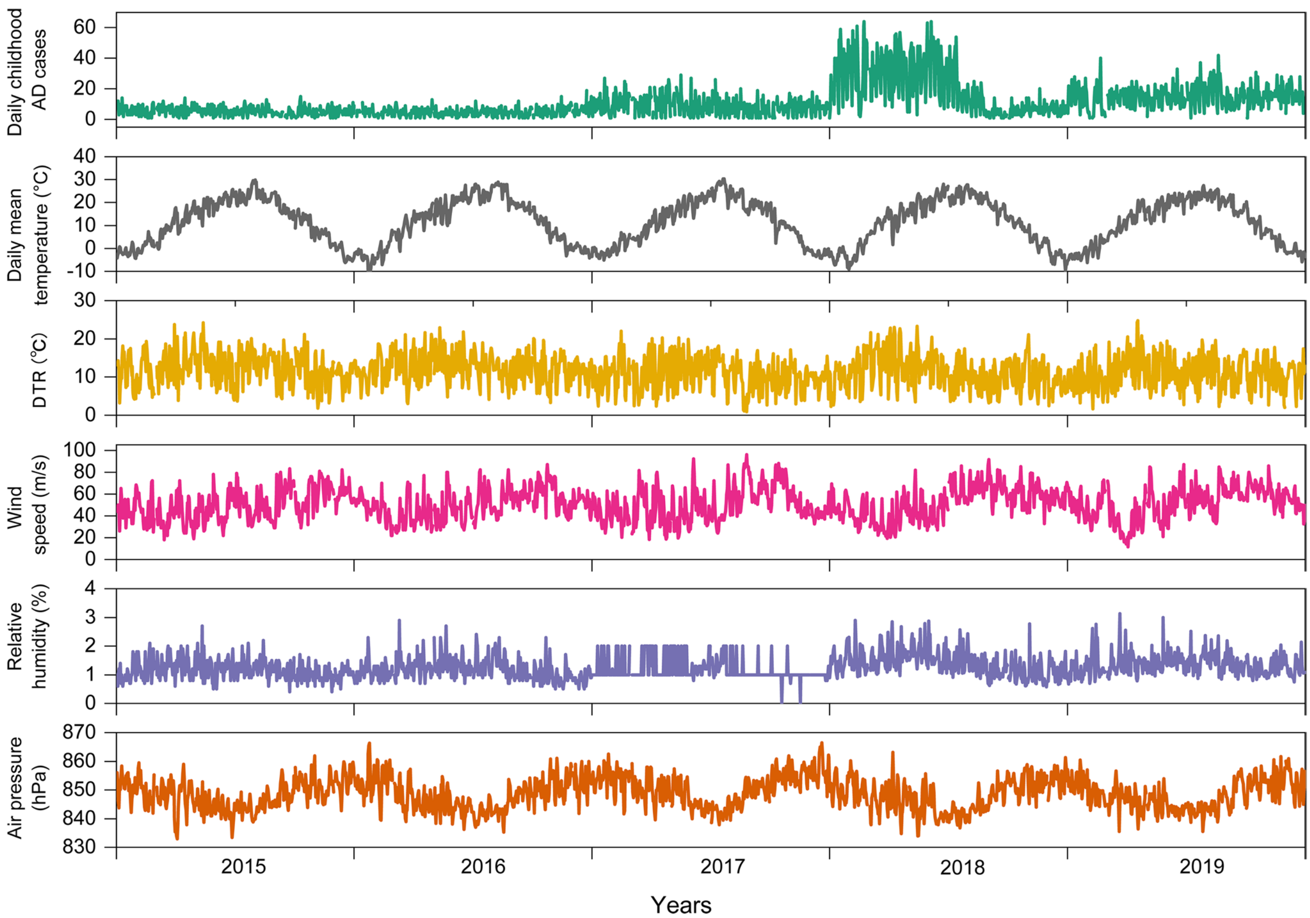

Fig. 2 The distribution of daily childhood AD cases and meteorological variables in Lanzhou, China, 2015–2019

Table 2 Spearman correlation analysis between meteorological factors and pollutants in Lanzhou from 2015 to 2019

Variables	Tmean	Tmax	Tmin	DTR	RH	AP	WS	SO_2	NO_2	PM_{10}
Tmean	1.000									
Tmax	0.970*	1.000								
Tmin	0.974*	0.904*	1.000							
DTR	0.233*	0.442*	0.032	1.000						
RH	–0.028	0.103	0.088*	–0.403*	1.000					
AP	–0.710*	–0.721*	–0.657*	–0.305*	0.137*	1.000				
WS	0.259*	0.211*	0.264*	–0.099*	–0.191*	–0.251*	1.000			
SO_2	–0.676*	–0.590*	–0.734*	0.157*	–0.251*	0.372*	–0.358*	1.000		
NO_2	–0.293*	–0.201*	–0.377*	0.336*	–0.173*	0.181*	–0.416*	0.571*	1.000	
PM_{10}	–0.396*	–0.298*	–0.462*	0.274*	–0.379*	0.181*	–0.246*	0.574*	0.460*	1.000

$^*P<0.05$

value of 1.033 (95% CI 1.049, 1.066) was observed, when RH was 32% at lag 21. The RR with the highest value was 1.166 (95% CI 1.094, 1.243) when WS was 3 m/s at lag 21. Figure 4 presented overall effects of meteorological factors on outpatient visits for childhood AD over 21 days. We observed that daily mean temperature was inversely associated with the risk of outpatient visits for childhood AD, WS, and DTR were positively correlated with the risk of outpatient visits. The correlation between RH and the risk of outpatient visits for childhood AD presented is reflected by a reverse "v" shape. Table 3 described single-day lag effects and cumulative effects of extremely meteorological factors on the risk of outpatient visits for childhood AD. Overall, extremely high or low temperature, extremely high

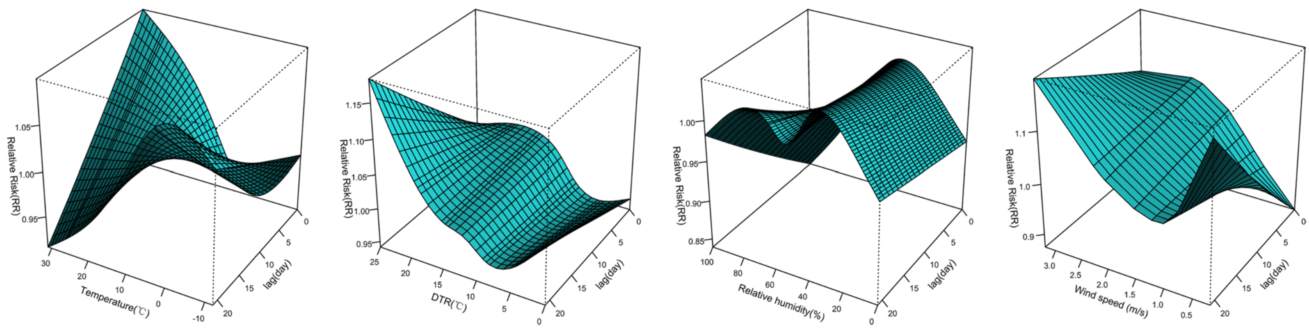

Fig. 3 Three-dimensional plot of the relationship between meteorological variables and childhood AD over 21 lag days

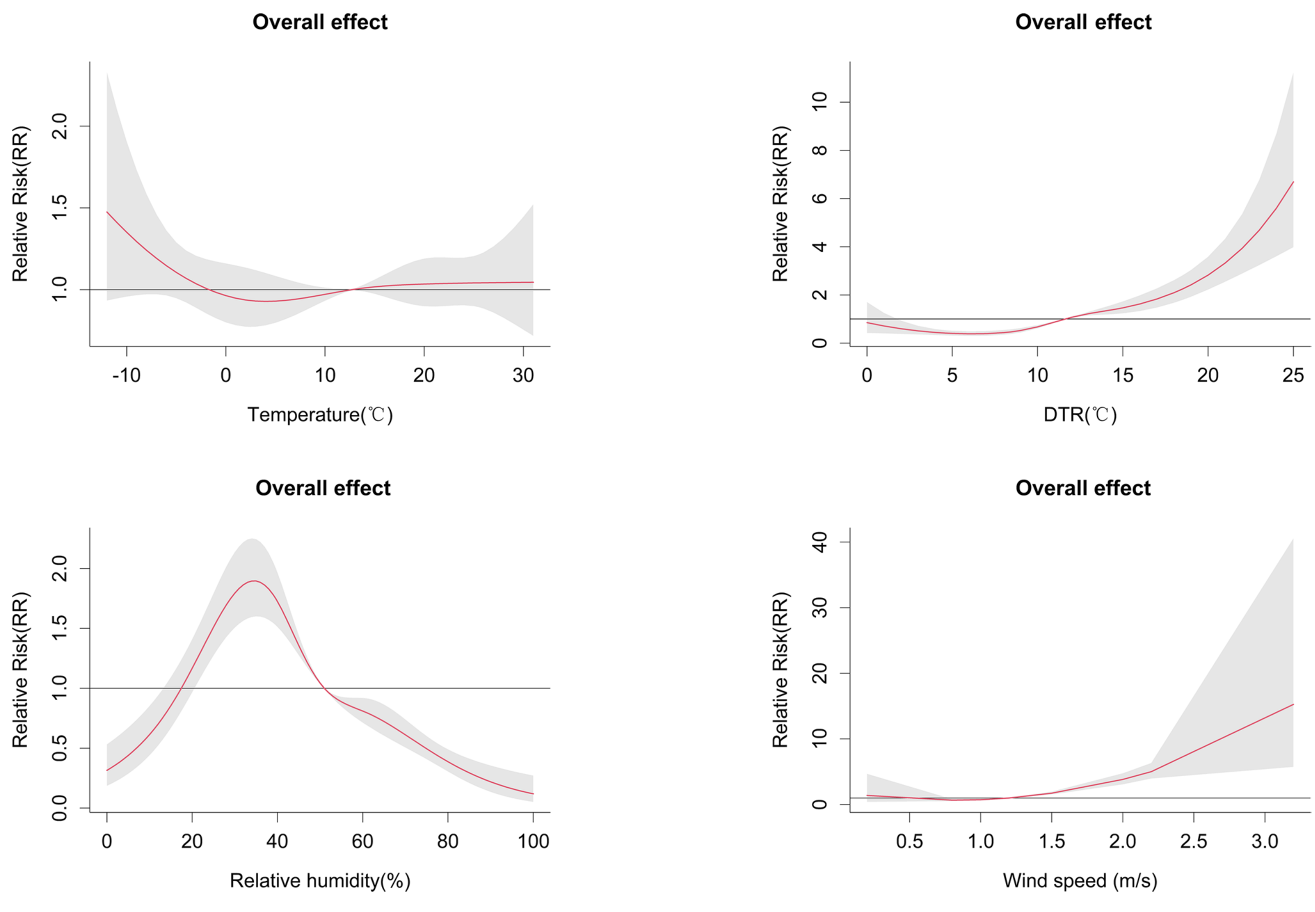

Fig. 4 The estimated overall effects of daily mean temperature, diurnal temperature range, relative humidity, and wind speed over 21 days. The red lines represent mean relative risks and the grey regions represent 95% CIs

DTR, extremely low RH, and extremely high WS increased the risk of outpatient visits for childhood AD. At lag 0–21, the effects of extremely high DTR and extremely high WS were profound, with maximum cumulative risks of 2.248 (95% CI 1.798, 2.811) and 3.834 (95% CI 3.086, 4.759) at lag 0–21, respectively.

Interaction analysis

Three-dimensional surface plots (Fig. S1) were used to reflect the interaction effects between childhood AD cases and meteorological factors. We can observe that the interaction between low temperature and RH was

Table 3 The relative risks of extremely meteorological factors on daily outpatient visits for childhood AD

Variables	Single-day lag				Cumulative-day lag			
	0	7	14	21	0–7	0–9	0–14	0–21
Cold effect	0.925 (0.902, 0.949)	0.976 (0.967, 0.986)	1.030 (1.022, 1.039)	1.087 (1.061, 1.114)	0.666 (0.579, 0.766)	0.650 (0.558, 0.757)	0.699 (0.605, 0.808)	1.069 (0.983, 1.162)
Hot effect	1.076 (1.053, 1.100)	1.026 (1.017, 1.035)	0.978 (0.971, 0.986)	0.933 (0.914, 0.953)	1.484 (1.317, 1.673)	1.531 (1.343, 1.744)	1.468 (1.294, 1.666)	1.042 (0.955, 1.136)
Low DTR effect	0.942 (0.921, 0.963)	0.955 (0.942, 0.968)	0.968 (0.956, 0.980)	0.982 (0.962, 1.001)	0.655 (0.569, 0.753)	0.601 (0.510, 0.707)	0.501 (0.409, 0.614)	0.422 (0.328, 0.542)
High DTR effect	1.024 (1.003, 1.045)	1.033 (1.021, 1.046)	1.042 (1.030, 1.054)	1.051 (1.031, 1.071)	1.253 (1.104, 1.423)	1.342 (1.159, 1.554)	1.629 (1.359, 1.951)	2.248 (1.798, 2.811)
Low RH effect	1.000 (0.984, 1.016)	1.015 (1.006, 1.024)	1.030 (1.021, 1.039)	1.046 (1.029, 1.062)	1.063 (0.964, 1.172)	1.103 (0.986, 1.233)	1.253 (1.092, 1.437)	1.637 (1.380, 1.943)
High RH effect	0.908 (0.891, 0.925)	0.947 (0.937, 0.957)	0.987 (0.976, 0.997)	1.028 (1.009, 1.048)	0.547 (0.490, 0.611)	0.499 (0.440, 0.566)	0.440 (0.377, 0.513)	0.473 (0.389, 0.576)
Weak WS effect	0.945 (0.924, 0.966)	0.969 (0.958, 0.981)	0.994 (0.983, 1.005)	1.020 (0.998, 1.042)	0.703 (0.615, 0.803)	0.667 (0.573, 0.777)	0.625 (0.523, 0.747)	0.665 (0.540, 0.818)
Strong WS effect	1.079 (1.057, 1.101)	1.068 (1.056, 1.081)	1.058 (1.046, 1.068)	1.047 (1.027, 1.068)	1.764 (1.555, 2.001)	2.005 (1.734, 2.317)	2.692 (2.256, 3.212)	3.832 (3.086, 4.759)

significant; however, no obvious pattern existed between WS and the interaction of temperature and RH.

Subgroup analysis

Figure S2 showed the lag effects of extreme meteorological factors on different gender and age subgroups. It indicated that extremely high and low temperatures increased the risk of outpatient visits for childhood AD. Extremely cold effect appeared on lag 11 and lasted for ten days. Extremely hot effect occurred on the current day and reached the maximum RR value of 1.076 (95% CI 1.035, 1.118), then lasted for 9 days. Extremely low DTR had a protective effect on the total and all subgroups. Extremely high DTR showed significant effects on the total and the remaining subgroups except the subgroup children aged 4–6 years. Effects of extremely high DTR emerged on the exposure day and lasted for the whole lag period. Extremely high RH was a protective factor, but extremely low RH could increase the risk of the total and all subgroups. Effects of extremely low RH occurred on lag 5 and reached a maximum at lag 21. Extremely high WS was associated with an increased risk of outpatient visits for childhood AD during the entire lag period, with a maximum RR of 1.079 (95% CI 1.051, 1.101) at lag 0. Extremely low WS seemed to appear a protective effect on childhood AD. Figure 5 presented cumulative effects of extremely meteorological factors on different subgroups at lag 0–21. As can be seen, effects of extreme temperatures showed little gender differences. Extremely low and extremely high temperatures had the most pronounced effects on children aged 7–14 years. The RR values were 2.178 (95% CI 1.715, 2.766) and 1.787 (95% CI 1.410, 2.266), respectively. Effects of extremely high DTR were greater for boys and children aged 0–3 years. The RR values were 2.448 (95% CI 1.818, 2.766) and 2.472 (95% CI 1.885, 3.295), respectively. Boys and children aged 0–3 years were more sensitive to extremely low RH and extremely high WS.

Sensitivity analysis

In sensitivity analyses, estimates showed little difference when *dfs* (3, 4, 5, and 6) for meteorological factors and (5, 6, 7, and 8) for time changed. Similar results were obtained when we changed the maximum lag days from 18 to 21, and the Q-AIC values of different models changed little (Fig. S3–S6). All results confirmed that the model was robust.

Discussion

The present study quantitatively evaluated the association between the number of outpatient visits for childhood AD and meteorological factors in Lanzhou during 2015–2019. This study showed that extremely high or low temperature, extremely high DTR, extremely low RH, and extremely high WS increased the risk of outpatient visits for childhood AD. Extremely high DTR and extremely high WS had greater influences on outpatient visits for childhood AD. Furthermore, the combination of low temperature and low RH can increase the risk of childhood AD.

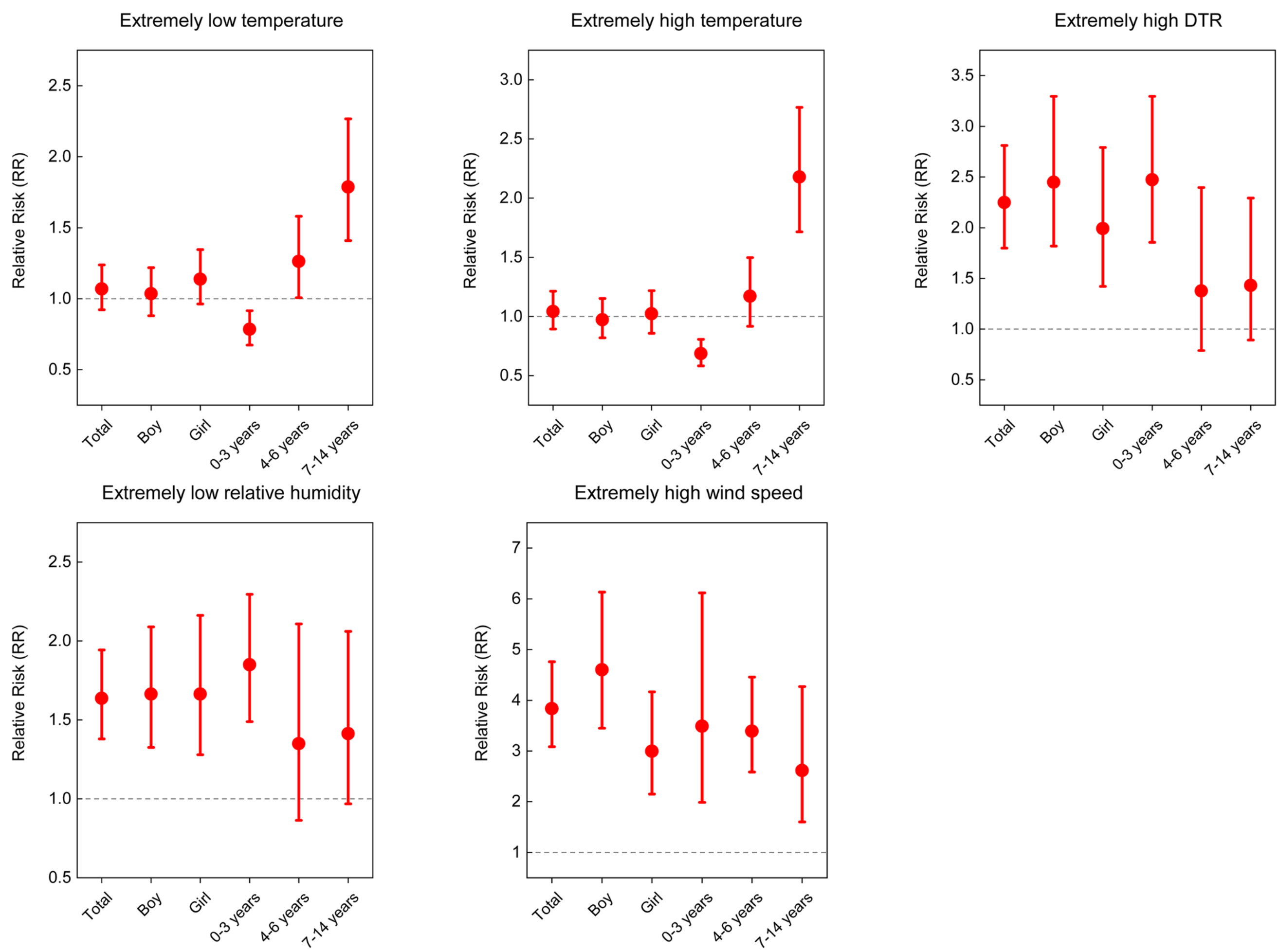

Fig. 5 The cumulative effects of extremely meteorological variables on different subgroups at lag 0–21. Y axis: RR and 95% CI

Our study found that both extremely high and low temperatures increased the number of outpatient visits for childhood AD. This finding was similar to most other studies. Some studies have shown that high temperature was an aggravating factor for childhood AD (Silverberg et al. 2013; Patella et al. 2020). There were also some studies indicated that low temperature increased the risk of clinical visits for childhood AD (Suárez-Varela et al. 2008; Hu et al. 2022). Several possible underlying mechanisms could explain this scenario. Murota & Katayama (Murota and Katayama 2016) claimed that thermal stimulation can cause dermal nerve fibers to release substance P and histamine to resulting in itching. A study on AD mouse models showed that the itching was aggravated in a warm environment (Seo et al. 2020), high temperatures activate the transient receptor potential vanilloid (TRPV) channel to generate pruritus symptoms (Andersen et al. 2017). Low temperature may cause impaired skin barrier function (Engebretsen et al. 2016). Halkier-Sørensen et al. (Halkier-Sørensen et al. 1995) used the hairless mouse model to demonstrate that cold exposure is not conducive to the recovery of the skin barrier. Liu et al. (Liu et al. 2018) demonstrated that cold stimulation can induce the release of inflammatory factors such as IL-4, IL-13, and TNF-α and cause inflammatory response. LaVoy et al. (LaVoy et al. 2011) claimed that immune imbalance exists in patients with AD, and immune imbalance plays a pivotal role in the development of AD; low temperature may cause immune imbalance triggering the occurrence and development of AD.

High DTR increased outpatient visits for childhood AD in this study, which is consistent with previous studies (Kim et al. 2017; Hu et al. 2022). A panel study in Korea showed that higher DTR was associated with more severe symptoms of childhood AD when DTR exceeded 14 °C (Kim et al. 2017). Another study in Shanghai showed that the number of outpatient visits for childhood AD increased at high DTR (Hu et al. 2022). One possible explanation is that changes in skin temperature increased pruritus intensity, any drops in skin temperature could cause histamine-induced itch, and an increase in skin temperature activated the thermosensitive channel, which also induced itch (Lewis et al. 2019). For extreme temperatures and high DTR, our results are in line with those being reported. The main reason for the similar results may be that extreme temperatures and high DTR are more likely to cause changes in the immune status and skin barrier.

In terms of humidity, existing research results showed inconsistency. One retrospective study suggested that high humidity was a risk factor for deterioration of AD (Onunu et al. 2007). Another study conducted in Spain suggested that humidity was positively associated with the incidence of childhood AD (Suárez-Varela et al. 2008). Studies carried out in Shanghai and Korea indicated that high humidity alleviates symptoms of pediatric AD, and the number of clinical visits for pediatric AD decreased under high humidity (Kim et al. 2017; Hu et al. 2020), which is similar to our results. The results of other clinical studies do not support these claims might as a result of different etiologic profiles. Some AD patients are colonized by *Staphylococcus aureus*. A high humidity environment is more favorable for the growth of *Staphylococcus aureus*. If patients with bacterial dysbiosis accounted for a higher proportion of total patients, high humidity may show harmful effects. Otherwise, if patients with skin barrier disruption accounted for a higher proportion of total patients, high humidity may show protective effects. Filaggrin (FLG) is a major skin barrier protein; low humidity environment can lead to FLG deamination and degradation (Cau et al. 2017). Thus, skin barrier function is disrupted under low humidity conditions. Furthermore, a human trial suggested the water content of skin decreased significantly in a low humidity environment (Cravello and Ferri 2008); low humidity can alter skin structure and lead to skin roughness increase (Eberlein-König et al. 1996).

The Influence of WS, our result contradicts the two previous studies (Li et al. 2018; Hu et al. 2020). We found that high WS increased the risk for childhood AD in this study. A study in Sichuan showed that no significant association was observed between AD outpatient visits and WS (Li et al. 2018). However, a recent study showed low WS was associated with an increased risk of clinical visits for childhood AD (Hu et al. 2020). A study conducted in Swiss showed that high WS helped to skin thermal transport and therefore attenuated pruritus of AD patients (Vocks et al. 2001). This disparity may be attributed to the different geographical locations (Hu et al. 2022). The maximum average WS differs by study location. The maximum values in Lanzhou, Shanghai, and Chengdu were 3.13 m/s, 6.1 m/s, and 41 m/s, respectively (Li et al. 2018; Hu et al. 2020). High WS in Lanzhou may not have any impact on the willingness of patients to attend the clinic. High WS at other two places were too high, which makes the patients may be reluctant to attend the clinic under such weather conditions. Less information is available regarding specific mechanisms. In a case–control study, Jung et al. (Jung et al. 2020) showed that exposure to wind mode leads to a decline in filaggrin degradation products (FDPS) of skin and a rise in skin PH for childhood AD patients compared with the wind-free mode of air conditioning. Thus, exposure to the wind mode aggravates AD. In addition, high wind speed leads to a reduced water content of the skin, as a result, the skin becomes rough and dry, aggravating AD symptoms (Singh et al. 2013).

Our findings indicate that the number of childhood AD outpatient visits significantly increased under low temperature combined with high humidity. To our knowledge, there is no study has evaluated such effects. Studies in Norway and Denmark suggest that AD with a higher incidence in winter (Hamann et al. 2018; Mohn et al. 2018). Their findings partly agree with our results because they shared similar cold and wet conditions, though, there is a need for further research in this area. For wet and cold environmental factors, it may favor the growth of bacteria and fungi. For wet and cold environmental factors, it may favor the long-term survival of bacteria and fungi. Bacteria and fungal may act as allergens to induce or aggravate AD.

Children under 14 years were divided into three subgroups in this study. Extreme temperatures had the greatest influence on children aged 7–14 years. The specific reason remains unclear. One possible reason is that children aged 7–14 years have more outdoor activities and more opportunities to expose to extreme temperatures (Zhang et al. 2019). Children aged 0–3 years was sensitive to extremely low RH, extremely high DTR and WS. Two reasons are possible. Firstly, skin thickness in children is related to age. Due to having thinner skin (Block et al. 2015), children of age are more sensitive to any changes in an external environment. Also, the immune system of their age period is immature and still developing (Ma et al. 2021), which makes them poor fighters in an adverse environment. Regarding the effect of extremely temperatures, effect from gender differences was not apparent. Boys usually have more outdoor activities, which naturally increase their sensitive response to extremely high DTR, extremely low RH, and extremely high WS than girls do.

Here are strengths about our study. Firstly, it is the first attempt to quantitatively assess outpatient visits risk of childhood AD and meteorological factors in Lanzhou city. Secondly, studies regarding the impact of DTR and WS on AD are very limited. Previous studies largely focused on meteorological factors, like ambient humidity and temperature. This study evaluated the effects of DTR and wind speed, and it updated our knowledge in this field. Thirdly, we performed stratified analyses by age and gender to identify sensitive populations, and the results indicated that gender- and age-specific preventative measures are needed.

Some limitations exist in our study. First, consider the ecological design that gives us restrictions to explore the potential cofactors, like individual lifestyle, genetics, and allergen. Such limits may lead to ecological fallacy. AD is a complex disease affected by multiple factors. Besides environmental factors, childhood AD outpatient visits are also influenced by genetic factors, microbial imbalance, and immune dysregulation (Langan et al. 2020; Yang et al. 2020). However, if we clinically practice testing relevant genes, immune cells, and skin microorganisms, that will be expensive and time-consuming. It is not surprising that patients will refuse these laboratory tests. In addition, individual lifestyle habits and allergen exposures also influence the onset of AD. For example, the use of personal care products containing fragrances can lead to aggravating the level of itching, and allergen exposure can aggravate inflammation (Kantor and Silverberg 2017). All these factors may be ignored and not as part of a medical record. In theory, this may have caused an overestimate of the risk estimation. AD is mainly treated at outpatient level, but can also include inpatient admission. We neglected this aspect in our study, which may have led our model to underestimate the risk of AD.

Conclusions

In this study, associations between meteorological factors and childhood AD are nonlinear. Extremely high or low temperature, extremely high DTR, extremely low RH, and extremely high WS increased the risk of outpatient visits for childhood AD. The interaction between low temperature and RH was significant. Children aged 7–14 years were most influenced by extremely temperatures. Boys and children aged 0–3 years were most affected by extremely DTR, RH, and WS. Public health departments should strengthen publicity and education about how meteorological factors affect childhood AD and develop gender- and age-specific preventative measures.

Abbreviations *AD*: Atopic dermatitis; *SCORAD*: Scoring Severity of AD; *LQI*: Life Quality Index; *DTR*: Diurnal temperature range; *RH*: Relative humidity; *WS*: Wind speed; *DLNM*: Distributed lag non-linear model; *GAM*: Generalized additive model; *RR*: Relative risk; *CI*: Confidence interval; *PM*: Particulate matter; SO_2: Sulfur dioxide; NO_2: Nitrogen dioxide; *TRPV*: Transient receptor potential vanilloid; *FDPS*: Filaggrin degradation products

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Author contribution Chunrui Shi and Fei Wang contributed to the design. Fei Wang led in writing the paper. Hui Nie contributed to the manuscript revision. All authors read and approved the final manuscript.

Data availability The data will be available from the corresponding author on reasonable request.

Declarations

Ethics approval Because this study did not involve human subjects or samples, it was deemed negligible-risk research and was exempt from ethical review by the Ethics Committee of The First Hospital of Lanzhou University; thus, no consent was required.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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