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Special Section:
Climate change and infectious diseases

Key Points:
- Investigated the relationship between extreme meteorological variables and the risk of Hand, Foot, and Mouth Disease infection
- Quantified the effect of extreme meteorological variables using the distributed lag non-linear model
- Revealed the effects of extreme meteorological variables on Hand, Foot, and Mouth Disease infections across 13 cities in Jiangsu Province

Correspondence to:
J. Wang,
njnuwjs@njnu.edu.cn

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Author Contributions:
Formal analysis: Xu Yang, Junshu Wang
Investigation: Guoming Zhang
Visualization: Zhaoyuan Yu
Writing – review & editing: Xu Yang, Junshu Wang, Guoming Zhang, Zhaoyuan Yu

Short-Term Effects of Extreme Meteorological Factors on Hand, Foot, and Mouth Disease Infection During 2010–2017 in Jiangsu, China: A Distributed Lag Non-Linear Analysis

Xu Yang[1,2], Junshu Wang[1,2], Guoming Zhang[3], and Zhaoyuan Yu[1,2]

[1]Key Laboratory of Virtual Geographic Environment, Nanjing Normal University, Ministry of Education, Nanjing, China, [2]Jiangsu Center for Collaborative Innovation in Geographical Information Resource Development and Application, Nanjing, China, [3]Health Information Center of Jiangsu Province, Nanjing, China

Abstract Hand, Foot, and Mouth Disease (HFMD) is an infectious disease that primarily affects young children. In densely populated Jiangsu Province in China, the impact of extreme meteorological factors on HFMD is a concern. We aimed to examine the association between extreme meteorological variables and HFMD infection risk using daily HFMD infections and meteorological data from 2010 to 2017 in Jiangsu Province. We used distributed lag non-linear model (DLNM) to analyze the data, which can effectively capture the nuanced non-linear dynamics and lag effects in the relationship between HFMD and extreme meteorological factors. Comparing the 10th and 90th percentiles of meteorological variables with their respective median values, our results showed that extremely low temperatures and high humidity were significantly associated with increased HFMD infection risk. The greatest effect of extremely low temperatures was observed at a lag of 1–2 days, elevating the risk by 18 ∼ 33% (RR = 1.18 ∼ 1.33). Extremely high humidity was found to increase the risk of infection, starting at a lag of 4 days. In contrast, extremely high temperatures, low humidity, and high wind speed were associated with reduced risk of infection at lag of 0–12 days, with the range of RR values being 0.60–0.98 for extremely high temperatures, 0.69–0.89 for extremely low humidity, and 0.84–0.98 for extremely high wind speed respectively. Our findings suggest that extreme meteorological factors can significantly impact the incidence of HFMD in Jiangsu Province, and highlight the need for effective public health protection measures during the periods of extreme meteorological condition, particularly for vulnerable populations.

Plain Language Summary Meteorological factors including temperature, humidity, rainfall and wind speed, have been recognized in previous studies as significant contributors to the spread, prevalence and severity of Hand, foot, and mouth disease (HFMD) outbreaks. In Jiangsu Province, the likelihood of experiencing such outbreaks due is high due to its dense population and substantial population movements, and it is crucial to comprehend the environmental factors driving HFMD in this region. To address this need, we collected daily HFMD infection and meteorological data from 2010 to 2017 from 13 cities in Jiangsu Province, and utilized a Distributed Lag Non-linear Model (DLNM) to evaluate the influence of extreme meteorological factors on HFMD infections. Our findings revealed that extremely low temperatures and high humidity increased the risk of HFMD infection, while extremely high temperatures, low humidity, and high wind speed decreased the risk of HFMD infection. The results will contribute to enhancing public health preparedness and response strategies, thereby reducing the societal burden of HFMD in Jiangsu Province and safeguarding the overall health and well-being of the population.

1. Introduction

Hand, foot, and mouth disease (HFMD) is a highly prevalent infectious disease that primarily affects children under 5 years of age. It is caused by a variety of enteroviruses, including Enterovirus 71 (EV71) and Coxsackievirus A16 (CV-A16) (Xing et al., 2014). HFMD can result in severe symptoms, such as aseptic meningitis, brainstem encephalitis, and cerebrospinal myelitis, and in some cases, can be life-threatening. The transmission of HFMD occurs primarily through direct contact with infected individuals, as well as through latent carriers who have a high rate of occult infection. In daily life, the virus mainly spreads through several routes, including close contact, respiratory droplets, and consumption of water and food contaminated with the virus (Li et al., 2018). The prevalence of HFMD in China has posed a substantial burden, primarily due to its vast population, which includes a significant number of vulnerable children. Additionally, China is undergoing rapid development and urbanization, resulting in densely populated urban areas and frequent mobility. These factors greatly amplify the risk of HFMD transmission. In 2008, a significant outbreak of HFMD occurred in Anhui Province, resulting in 22 fatalities (Y. Y. Zhang et al., 2010). Since the disease was classified as a category C infectious disease in 2008, a total of 25,006,262 cases and 3,695 deaths nationwide have been reported as of 2022, with the majority of the cases affecting children under the age of 5 (J. Zhang, 2019). Jiangsu Province experiences four distinct seasons, with concurrent rainfall and high temperatures, particularly during the hot and humid summer months. The yearly average temperature ranges between 13.6°C and 16.1°C, with summer temperatures reaching up to 25.9°C. The combination of high temperatures and humidity in summer creates an ideal environment for the transmission of HFMD, prolonging the survival of the virus and increasing the risk of infection.

The increasing frequency and intensity of extreme weather events, exacerbated by global climate change, pose a serious threat to human well-being. According to the World Health Organization (WHO), between 2030 and 2050, climate change is projected to result in an additional 250,000 deaths annually, primarily due to malnutrition, malaria, diarrhea, and heat stress (Lugten & Hariharan, 2022). Extreme weather events have a significant impact on the transmission and spread of infectious diseases, presenting a major challenge to global public health. Climate change has led to an increase in the frequency, intensity, and duration of extreme weather events such as heat waves, droughts, floods, cyclones, and storms. These events directly and indirectly influence the dynamics of infectious diseases through various mechanisms (Anyamba et al., 2020). Elevated temperatures can expand the geographical range of disease-carrying vectors, such as mosquitoes, potentially leading to the transmission of diseases like malaria, dengue, and Zika to previously unaffected regions. Additionally, flooding can contaminate water sources with pathogens, increasing the susceptibility to waterborne diseases like cholera and dysentery (Chala & Hamde, 2021). Consequently, understanding the relationship between meteorological factors and the incidence of infectious diseases has become an important area of research in public health.

In the case of HFMD, meteorological factors such as temperature, relative humidity, precipitation and wind speed have been identified as key factors influencing the spread, prevalence and severity of HFMD outbreaks (Ling et al., 2011; Z. Liu et al., 2020; Nguyen et al., 2017; Wang et al., 2011). DLNM has been used to investigate the temporal lagged association between daily temperature and HFMD in Chengdu, China, finding that temperature plays a significant role in the incidence of the disease (Yin et al., 2016). In a study conducted in Shijiazhuang, both high and low temperatures were found to increase the risk of HFMD infection, with high temperatures having a more pronounced effect. The infectivity of the virus increases within a specific temperature range as temperature rises, and the virus remains contagious even in low-temperature environments (R. Liu et al., 2022; Rajtar et al., 2008). However, other studies have indicated that high temperatures may reduce outdoor activities among residents, leading to less contact with others and potentially reducing the risk of infection (Chen et al., 2014). A study in Wuhan revealed that temperature exhibits an approximate M-shaped relationship with HFMD, while relative humidity shows an inverted V-shaped relationship with HFMD (Hao et al., 2020). The study in Guilin indicates that extremely high wind speeds have a protective effect as they can diminish the risk of HFMD by dispersing and carrying away infectious agents present in the air or on the surfaces of objects (Yu et al., 2019). In contrast, extreme precipitation has been found to increase the incidence of HFMD among children in Hefei, China (Cheng et al., 2014). Overall, the relationship between meteorological factors and the incidence of HFMD highlights the complex interplay between climate change, extreme weather events, and infectious diseases, emphasizing the need for effective public health measures and strategies to mitigate their impact.

However, most existing studies have focused on single cities or small regions, which limits their ability to capture the large-scale effects of extreme meteorological factors on HFMD infection in the public. Additionally, due to variations in socio-economic conditions, healthcare infrastructure, and residents' lifestyle differences across regions, research findings on HFMD from other areas may not be directly applicable to Jiangsu Province. Therefore, it is necessary to investigate 13 cities in Jiangsu Province as the study area to explore the impact of extreme meteorological factors on the incidence of HFMD among residents in these cities. Furthermore, existing studies have mostly focused on the impact of temperature and relative humidity on HFMD transmission, neglecting other meteorological factors such as wind speed and precipitation. In our research, we will comprehensively consider these various meteorological factors, including temperature, relative humidity, wind speed, and precipitation, to fully understand their roles in HFMD transmission. It will be very useful to capture the true risk factors in predicting the occurrence of HFMD for determining interventions to address the effects of the disease on public health. Identifying and understanding the key factors contributing to the spread of HFMD is crucial for developing targeted interventions and preventive measures. These interventions may include early warning systems,

Figure 1. Geographic Location Map of Jiangsu Province and 13 cities.

educational campaigns, improved hygiene practices, and vaccination programs. By addressing the specific risk factors associated with HFMD, interventions can be tailored to effectively reduce the impact of the disease, protect vulnerable populations, and promote overall public health and well-being.

This study aims to find the correlation between extreme meteorological factors, including temperature, relative humidity, wind speed, precipitation, and the susceptibility to HFMD among the population of Jiangsu Province from 2010 to 2017. By analyzing the data during this period, we aim to identify high-risk periods and develop targeted interventions to mitigate the spread of HFMD under extreme meteorological conditions. By studying the impact of extreme meteorological factors on the incidence of HFMD in Jiangsu Province, we can gain valuable insights into the environmental drivers of the disease in this region. The findings will contribute to enhancing public health preparedness and response strategies, thereby reducing the societal burden of HFMD in Jiangsu Province and safeguarding the overall health and well-being of the population.

2. Materials and Methods

2.1. Study Area

This study was conducted in Jiangsu Province, located on the eastern coast of mainland China and covers a total area of 107,200 square kilometers, stretching from 116°18' to 121°57'E and 30°45' to 35°20'N (Figure 1). Geographically, Jiangsu spans from north to south and falls within the East Asian monsoon climate zone, characterized by distinct seasons and simultaneous rain and heat. The region is demarcated by the Huai River and Main Irrigation Channel of North Jiangsu, with the area north of the Huai River experiencing a warm temperate humid and semi-humid monsoon climate, and the area south of the Huai River exhibiting a subtropical humid monsoon climate. Jiangsu Province consists of 13 prefecture-level cities, including Xuzhou, Lianyungang, Suqian, Huai'an, Yancheng, Nanjing, Yangzhou, Taizhou, Zhenjiang, Nantong, Changzhou, Wuxi, and Suzhou. Jiangsu Province has resident a population of 80.29 million, and ranks as the fifth most densely populated province in China, with a population density of 749 people per square kilometer. The province has a large number of children who are susceptible to HFMD, making it an ideal region for studying the correlation between extreme meteorological factors and the susceptibility to the disease. The large population provides favorable conditions for the rapid spread of HFMD. Urban areas, schools and childcare centers within Jiangsu Province serve as potential hotspots for disease transmission. In addition, as a significant transportation hub, Jiangsu Province attracts a large influx of domestic and international travelers, which increases the risk of introducing new strains of HFMD or importing cases from other regions. The demographic data from the Jiangsu Province Statistical Yearbook (2018) was used to analyze the total population, including resident population by region, age composition, and male to female ratio.

2.2. Data Collection

The study mainly relied on four types of data, including demographic data, meteorological data, HFMD infection data, and administrative map data to investigate the correlation between extreme meteorological factors and the susceptibility to HFMD in Jiangsu Province. Demographic data was obtained from Jiangsu Province Statistical Yearbook, while the HFMD data was collected from the Universal Health Information Platform of Jiangsu Province, which provided daily records of HFMD cases for 13 cities in Jiangsu Province from 2008 to 2017. The data set utilized ICD-10 diagnostic codes for categorizing and diagnosing cases of HFMD, including information such as the region's name, date, and the number of reported cases. A total of 924,647 HFMD cases from 1st January 2010 to 31st December 2017 were selected as our research data set due to substantial missing data in 2008 and 2009. The meteorological data for the same period were collected from the European Center for Medium-Range Weather Forecasts (ECMWF) fifth-generation global atmospheric reanalysis (ERA5). This data set consisted of variables such as mean temperature, dew point temperature, v-component of wind (the northward component of the wind), u-component of wind (the eastward component of the 10 m wind), precipitation and other related parameters with a grid with resolution of $0.25 \times 0.25°$. By weighting and averaging various meteorological indicators on a daily basis, the values of each grid point were combined to calculate the average within the grid, allowing the aggregation of grid data to the city level. Relative humidity was obtained through the calculation of temperature and dew point temperature. Wind speed was derived by summing the squares of the v-component of wind and the u-component of wind and then taking the square root. The administrative zone map data was obtained from the Yangtze River Delta Science Data Center, National Earth System Science Data Sharing platform.

2.3. Model Analysis

According to existing studies, it has been observed that meteorological factors have a non-linear impact on human health and exhibit lag effects (Hu et al., 2018; Y. Zhang et al., 2017). The occurrence of HFMD on a daily basis is considered a low probability event and follows characteristics of a Poisson distribution. In addition, to address the issue of overdispersion, a Quasi-Poisson model is adopted as the link function for fitting the model (Gasparrini, 2014; Xu et al., 2019). The DLNM is a flexible non-linear model that can account for lag effects and non-linear associations between meteorological factors and the occurrence of HFMD. We used the generalized linear model combined with the Distributed Lag Non-linear Model (DLNM) to analyze the impact of extreme weather factors on the occurrence of HFMD in Jiangsu Province. The DLNM model takes into account long-term trends, weekly effects, and holidays and other factors and other factors that may affect the occurrence of HFMD. The DLNM basic expression is as follows:

$$\log[E(Y_t)] = \alpha + cb(X_i) + ns(Time, df) + Dow_t + Holiday_t$$

Where t denotes the observation date, Y_t represents the number of HFMD cases on day t, α represents the intercept; the cross-basis matrix, cb, represents the relationship between HFMD cases and various meteorological factors, such as mean temperature, relative humidity, wind speed, and precipitation. The term (X_i) represents these meteorological factors, while ns denotes the natural cubic spline functions used to capture complex relationships. The time component includes seasonal and long-term trends to see if the experimental results are cyclical. Additionally, the variables Dow_t and $Holiday_t$ represent the day of the week and public holidays respectively. In

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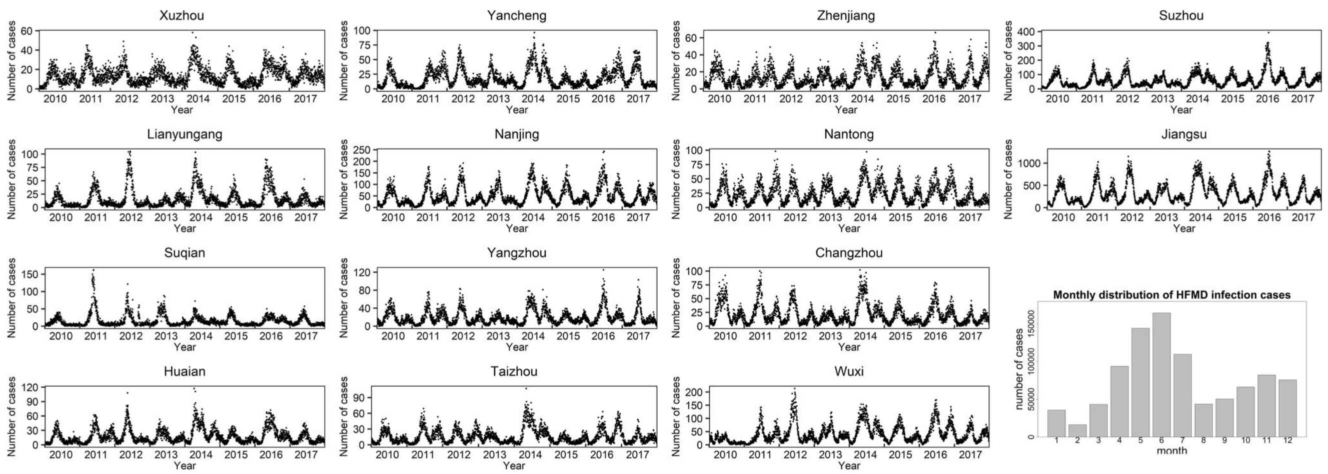

Figure 2. Temporal distribution of HFMD infection cases from 2010 to 2017 in 13 cities and in Jiangsu Province, and the monthly distribution of HFMD infection cases in Jiangsu Province.

the variable Holidayt, holiday settings are represented as 1, while weekdays are represented as 0. As for the variable Dowt, Monday is represented as 1, Tuesday as 2, and so on. The effects of extreme meteorological factors on HFMD infection were expressed as the relative risk (RR), calculated by the following formula:

$$RR = W^{p}\hat{\eta}$$

$$\text{SE} = \sqrt{diag\left(W^{p}\,V(\hat{\eta})\,W^{pT}\right)}$$

$$95\%CI = \left(e^{(RR-1.96*SE)}, e^{(RR+1.96*SE)}\right)$$

$\hat{\eta}$ is the vector of estimated coefficients obtained from the model fitted, which includes the matrix of cross-basis functions W; W^{p} is the matrix of cross-basis functions at lag p. SE is the standard error of RR; $V(\hat{\eta})$ is the variance–covariance matrix of the estimated coefficients ($\hat{\eta}$); W^{pT} is the transpose of the matrix of cross-basis functions at lag p; $\sqrt{diag(\ldots)}$ denotes taking the square root of the diagonal elements of the matrix within.

Each variable's degrees of freedom (df) were determined using the Akaike Information Criterion for Quasi-Poisson's (Q-AIC). The degrees of freedom (df) for the time component were set to seven. Moreover, considering the incubation period of HFMD and previous studies, a lag of 12 days with a relatively low Q-AIC value was chosen to investigate any potential lagged associations (Y. Liu et al., 2021; Luan et al., 2021; Yu et al., 2019). In this analysis, meteorological factors were classified as extreme weather if they exceeded 90% or fell below 10%. Effects were expressed as relative risk (RR) by comparing the 10th and 90th percentiles of meteorological variables with their respective medians. This was done to illustrate the impact of extreme weather factors on HFMD infection. It's worth noting that, since the 10th percentile of precipitation was 0 mm, only the impact of extremely high precipitation (90th percentile) on HFMD infection was studied. The “dlnm” package in R (version:4.2.2) was utilized for data processing and statistical analysis. The DLNM model was constructed using this package, and a two-sided p-value < 0.05 was set as the level of statistical significance.

3. Results

3.1. Descriptive Analysis

During the period from 2010 to 2017, a total of 924,647 cases of HFMD were reported in Jiangsu Province. On average, there were 316 cases reported daily. The male-to-female ratio of reported cases was 1.53:1, with the majority of cases (97.7%) occurring in children under the age of five. Among the 13 cities in Jiangsu Province, Suzhou had the highest number of reported cases, while Zhenjiang had the lowest.

Table 1 shows the statistics data for meteorological factors in 13 cities of Jiangsu Province from 2010 to 2017. During the study period, the median ranges for temperature, relative humidity, wind speed, and precipitation in the 13 cities were 16.18 ~ 18.09°C, 67.68 ~ 74.50%, 2.32 ~ 2.99 m/s, and 0.01 ~ 0.19 mm, respectively. The 90th percentile ranges for temperature, relative humidity, wind speed, and precipitation were 27.05 ~ 29.07°C, 85.51 ~ 88.63%, 3.77 ~ 4.87 m/s, and 5.99 ~ 11.74 mm, respectively. The 10th percentile ranges for temperature, relative humidity, and wind speed were 1.31 ~ 4.53°C, 44.95 ~ 56.61%, and 1.02 ~ 1.30 m/s, respectively.

Figure 2 presents the temporal distribution of HFMD infection cases in the 13 cities and the overall distribution in Jiangsu Province from 2010 to 2017. Additionally, it also shows the monthly distribution of HFMD infection cases in Jiangsu Province. It can be observed that HFMD cases exhibit distinct pattern of peaks and troughs, and the highest concentration occurs between May and July. This observation highlights the seasonal clustering of HFMD outbreaks in the region.

3.2. Distributed Lagged Effects of Extreme Meteorological Variables on HFMD Infection

Figure 3 illustrates the distributed lag effects of extreme meteorological variables at different lag days (0–12 days) on the risk of HFMD infection. The results reveal distinct patterns for various meteorological factors. For 13 cities, extremely low temperatures exhibit a lower risk of HFMD infection on the same day, peaking on the second or third day. The risk of infection increases by 18%–33% (RR = 1.18 ~ 1.33) across 13 cities, gradually declining thereafter. Conversely, extremely high temperatures exhibit an opposite effect, reaching their peak on the same day and rapidly decreasing thereafter, eventually stabilizing. The impact of extremely low humidity shows a “U” shape, with the risk of HFMD infection decreasing from a 2-day lag and reaching its lowest point after 6 days of lagging. On the other hand, the effect of extremely high humidity is not evident during the first 3 days, but the risk of HFMD infection starts to increase around the fourth day. On the first day of extremely low wind speeds, there is a higher risk of HFMD infection, which subsequently decreases. However, the aggravating effect on HFMD infection is only significant in Xuzhou, Lianyungang, Yangzhou, and Taizhou. In other regions, the impact of extremely low wind speeds is not significant. Conversely, on the first day of extremely high wind speeds, the risk of HFMD infection is initially extremely low but increases thereafter. Overall, extremely high wind speeds reduce the risk of HFMD infection. As for precipitation, except for Suqian, where there is a higher risk of HFMD infection due to extremely high precipitation lasting for 9 days, the impact of high precipitation on HFMD is not significant in other regions. Additionally, the lowest risk of infection occurs on the 12th day.

The results of our analysis suggest that the impact of extreme meteorological variables on the risk of HFMD infection varies depending on the variable and the time delay involved. Extremely low temperatures reduce the risk of HFMD infection on the same day, while extremely high temperatures increase the risk. The impact of extremely low humidity on HFMD infection risk shows a “U” shape, and the effect of extremely high humidity has a lag, often starting on the fourth day. Extremely low wind speed exacerbates the risk of HFMD infection in some cities, while extremely high wind speed reduces the risk. The impact of extremely high precipitation on HFMD is not significant. These findings highlight the complex relationship between extreme meteorological variables and the risk of HFMD infection, emphasizing the importance of considering different lag periods and regional variations in mitigating and managing HFMD outbreaks.

3.3. Cumulative Effects of Extreme Meteorological Variables on HFMD Infection

Table 2 shows the cumulative effects of various meteorological factors, including extreme temperatures, relative humidity, wind speed, and precipitation on HFMD infection in 13 cities of Jiangsu Province. The findings indicate that the highest RR value was associated with extremely high humidity in Suzhou during a lag period of 0–12 days (RR = 1.42, 95%CI: 1.29–1.55). In contrast, the lowest RR value was observed for extremely high temperatures in Changzhou during the same lag period (RR = 0.60, 95%CI: 0.52–0.70). The findings suggest that extremely low humidity and high wind speed can reduce the risk of HFMD infection in all the 13 cities. However, extremely high temperature was found to increase the infection risk in Xuzhou and decrease it in the other 12 regions. Additionally, extremely high precipitation reduced the risk of infection in areas outside Huai'an. The impact of extremely high humidity was found to elevate the infection risk in all areas except Taizhou. The effects of extremely low temperature and wind speed on the risk of HFMD infection varied across each city. In summary, extreme humidity exhibited the most significant impact on the risk of HFMD infection. Extremely low humidity reduced the risk and high humidity exacerbated the risk.

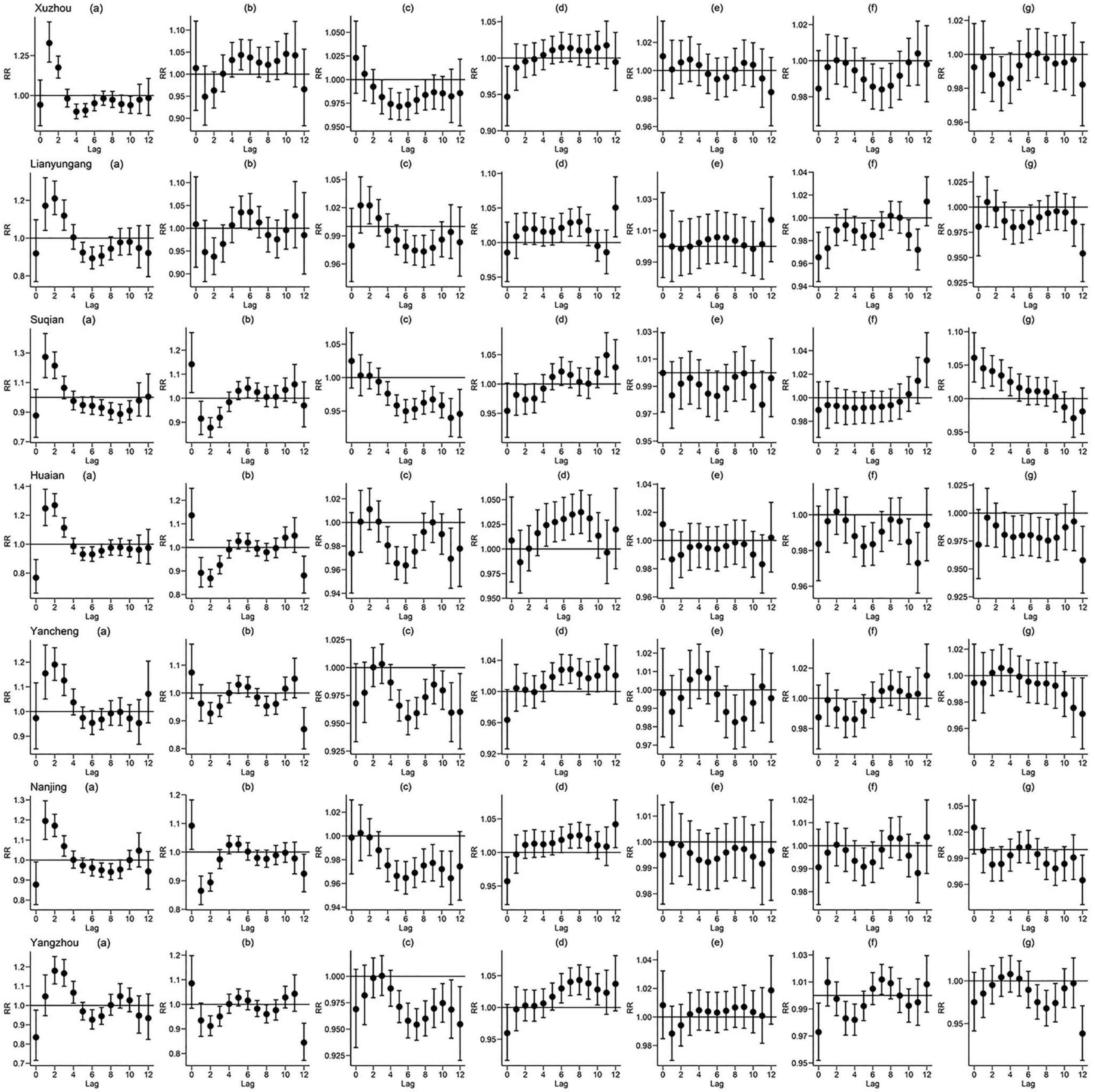

Figure 3. The distributed lagged effects of extreme meteorological variables on HFMD infection at various lag days. (a) extremely low temperature; (b) extremely high temperature; (c) extremely low humidity; (d) extremely high humidity; (e) extremely low wind speed; (f) extremely high wind speed; (g) extremely high precipitation.

The results reveal that extremely low temperatures and high humidity increase the risk of HFMD infection to a certain extent in Jiangsu Province. The impact of extremely low temperatures on the increased risk of HFMD infection starts on the first day after the occurrence of extremely low temperatures. In Xuzhou, the impact persists until the second day, while in Lianyungang, Suqian, Huai'an, and Nanjing, it extends until the third day. In other cities, the impact continues until the fourth day. On the other hand, extremely high humidity exacerbates the risk of HFMD infection, with the effects typically manifesting 1–2 days later and lasting for a duration of 9–12 days. Conversely, extremely high temperatures, low humidity and high wind speed play a role in reducing the risk of

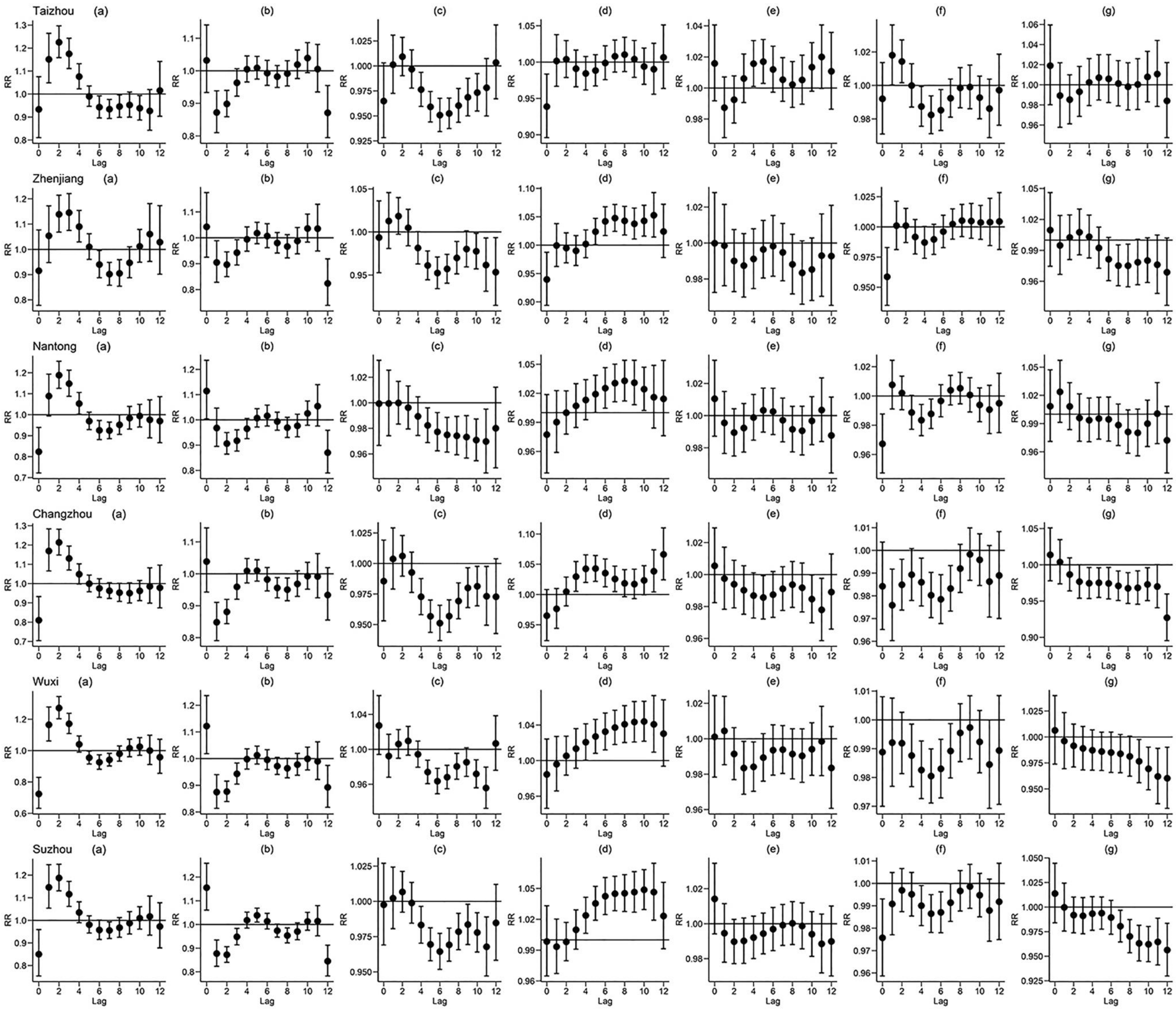

Figure 3. (Continued)

infection. Over the lag period of 0–12 days, extremely high temperatures decreased the risk of infection by 2%–40% in 12 cities, excluding Xuzhou. Changzhou had the lowest cumulative infection risk (RR = 0.60, 95% CI: 0.52–0.70). Extremely low humidity decreased the risk of HFMD infection by 11%–31%. Suqian experienced the most significant protective effect of extremely low humidity (RR = 0.69, 95% CI:0.63–0.76). Extremely high wind speeds reduced the risk of infection by 2%–16%, with Changzhou having the lowest infection risk under such conditions (RR = 0.84, 95% CI:0.78–0.90).

4. Discussion

The study utilized DLNM to investigate the impacts of extreme weather conditions, such as temperature, relative humidity, wind speed, and precipitation on the incidence of HFMD among residents in Jiangsu Province. At 1–2 days lag, the impact of temperature is most significant, with extremely low temperatures greatly increasing the risk of HFMD infection, while extremely high temperatures have the opposite effect, significantly reducing the risk of HFMD. Extremely low humidity shows a protective effect with a lag of 6 days. The impact of extremely high humidity begins to manifest after a lag of 3 days, with the risk of HFMD infection increasing daily. It can be

Table 1
The Statistics for Meteorological Factors in 13 Cities of Jiangsu Province From 2010 to 2017

	Temperature (°C)			Relative humidity (%)			Wind speed (m/s)			Precipitation (mm)	
City	Median	10th	90th	Median	10th	90th	Median	10th	90th	Median	90th
Xuzhou	16.55	1.31	27.62	67.68	44.95	85.51	2.32	1.09	3.77	0.01	5.99
Lianyungang	16.18	1.33	27.05	70.72	46.92	86.49	2.34	1.02	3.91	0.01	6.31
Suqian	16.53	1.54	27.57	71.52	49.82	86.78	2.37	1.11	3.90	0.01	6.68
Huai'an	16.57	2.00	27.57	71.22	50.30	87.00	2.48	1.14	4.02	0.03	7.86
Yancheng	16.51	2.36	27.30	71.76	50.07	87.14	2.55	1.16	4.20	0.05	9.05
Nanjing	17.51	3.61	28.34	73.03	53.95	88.63	2.54	1.19	4.13	0.11	11.02
Yangzhou	17.12	3.22	27.93	72.65	53.11	88.51	2.54	1.21	4.11	0.08	10.88
Taizhou	17.09	3.03	27.86	71.97	51.78	87.97	2.54	1.20	4.09	0.06	10.82
Zhenjiang	17.23	3.36	28.10	73.22	54.01	88.57	2.54	1.18	4.11	0.08	11.29
Nantong	17.52	3.87	28.39	74.50	56.41	88.56	2.73	1.27	4.46	0.12	10.47
Changzhou	17.73	3.85	28.75	73.52	55.24	88.50	2.59	1.19	4.24	0.11	10.51
Wuxi	17.83	4.19	28.92	73.60	55.78	88.05	2.99	1.30	4.87	0.16	11.28
Suzhou	18.09	4.53	29.07	74.09	56.61	88.14	2.91	1.28	4.81	0.19	11.74

Note. "10th" represents the 10th percentile of a meteorological variablele, "median" represents the median of the meteorological variable, and "90th" represents the 90th percentile of the meteorological variable.

observed that there is a pronounced lag in the influence of extreme meteorological factors on HFMD infection, with the risk of HFMD changing significantly several days after the occurrence of extreme weather. This may be due to HFMD has an incubation period, and infected individuals only show noticeable symptoms after a certain period. Additionally, extreme weather may affect the human immune system, making the body more susceptible to viral infections. This influence may take some time to manifest in the immune system, resulting in a lag in the risk of infection.

Table 2
The Cumulative Relative Risk of HFMD Infection Associated With Extreme Meteorological Variables at Lag 0–12 Days During 2010–2017 in Jiangsu

	Cumulative relative risk and 95% CI						
City	Temperature (10th vs. 50th)	Temperature (90th vs. 50th)	Relative humidity (10th vs. 50th)	Relative humidity (90th vs. 50th)	Wind speed (10th vs. 50th)	Wind speed (90th vs. 50th)	Precipitation (90th vs. 50th)
Xuzhou	16.55	1.31	27.62	67.68	44.95	85.51	2.32
Lianyungang	16.18	1.33	27.05	70.72	46.92	86.49	2.34
Suqian	16.53	1.54	27.57	71.52	49.82	86.78	2.37
Huai'an	16.57	2.00	27.57	71.22	50.30	87.00	2.48
Yancheng	16.51	2.36	27.30	71.76	50.07	87.14	2.55
Nanjing	17.51	3.61	28.34	73.03	53.95	88.63	2.54
Yangzhou	17.12	3.22	27.93	72.65	53.11	88.51	2.54
Taizhou	17.09	3.03	27.86	71.97	51.78	87.97	2.54
Zhenjiang	17.23	3.36	28.10	73.22	54.01	88.57	2.54
Nantong	17.52	3.87	28.39	74.50	56.41	88.56	2.73
Changzhou	17.73	3.85	28.75	73.52	55.24	88.50	2.59 1
Wuxi	17.83	4.19	28.92	73.60	55.78	88.05	2.99
Suzhou	18.09	4.53	29.07	74.09	56.61	88.14	2.91

Note. "10th" represents the 10th percentile of a meteorological variable, "median" represents the median of the meteorological variable, and "90th" represents the 90th percentile of the meteorological variable.

On the first day of extreme temperatures, there is a contrasting effect on the risk of HFMD infection, where extremely low temperatures decreased the risk, while extremely high temperatures have the opposite effect. This disparity may be attributed to the different transmission capabilities of the virus at different temperatures. The virus is more likely to replicate and spread under high-temperature conditions, increasing the risk of HFMD infection. However, the impact of temperature on the risk of HFMD infection reverses in the following days. Extremely low temperatures showed the greatest effect at 1–2 days lag, elevating the risk by 18 ∼ 33% (RR = 1.18 ∼ 1.33) across 13 cities. Extremely low temperatures can weaken the body's immune function and reduce the ability to resist viral invasion, thereby increasing the risk of infection. Conversely, over the lag period of 0–12 days, extremely high temperatures decreased the risk of HFMD infection by 2%–40%. The reduced risk of infection in extremely high temperatures may be attributed to residents engaging in fewer outdoor activities and reducing interpersonal contact (Suminski et al., 2008).

In this study, extreme relative humidity emerged as a key factor influencing the transmission of HFMD. Extremely high humidity exacerbates the risk of HFMD infection, with the effects typically manifesting 1–2 days after exposure and lasting for a duration of 9–12 days. On the other hand, extremely low humidity decreases the risk of HFMD infection by 11%–31%. The reasons for the impact of extreme humidity on HFMD transmission are complex and multifaceted. First, pathogens associated with HFMD undergo rapid development under extremely high humidity conditions, exhibiting increased their survival and transmission capabilities (Bo et al., 2020; Luo et al., 2020). Secondly, children, who are often affected by HFMD, possess immature immune systems, making them more vulnerable to infection under conditions of high humidity. In extremely high humidity conditions, reduced sweating and slower metabolic rate may increase the likelihood of viral invasion into the body, consequently raising the risk of HFMD infection (Yang et al., 2015). Finally, airborne droplets carrying the virus remain suspended in the air for longer durations, thereby increasing the risk of human exposure to the virus.

The results of this study indicate that extremely high wind speeds reduce the risk of infection by 2%–16%, consistent with previous findings by Pham et al. (2015) in Vietnam and Wu et al. (2017) in Hunan. This may be attributed to the fact that extremely high wind speeds often reduce the time people spend outdoors and decrease the frequency of interpersonal contact, thereby limiting opportunities for viral transmission. Additionally, extremely high wind speeds have the effect of dispersing and diluting the concentration of HFMD viruses in the air, thereby reducing the probability of airborne transmission. In contrast to previous related research (Cheng et al., 2014; Q. Zhang et al., 2019), this study also found that extreme precipitation reduced the risk of HFMD. The potential reason for this divergence may be the higher level of urbanization and the more advanced urban water management system in the study area, Jiangsu Province. This mitigated the occurrence of water pollution under conditions of extreme precipitation, thereby minimizing the risk of virus transmission through contaminated water. Additionally, people tend to reduce their outdoor activities during rainy weather, which decreases the probability of mutual transmission among individuals.

However, it is important to acknowledge the limitations of this study. Firstly, the lack of gender and age classification in our HFMD infection data prevents us from analyzing the impact of extreme weather factors on HFMD infections in different demographic groups. Secondly, due to the relatively uniform climatic conditions across different regions in Jiangsu Province, the impact of regional differences on HFMD infections is not significant. We also did not consider the effects of the combined effects of different meteorological factors on HFMD infections, in addition to other types of factors (e.g., the level of economic development, the construction of healthcare facilities, and the living habits of the population) that could have an impact on the results of the experiment. In the future, it is essential to consider and incorporate more relevant factors for in-depth research in different regions.

5. Conclusions

In this study, we have found that extreme meteorological factors have a significant impact on the incidence of HFMD. Extremely low temperatures and high humidity elevate the risk of HFMD infections, whereas extremely high temperatures, low humidity, and high wind speeds reduce the risk of HFMD infection. Other extreme meteorological factors, however, did not have a uniform impact on HFMD infections in the 13 cities of Jiangsu Province, which may be due to different levels of socio-economic development, medical care, and governmental public health policies among the cities. Compared to previous studies that focused on individual cities or small regions, this study broadened its scope to include all 13 cities in Jiangsu Province. It provides a macro perspective and quantifies the impact of extreme weather factors on the incidence of HFMD, making the results more representative and reflecting the widespread impact of extreme meteorological factors on public health. In addition, previous studies have mainly focused on the impact of temperature on the risk of HFMD infection, this study enriches the meteorological driving factors of the disease by exploring the role of other climatic conditions such as relative humidity, wind speed, and precipitation. It deepens our understanding of the influence of extreme weather on the risk of HFMD infection. Furthermore, our analysis is based on daily data, which provides more accurate results compared to studies conducted on a weekly or monthly time scale.

Jiangsu province, as one of the densely populated provinces in China, exhibits high levels of urbanization and social development. As a crucial transportation hub, it experiences frequent population movements and has a large number of children who are susceptible to HFMD infection. This poses significant risks for the transmission of HFMD. Investigating the environmental drivers of HFMD infections in this region holds paramount importance for infectious disease prevention and urban development. Considering the limited research on the factors influencing HFMD infections in Jiangsu Province, this study fills a critical gap. The research findings can guide health authorities in formulating more targeted policies for HFMD prevention and control. Simultaneously, it can enhance public awareness of HFMD susceptibility, fostering self-protection consciousness to reduce disease transmission and elevate public health standards.

Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

Data Availability Statement

The HFMD data were collected from the Universal Health Information Platform of Jiangsu Province. The meteorological data for the same period were collected from the European Centre for Medium-Range Weather Forecasts (ECMWF) fifth-generation global atmospheric reanalysis (ERA5) (Hersbach et al., 2023). The administrative zone map data were obtained from the Yangtze River Delta Science Data Center, National Earth System Science Data Sharing Infrastructure, National Science & Technology Infrastructure of China (Yangtze River Delta Science Data Center, 2002).

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