Spatial-temporal mapping of hand, foot and mouth disease in relation to climate factors in Xinjiang, China from 2008 to 2016

ling xie (1428375964@qq.com)
Xinjiang University https://orcid.org/0000-0002-1033-0420
Ruifang Huang
Xinjiang Uygur Autonomous region center for disease control and prevention
Hongwei Wang
Xinjiang University
Zhengqing Xiao
Beijing University of Posts and Telecommunications

Research article

Keywords: HFMD, air temperature, precipitation, spatial temporal analysis, Xinjiang Uygur Autonomous Region.

Posted Date: May 13th, 2020

DOI: https://doi.org/10.21203/rs.2.17027/v2

Abstract

[Objectives]: The study mainly aims to depict the epidemiological characteristics of hand, foot and mouth disease (HFMD) in Xinjiang, China and evaluate the effects of meteorological factors on the incidence of HFMD through spatiotemporal analysis. This study provides substantial evidence for HFMD control and prevention.

[Methods]: With the data from the national surveillance data of HFMD and meteorological parameters in the study area from 2008 to 2016. We first employed GeoDetector Model to examine the effects of meteorological factors on HFMD incidence in Xinjiang, China and to test the spatial-temporal heterogeneity of HFMD risk, and then the spatial autocorrelation was applied to examine the temporal-spatial pattern of HFMD.

[Results]: From 2008 to 2016, the HFMD distribution showed a distinct seasonal pattern and HFMD cases typically occurred between May and July, peaking in June, in Xinjiang. The relative humidity, precipitation, air pressure and temperature had more influence than other risk factors on HFMD incidence with explanatory powers of 0.30, 0.29, 0.29 and 021($p<0.000$), respectively. The interactive effect of any two risk factors would enhance the risk of HFMD and there was a nonlinear enhancement between any two risk factors interactive effect. The spatial relative risks in Northern Xinjiang were higher than in Southern Xinjiang. Global spatial autocorrelation analysis indicated the spatial dependency on the incidence of HFMD in 2008, 2010, 2012, 2014 and 2015. The spatial dependency was the negative spatial autocorrelation in 2009. The incidence of HFMD in Xinjiang presented a random distribution pattern in 2011 and 2016.

[Conclusion]: Our findings show that the risk of HFMD in Xinjiang showed significant spatiotemporal heterogeneity. The monthly average relative humidity, monthly average precipitation, monthly average air pressure and monthly average temperature factors might have stronger effects on the HFMD incidence in Xinjiang, China, compared with other factors. The distribution of HFMD in Xinjiang is different from other temperate continental climate zones due to the large difference in climate and latitude between Southern and Northern Xinjiang and their arid and semi-arid geographical environment. These associations draw attention to climate-related health issues and will help in establishing accurate spatiotemporal prevention of HFMD in Xinjiang, China.

Background

Hand, foot and mouth disease (HFMD) is an infectious disease related to various enteroviruses that mostly affect children below 5 years old [1]. Its pathogens are typically coxsackieviruses (coxsackievirus A16 (CVA16)) and enteroviruses (enterovirus 71 (EV71)) [2-5]. Its clinical manifestations mainly include mouth ulcers, fever, and vesicles on the hands, feet, and mouth[6]. Most HFMD patients can fully recover since HFMD is a self-limited disease, but some patients may develop severe life-threatening complications and even death[3]. HFMD is transmitted through direct contact with feces, respiratory droplets, and blister fluid of infective patients or the contaminated environment[5].

In recent years, HFMD outbreaks have been reported frequently in Asian countries such as Vietnam, Thailand, Singapore, Malaysia and China [7], causing widespread public health concerns. In 2014, China had an unprecedented number of large-scale outbreaks of HFMD, with the cumulative number of cases reaching 2,778,861[8]. In May 2008, HFMD was added to Category C of notifiable diseases for disease surveillance in China[9]. Thus, HFMD is increasingly widely concerned.

At present, several studies have extensively explored the correlation between HFMD and meteorological factors such as relative humidity [1,10-11], precipitation [11] and temperature [11-12]. The occurrence of HFMD showed apparent different characteristics in countries or regions with distinct climate conditions [13]. In Vietnam[14], HFMD increased 7% (RR:1.07; 95%CI: 1.052–1.088) and 3.1% (RR: 1.031, 95%CI: 1.024–1.039) for 1 °C increase in monthly temperature above 26 °C and 1% increase in monthly humidity above 76%.Whereas HFMD decreased 3.1% associated with a 1mm increase in monthly cumulative rainfalls. In South Korea[15], at an average temperature below 18°C, the HFMD rate increased by 10.3% for every 1°C rise in average temperature (95% CI: 8.4, 12.3%). We also saw a 6.6% increase in HFMD rate (95% CI: 3.6, 9.7%) with every 1% increase in relative humidity under 65%, with a 1.5% decrease in HFMD rate observed (95% CI: 0.4, 2.7%) with each 1% humidity increase above 65%. Annual HFMD incidence of counties was positively associated with the average annual temperature (RR: 1.171, 95% CI: 1.0435 – 1.3134) in Sichuan, China [16]. The climatic types of arid and semi-arid regions in Northwest China are obviously different from the above research areas. The basic quantitative study on meteorological factors and HFMD in Xinjiang is to explore the determinants of meteorological driving factors of HFMD.

To our knowledge, previous studies adopted different methods from different perspectives to explore the relationship between HFMD incidence and meteorological factors. In summary, it can be divided into four categories: Establish a mathematical model to predict the incidence of HFMD, for example, seasonal auto-regressive integrated moving average (SARIMA) models[3], SIR model[17]. The risk model of HFMD was estimated by the variation of meteorological factors: time-series Poisson regression models[5]. Meteorological factor changes and time lag model of HFMD: the generalized additive model [18], the negative binomial multivariable regression model [19], the distributed lag non-linear model[20]. Determinants of the drivers of HFMD: spatial panel data models [21], GeoDetector models [13]. In order to quantify the determinant powers of driving factors of HFMD in Xinjiang, the Geographical detector is the most suitable model. It is a set of statistical methods for detecting spatial differentiation and good at revealing the driving forces behind it.

Most of the previous studies concentrated in areas with high HFMD incidence, which are often characterized by high population density. The climate in high incidence areas is often temperate to humid, such as Hong Kong[19], Guangdong[12], Guangxi[22] and Jiangsu [23] provinces. However, the spatiotemporal heterogeneity of HFMD under the influence of meteorological factors in Northwest China was seldom studied. In general, the study on HFMD in arid and semi-arid regions is still limited; more research on such climates would potentially make the mechanism of HFMD transmission clearer under different climate conditions.

It was reported that the HFMD ranks the first in the number of class C infectious diseases in Xinjiang, 2019[24], and the number of cases increases gradually each year, but the relationship between HFMD and meteorological factors in Xinjiang has not been proved. In this study, we analyze the spatial-temporal heterogeneity of HFMD and its relationship with meteorological factors in Xinjiang at the county scale, which is located in Northwest China having a semi-arid climate to shed more light on the mechanisms of HFMD transmission in those regions. The objectives of this study are: Firstly, to understand the spatiotemporal distribution characteristics of HFMD from 2008 to 2016 in Xinjiang, China. Secondly, to quantify the determinant powers of meteorological driving factors of HFMD. Thirdly, to detect the relative risk of HFMD under different meteorological elements by risk detectors. Fourthly, to explore the global spatial autocorrelation and of the incidence of HFMD among different years in Xinjiang from 2008 to 2016. This study aims to provide countermeasures and suggestions for further public health interventions.

Methods

2.1 Study area

Xinjiang Uygur Autonomous Region is the largest provincial administrative region in China. The area is $166*10^4$ km^2 and the population was 2486.76 million in 2018. Xinjiang locates in the geographical center of Eurasia (34.3°–49.5°N, 73.5°–96.3°E) and neighbors Russia, Kazakhstan, Kyrgyzstan, Tajikistan, Pakistan, Mongolia, India and Afghan from north to south. The mountains border Xinjiang on three sides and the Tianshan Mountains cuts across Northern Xinjiang. As a typical arid and semi-arid area, Xinjiang has a temperate continental climate. The annual mean temperature ranges from 9°C to 12°C and the annual precipitations in Northern and Southern Xinjiang are respectively 210mm and less than 100mm, displaying an uneven spatial distribution pattern. The Tianshan Mountains have a higher level of precipitation, whereas Southern Xinjiang suffers severe water stress. The dominant wind throughout the year is northwest wind (Wei et al. 2019). Fig. 1 shows the geographical location of Xinjiang.

2.2 Data sources

Data on HFMD were provided by the Chinese Centre for Disease Control and Prevention (CDC). HFMD incidence in China was reported to the CDC via the China Information System for Disease Control and Prevention, the national disease report system, by the physicians treating the disease and public health personnel. The data of daily HFMD cases in Xinjiang from January 1, 2008 to December 31, 2016 were from China Information System for Disease Control and Prevention. The collected patient's data include gender, age, living address, types of patients, the onset date of symptom and confirmation time of symptom. Meteorological data were obtained from the China Meteorological Data Sharing Service System [25], including daily average temperature (TEM), daily average relative humidity (RHU), daily average barometric pressure (PRS), daily cumulative precipitation (PRE), daily average evaporation (EVP), daily average wind speed (WIN) and daily sunshine duration (SSD). Monthly average temperature, relative humidity, barometric pressure, precipitation, evaporation, wind speed and sunshine duration were computed or aggregated from daily weather data. The monthly county-level meteorological variables were estimated by using ordinary spatial kriging methods based on 66 meteorological surveillance stations within Xinjiang conducted by ArcGIS10.1. The 66 meteorological surveillance stations are mapped in Figure 1.

2.3 Methods

Due to technological limitations, the Methods subsection is only available as a download in the supplementary files.

Results

3.1 Descriptive analysis

In total, 56,379 HFMD cases were reported from 2008 to 2016 in Xinjiang, with a daily average of 17.2 cases and the annual average incidence was 25.27/10,000. Fig. 2 shows the monthly distributions of HFMD cases and meteorological variables in Xinjiang from 2008 to 2016. The monthly HFMD distribution showed a distinct seasonal pattern over the period and HFMD cases typically occurred between May and July, peaking in June. The annual morbidity among males was about 1.5 times higher than that of females. Children under 5 years old were at the highest risk of HFMD. Most cases (86.2%) were dispersed children who did not go to kindergarten or school. A descriptive summary of the meteorological and socioeconomic variables is shown in Table 1.

3.2.1Factor detector analysis

As shown in Table 2, the determinant power of the average relative humidity was obviously associated with the incidence of HFMD ($q = 0.30$), indicating that the average relative humidity mainly explains the spatial heterogeneity of the incidence of HFMD. Precipitation, barometric pressure, temperature and sunshine duration were also associated with the incidence of HFMD in Xinjiang, having explanatory powers q of 0.29, 0.29, 0.21 and 0.20, respectively. The study reveals that humidity, precipitation and barometric pressure were three dominant factors influencing the transmission of HFMD in the semi-arid regions.

3.2.2Interaction detector:

The study found that the interaction of any two risk factors has greater explanatory power than any single metrological factor. Compared with their individual impact, they most presented the effect of “nonlinear enhance” or “bivariate enhance”. As shown in Table 3, the q statistics of average relative humidity was 0.3, which increased to 0.5 after accounting for the interactive effect of average barometric pressure on the HFMD incidence. As 0.5 is significantly higher than 0.3 (q statistics of average relative humidity) and 0.29 (q statistics of average barometric pressure), the result indicated that relative humidity and barometric pressure has a significantly bivariate enhanced interactive associations on the incidence rate of HFMD. The explanatory power of average relative humidity increased to 0.39 after considering the interactive effect of precipitation on HFMD incidence. The coupled impact of average relative humidity (q=0.3) and average wind speed (q=0.07) played an important role in HFMD, with an explanatory power of 0.43 (Table 3). High average relative humidity and high average wind speed were associated with a high incidence of HFMD. The interaction of these risk factors could effectively explain the spatial heterogeneity of the HFMD, and the selected risk factors had a tendency of strengthening interaction.

3.2.3Risk detector analysis

Figure 6 showed the relative risk (RR) of HFMD with different meteorological factors from 2008 to 2016 in Xinjiang. Actually, the distribution of RR in space was not the same every year, and there were certain changes. Specifically, the spatial RRs in counties in Northern Xinjiang were higher than the counties in Southern Xinjiang, implying that these counties have relatively higher HFMD risk. Conversely, counties in Southern Xinjiang generally have lower RRs. The Northern Xinjiang had a higher average relative humidity, suitable temperature and precipitation level, resulting in a higher RR of HFMD. The southern regions were affected by the Taklimakan desert, high temperature, low relative humidity, precipitation and air pressure, and the risk of HFMD is relatively low. We found that the lowest RR of HFMD in Khotan, during the study period. According to the following meteorological risk factor charts, Urumqi, Tacheng Prefecture, Changji Prefecture and Ili Kazak Autonomous Prefecture are the high RR areas of HFMD in Northern Xinjiang. It may be ascribed to the higher average relative humidity and sufficient precipitation in the above areas. These areas are suitable for the growth and transmission of the HFMD virus.

We found that when the monthly average precipitation exceeded 0.94mm, the incidence of HFMD decreased. There was an inverted V-shape association between temperature and HFMD. A similar pattern was observed for the association between the monthly average relative humidity and HFMD, the monthly average sunshine duration and HFMD, the monthly average wind speed and HFMD. When the monthly average temperature was 8.81 °C, the HFMD reached a peak. The incidence of HFMD increased along with the monthly average relative humidity and the monthly average sunshine duration, reached a peak when the monthly average relative humidity was at 61.1% and the monthly average sunshine duration was at 7.78 hours and then decreased afterwards, respectively. Risk detector value presented a logarithmic relationship between the monthly average evaporation and HFMD, an exponential relationship between the monthly mean air pressure and HFMD. With regards to the association between the monthly average wind speed and HFMD, the incidence of HFMD was the highest when the monthly average wind speed is less than 2.52m/s.

3.3 Spatial autocorrelation of HFMD incidence

Moran's I value was calculated by global spatial autocorrelation analysis. Moran scatter diagram (Fig.5) shows the results of the global spatial autocorrelation test, demonstrating a highly statistically significant spatial autocorrelation difference of HFMD at the state level in Xinjiang each year from 2008 to 2016. The Moran's I values (Table 4) ranged from -0.135 to 0.202 ($P < 0.05$), indicating the spatial dependency on the occurrence of HFMD in 2008, 2010, 2012, 2014 and 2015. Moran's I value in 2009 was -0.135, indicating that there was a negative spatial autocorrelation of HFMD in Xinjiang. Moran's I values in 2011 and 2016 were respectively -0.066 and -0.00018, indicating that the incidence of HFMD in Xinjiang presented a random distribution pattern. Bayingolin Mongol Autonomous Prefecture showed the high-high spatial autocorrelation of HFMD incidence, whereas Kashgar, Hotan, Aksu and Kizilsu Kirghiz Autonomous Prefecture showed the low-low spatial autocorrelation of HFMD incidence in 2008 and 2010. From 2011 to 2016, Urumqi always showed the high-high spatial autocorrelation of HFMD incidence.

Discussion

Although the correlation between climatic factors and HFMD incidence has been extensively explored[6,15], the relationships between HFMD occurrence and meteorological factors in Xinjiang where typical arid and semi-arid areas were interpreted with daily HFMD surveillance data for the first time in the study. The relationship interpretation can help the prevention and control of HFMD in this climate environment (Xinjiang and other regions in Central Asia).

Previous studies have shown that the response of HFMD incidence with respect to climate change differs. In temperate regions, HFMD outbreaks occurred in summer or early fall [5] when temperature rise and precipitation increase occurred lately. Therefore, HFMD incidence in temperate regions was different from that in tropical and subtropical regions [18,33]. Meteorological factors were positively or negatively correlated with HFMD incidence in a threshold range. For example, a study conducted in Wuhan, the capital city of Hubei province located in South China, showed that temperature ranging from 20 to 25 °C prevents HFMD infections in Wuhan [34]. Other climate conditions may also have a threshold effect. A study conducted in mainland China showed that relative humidity between 80.59 to 82.55% would lead to a higher risk of HFMD [35]. However, the monthly average relative humidity between 51.52 to 61.10% and monthly average precipitation ranging from 4.42 to 8.81 °C would lead to a higher risk of HFMD in Xinjiang. Enteroviruses are resilient to the gastrointestinal environment, but their stability in the ambient environment depends on humidity and temperature [36]. Moreover, moderate monthly cumulative precipitation partly maintained the HFMD epidemic in the study period. Precipitation might affect water sanitation and facilitate disease transmission due to the increased contact rate of droplets, which mainly carries the HFMD virus [20]. High precipitation promoted the attachment of the HFMD virus and increased the exposure probability [1]. In a study in Japan, with the increase in temperature, Herpangina & HFMD incidence increased. In a warm environment, the transmission of the HFMD virus was enhanced, but cold and hot climate limited the transmission [23,6,5]. In this study, the relationship between monthly average relative humidity and HFMD relative risk represents inverted V-shape, a similar pattern was observed for the association between the monthly average temperature and HFMD, the monthly average precipitation and HFMD, the monthly average sunshine duration and HFMD, the monthly average wind speed and HFMD. It indicates that there is a non-linear relationship between meteorological factors and the risk of HFMD in Xinjiang. It's worth noting that risk detector value presented a logarithmic relationship between the monthly average evaporation and HFMD, an exponential relationship between the monthly mean air pressure and HFMD. This is different from previous research results.

In order to further explore the relationship between meteorological factors and HFMD incidence, in this study, GeoDetector was adopted to explore the spatial and temporal heterogeneity and its interactive effects on the HFMD incidence in Xinjiang and spatial autocorrelation analysis was applied to examine the spatial pattern of HFMD in Xinjiang. The results demonstrated that HFMD incidence showed obvious regional differentiation, displaying a dynamic spatial-temporal distribution. The distribution of HFMD was mainly concentrated in Northern Xinjiang. The incidence of HFMD in Southern Xinjiang might be ascribed to the precipitation stress. The incidence of HFMD in Urumqi, Changji Prefecture, Tacheng Prefecture and other areas in Northern Xinjiang was obviously worthy of in-depth investigation. In 2012 and 2016, the density of HFMD exceeded 7000 cases in a single grid of the focal area. Spatially, the focal area of HFMD incidence was located in Urumqi and regional centers. These focal areas have a well-developed economy, the fast highway system, and the large heterogeneous migrant population, which increases the HFMD risk [16].

In the study, the majority of HFMD cases were children less than 5 years old. Obvious seasonal peaks occurred between May and July. The results were similar to previous studies [21,12]. However, some other studies reported a different timing of the HFMD outbreak. We found that the highest peak was in September [22] and the second highest peak was in May in Guangxi, while the peak of HFMD in Shandong was observed in July [37]. Potential reasoning was that the differences in temperature, precipitation and humidity among different regions resulted in the differences in the seasonal variation of HFMD.

The global spatial autocorrelation analysis results demonstrated that the area with the high HFMD incidence was different from the high spatial autocorrelation area of HFMD in Xinjiang. Urumqi has always shown the high spatial autocorrelation of HFMD incidence because the incidence of HFMD in Urumqi remained high over the years and the adjacent area also had a high incidence of HFMD. Multiple regions showed low spatial autocorrelation because the incidence of HFMD had inter-annual variation in several regions, with a low incidence of HFMD in adjacent areas, such as Aksu and Ili Kazak Autonomous Prefecture.

Due to the large area, complex climatic states, and population density in various parts of Xinjiang, it is difficult to grasp the influences of meteorological factors on HFMD transmission [36]. In the study, we quantitatively proved that HFMD cases were correlated with meteorological factors in Xinjiang Uygur Autonomous Region, Northwest China. The findings provide the basis for HFMD prevention.

The present study has some limitations. First, there were only 66 meteorological surveillance stations in Xinjiang; ordinary kriging interpolation results might not cover all variations of the meteorological variables at the county level. However, this was more accurate than using the same meteorological data on all counties in each city. Second, we estimated spatiotemporal variations in HFMD at the scale of counties and months; we did not include the factors at an individual and pathogenic levels, such as personal hygiene, educational background, incomes of the children's parents, living conditions, and composition of major pathogens. Further studies should consider the potential impacts of these factors. Third, the result should be examined via different investigation techniques, such as geographically weighted regression (GWR). With GWR, spatially changing relationships between variables can be explored [38,39]. GWR will be applied in our study on the relationship between HFMD incidence and potential impact factors.

Conclusions

The findings of our study indicated that the spatial-temporal distribution of HFMD risk in Xinjiang, China, was non-homogeneous. The higher relative risk counties mainly gathered in Northern Xinjiang. Meteorological factors, such as monthly average relative humidity, monthly average precipitation, monthly average barometric pressure and monthly average temperature, might be the driving factors of HFMD in Xinjiang. The high relative risk areas and high spatial correlation areas of HFMD all point to the Northern Xinjiang. Therefore, in the high incidence of HFMD season and relative risk areas, we can reduce environmental exposure and contact transmission to decrease the spread of HFMD.

Declarations

Acknowledgements

We would like to extend our thanks to Xinjiang Center for Disease Control and Prevention, China for sharing data on Xinjiang hand, foot and mouth disease not referring to patient's privacy information.

Authors' Contributions

HW W were in charge of the conception, design of study and revised the manuscript. L X wrote the manuscript and revised it critically for intellectual content. ZQ X undertook in data analyzed and helped to revise the manuscript. RF H provided HFMD data. All authors read and approved the final manuscript.

Availability of data and materials

The meteorological data used in the study were available from National Meteorological Information Center (http://data.cma.cn/). The vector map data was applied from Resource and Environment Data Cloud(http://www.resdc.cn/) with official permission. The datasets of HFMD generated during and analyzed during the current study are not publicly available due to confidentiality requirements but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Consent to publish

Not applicable.

Ethics approval and consent to participate

This study was reviewed and approved by the Ethics Committee of the Xinjiang Center for Disease Control and Prevention, China. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees. We aggregated the HFMD for each day at the county level (excluding the Xinjiang production and construction corps), not referring to patient’s privacy information.

Funding

This work was supported by the National Natural Science Fund of China (Grant No 4186010245), Additionally, the funding body in the study had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Abbreviations

HFMD: Hand, foot and mouth disease; CA16: coxsackievirus A16; EV71: enterovirus 71; RR: relative risk; CDC: Chinese Centre for Disease Control and Prevention; TEM: temperature; RHU: relative humidity; PRS: pressure, PRE: precipitation; EVP: evaporation; WIN: wind speed; SSD: sunshine duration; EN: Enhance (nonlinear); EB: Enhance (bivariate); ID: Independent; E: Enhance.

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Tables

Table 1 Descriptive statistics of meteorological variables

Covariates	Minimum	25% Percentile	Median	75% Percentile	Maximum
Average relative humidity (%)	32.35	41.64	51.52	61.11	70.69
Average temperature (∘C)	0.01	4.42	8.82	13.23	17.63
Cumulative precipitation (mm)	0.02	0.49	0.95	1.42	1.91
Sunshine duration (hour)	5.72	6.8	7.89	8.97	10.05
Average wind speed (m/s)	0.84	1.68	2.53	3.37	4.21
Average barometric pressure(hPa)	699.42	777.75	856.08	934.41	1012.74
Average evaporation (mm)	0.16	1.92	3.68	5.44	7.2

Table 2 Explanatory power of each impact factor on the incidence of HFMD in Xinjiang

	EVP	PRE	PRS	RHU	SSD	TEM	WIN
q statistic	0.11	0.29	0.29	0.30	0.20	0.21	0.07
p value	0.000	0.000	0.000	0.000	0.005	0.000	0.005

Table 3 The value of q for interactions between pairs of factors on the incidence of HFMD.

Covariates	EVP	PRE	PRS	RHU	SSD	TEM	WIN
EVP	0.11						
PRE	0.34EB	0.29					
PRS	0.35EB	0.37EB	0.29				
RHU	0.35EB	0.39EB	0.50EB	0.30			
SSD	0.21E	0.33EB	0.40EB	0.38EB	0.20		
TEM	0.34EN	0.33EB	0.41EB	0.37EB	0.34EB	0.21	
WIN	0.25EN	0.36ID	0.36ID	0.43EN	0.35EN	0.32EN	0.07

Note: EN: Enhance (nonlinear), EB: Enhance (bivariate), ID: Independent, E: Enhance

Table 4 Results of the spatial autocorrelation test on HFMD cases in Xinjiang from 2008 to 2016.

Years	2008	2009	2010	2011	2012	2013	2014	2015	2016
Moran’s I	0.144	-0.135	0.202	-0.066	0.120	0.056	0.134	0.146	-0.001
Z-score	1.904	-0.647	2.832	0.042	1.933	1.181	2.092	2.146	0.625
P values	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05

Figures

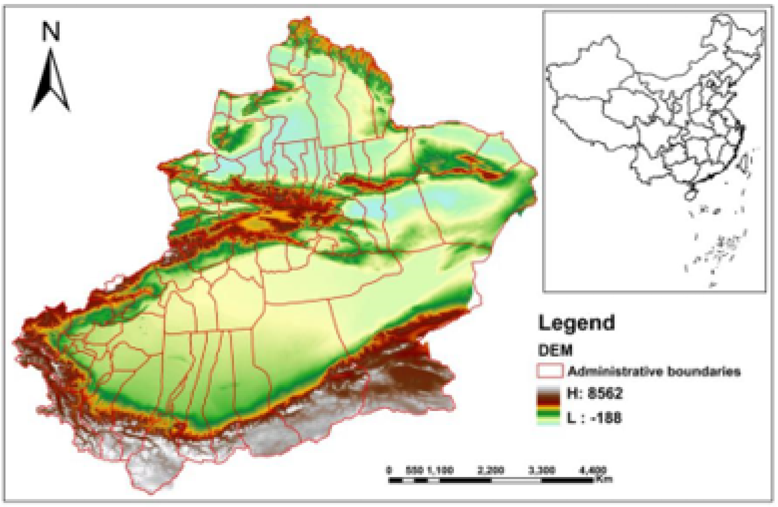

Figure 1

Geographical location of the study area in China Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

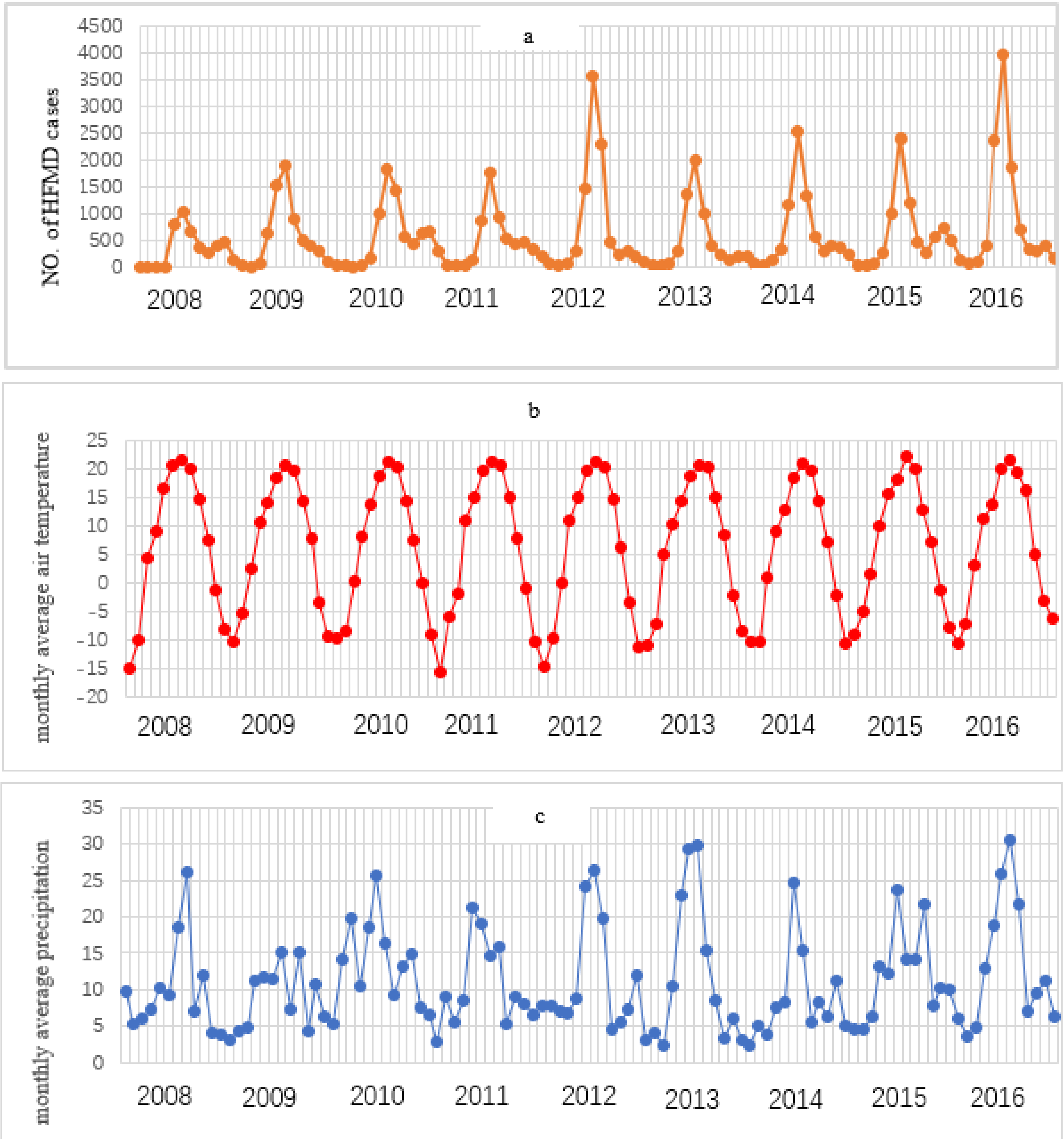

Figure 2

Time series of monthly data of HFMD cases (a), temperature (b) and precipitation (c) in Xinjiang, China from 2008 to 2016 (unit: Temperature(°C), precipitation (mm))

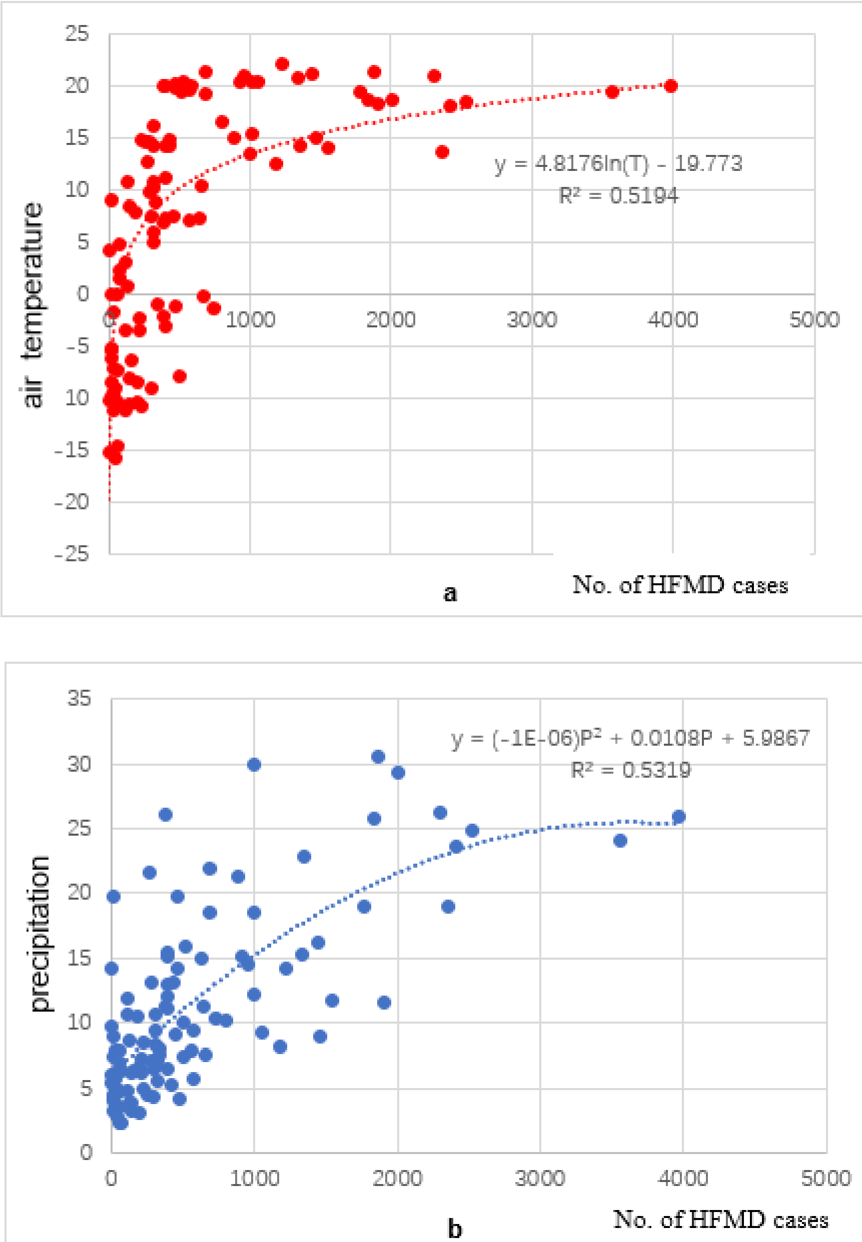

Figure 3

Fitting curve of meteorological factors (mean monthly temperature (a) and mean monthly precipitation (b)) and HFMD cases (unit: temperature (°C), precipitation (mm)).

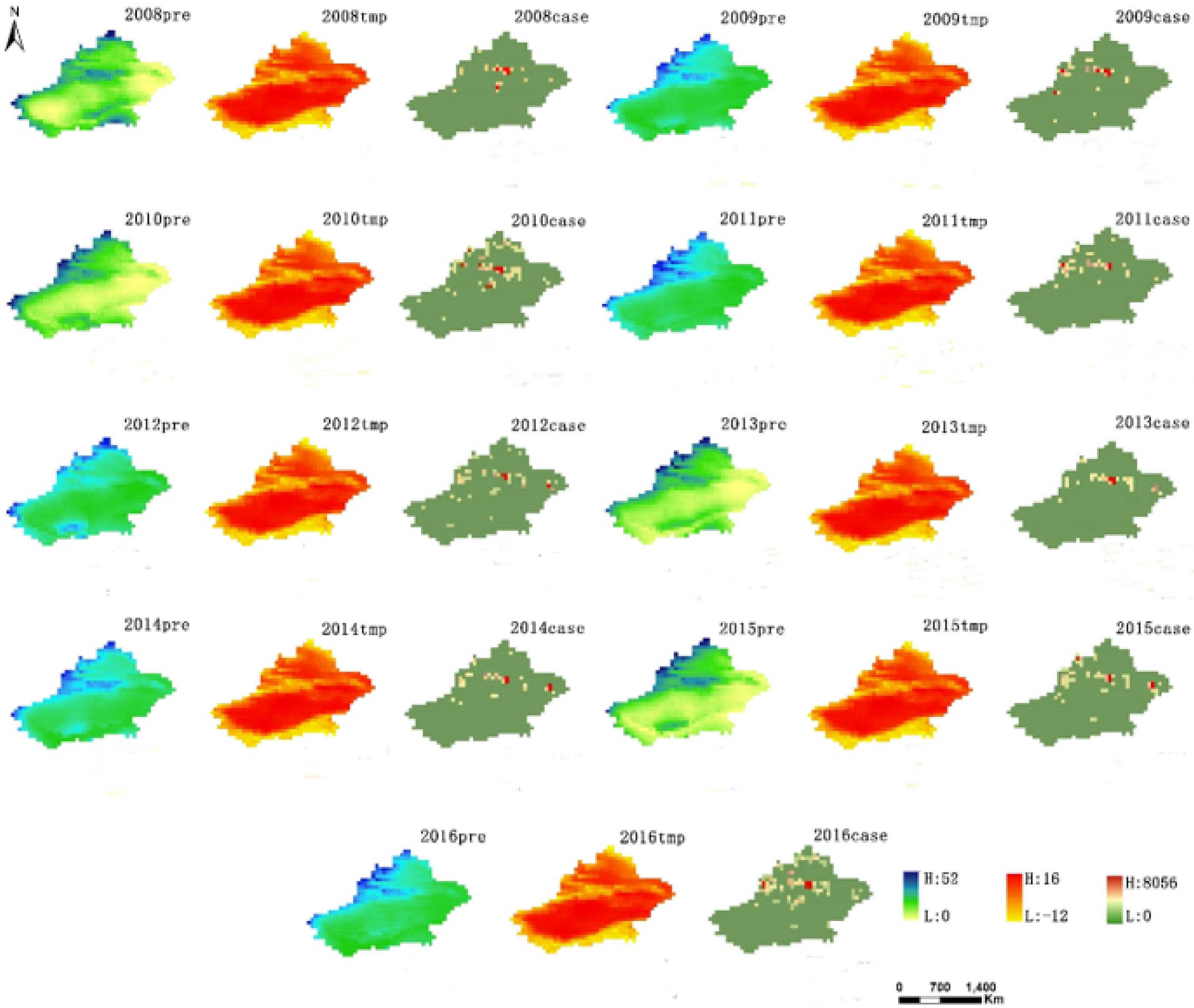

Figure 4

Raster data of mean annual temperature, precipitation and HFMD cases in the study area from 2008 to 2016.

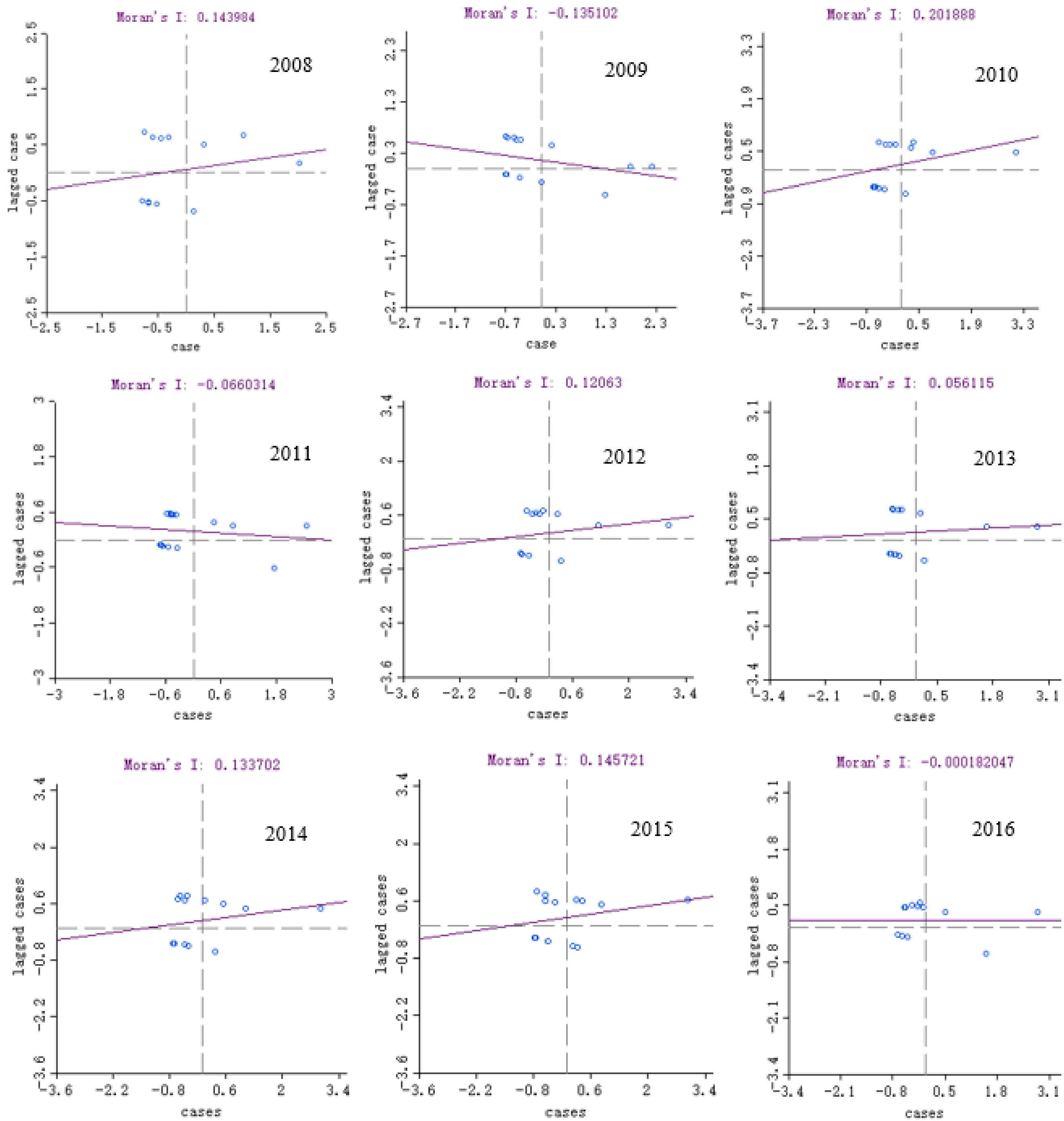

Figure 5

Moran scatter diagram of Xinjiang HFMD from 2008 to 2016.

Supplementary Files

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- methods.docx