Estimating the Influence of High Temperature on Hand, Foot and Mouth Disease Incidence in China

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Abstract

The burden of disease caused by ambient high temperature has become a public health concern, but the association between high temperature and hand, foot and mouth disease (HFMD) remain indistinct. We used Distributed Lag Non-linear Model (DLNM) to estimate the burden of disease attribute to high temperature, adjusting for long-term trend and weather confounders. Total 18167455 cases were reported in 31 Chinese provinces, the incidence of HFMD showed a gradually increasing trend from 2008 to 2017 in China. Minimum Mortality Temperature (MMT) was mainly concentrated at 17°C to 23°C in the age group less than 5 years old, 18°C to 25°C in the age group 6~10 years old and 19°C to 27°C in the age group above 10 years old. The greatest RR in age group 0~5 years old was 2.06 (95%CI: 1.85~2.30) in Heilongjiang, and the lowest RR was 1.02 (95%CI: 1.00~1.05) in Guangdong; the greatest RR in age group 6~10 years old was 2.24 (95%CI: 1.72~2.91) in Guizhou, and the lowest RR was 1.01 (95%CI: 0.97~1.12) in Tianjin; the greatest RR in the age group over 10 years old was 2.53 (95%CI: 1.66~3.87) in Heilongjiang, and the lowest RR 1.02 (95%CI: 0.71~1.46) in Henan. We found the positive association between high temperature and HFMD in China.

Introduction

Hand, foot and mouth disease (HFMD) is a common infectious disease mainly occurring in children under 5 years old. It is mainly caused by Coxsackievirus A16 (CV-A16) and Enterovirus 71 (EV71) (Saguil et al., 2019). HFMD is mainly characterized by respiratory symptoms such as fever, runny nose and herpes in hands, feet and mouth. Some severe patients will have meningitis, encephalitis, encephalomyelitis, pulmonary edema and circulatory disorders, which will leave sequelae and even lead to death (Cox et al., 2018). At present, there is no effective vaccine to prevent HFMD. Finding risk factors and improving prevention strategies are very important for children's health.

As a consequence of global climate change, extreme high temperature had a serious impact on human health. High temperature is also a common meteorological disaster, which has a certain impact on people's daily life, health and various departments of the national economy (Roye et al., 2020). As we know, high temperature will increase the death and morbidity of diseases to a certain extent, especially cardiovascular diseases, respiratory diseases and so on (Luan et al., 2017; Song et al., 2018). The standard of high temperature heat wave is mainly based on the degree of impact or harm of high temperature on human body. At present, there is no unified and clear standard of high temperature heat wave in the world. Therefore, it is of great significance to explore different heat wave standards for different populations and diseases. However, there are few studies on the impact of high temperature on infectious diseases, and we have not paid enough attention to it. In order to cope with the heat weather in the future, we should not only pay attention to the impact of high temperature on death, but also pay more attention to its impact on infectious diseases, especially in the current situation of Corona Virus Disease 2019 prevention and control is still pressing.

Current studies (Caminade et al., 2019; Dennis et al., 2018) have found that in addition to human, biological and ecological determinants, the impact of climate factors on the emergence and recurrence of infectious diseases has attracted more and more attention. These temperature changes may affect the spread of many serious infectious diseases. Understanding the link between climate change and ecological change is a decisive factor in the emergence and redistribution of diseases, which will eventually help to optimize prevention strategies. The correlation between meteorological factors and HFMD has been confirmed by relevant studies, but there is a lack of research on the temperature early warning threshold of HFMD.

China has a vast territory. From south to north, there are tropical, subtropical, warm temperate, temperate and cold temperate regions. Tibet and Qinghai belong to special plateau climate regions. From west to East, the altitude gradually decreases. The altitude of the western plateau is more than 4000 meters, that of the central basin and mountainous areas is 1000-2000 meters, and that of the eastern plain and hilly areas is less than 500 meters. We know that with the increase of altitude, the temperature will decrease. Due to different climatic zones and altitudes, the temperature varies greatly between different provinces in China. The average temperature difference between the northern and southern regions is more than 20°C, and the average temperature difference can exceed 10°C even at the same latitude. Therefore, according to the actual situation of

different regions, personalized research on temperature is of great significance to the incidence of hand, foot and mouth disease.

Based on the incidence data of HFMD and meteorological data in 31 provinces of China, this study want to evaluate the regional differences of the impact of temperature on the incidence of HFMD, explore the minimum incidence temperature HFMD, and use the minimum incidence temperature as a reference for formulating temperature early warning, which provides a basis for formulating reasonable protective measures against ambient temperature. We integrate the high temperature information with the incidence information of HFMD and put forward early warning information, which is very important to reduce the adverse impact of current and future diseases on health, especially the health protection of children.

Material And Methods

Data sources

The number of HFMD cases was collected from the National Population and Health Science Data Sharing Platform (<https://www.ncmi.cn/>). These data were obtained through the Data-center of China Public Health from May 2008 to December 2017. The age group is divided into groups under 10 years old and over 10 years old. Under 10 years old, we are divided into groups according to one year old. The study covers 31 Chinese provinces including Anhui, Beijing, Fujian, Gansu, Guangdong, Guangxi, Guizhou, Hainan, Hebei, Henan, Heilongjiang, Hubei, Hunan, Jilin, Jiangsu, Jiangxi, Liaoning, Inner Mongolia, Ningxia, Qinghai, Shandong, Shanxi, Shaanxi, Shanghai, Sichuan, Tianjin, Tibet, Xinjiang, Yunnan, Zhejiang and Chongqing.

We collected mean temperature, pressure and relative humidity for the same period, meteorological data was collected from the China Meteorological Data Sharing Service System (<http://data.cma.cn/>).

Statistical analysis

Current studies widely used distributed lag non-linear model (DLNM) to assess the effect of ambient temperature on health, the formula was illustrated as follows (Gasparrini,2014; Gasparrini et al., 2010):

$$Y_t = \alpha + NS(\text{Time}, T*7) + NS(\text{Humidity}, 3) + NS(\text{Pressure}, 3) + \gamma \text{Dow} + \eta \text{Holiday} + \beta \text{Temperature}$$

Where α was the intercept; γ , η and β represented coefficients; the model adopted natural cubic spline curve, $NS(\text{Time})$ was used to control effects of long-term trend and seasonality, $NS(\text{Humidity})$ was used to control effects of relative humidity, $NS(\text{Pressure})$ was used to control effects of pressure, and the df of them was 7, 3 and 3 respectively; Dow represented day of the week and Holiday represented public holidays, these two categorical variables in the model was used to stand for their confounding effects. Considering the cumulative effect and the lag effect, we choose the lag days at 7; df means the degrees of freedom. We chose the 10th, 75th, and 90th percentiles distribution of mean temperature as three internal knots to estimate the exposure-response relationship in the model.

Referring to previous relevant studies (Gasparrini et al., 2015), we defined high temperature as the 95th percentile of temperature higher than the mean temperature in this research. Minimum Morbidity Temperature (MMT) represented the temperature corresponding to the point with the lowest relative risk, which can be regarded as the optimal temperature. The effective range of the mean temperature was defined between the 1st percentile (P1) and the 99th percentile (P99) of the time series. The basis of MMT is the best linear unbiased prediction for cumulative exposure response associations for each province, namely the lowest percentile incidence rate between 1st and 99th percentiles.

Sensitivity analyses were presented at Supplementary **Fig. S1**. R software (version 4.1.1) was used to analyze the data, and DLNM package was applied.

Results

From 2008 to 2017, the incidence of HFMD showed a gradually increasing trend in China, with less incidence in winter and a peak in summer (Fig. 1).

Table 1 presents the summary of HFMD cases and weather conditions during the study period. A total of 18167455 cases were reported in 31 Chinese provinces. Guangdong had the largest number of cases (2910068 cases), other provinces and cities with a large number of cases included Guangxi (1907353 cases), Hunan (1255729 cases), Zhejiang (1143235 cases) and Jiangsu (1037181 cases), and Tibet had the least number of cases (10253 cases). The range of mean temperature was from 3.4°C to 25.1°C, the highest mean temperature was in Hainan and the lowest in Heilongjiang. The range of relative humidity and pressure was from 46.5–80% and 671.1Kpa to 1016.3Kpa respectively.

As shown in the **Fig. 2**, HFMD cases mainly occurred from April to July, which accounting for 58% of the total number of cases. From August to December, the incidence of HFMD was relatively stable, accounting for about 34% of the total cases. From January to March, the incidence of HFMD was the least, accounting for about 18% of the total incidence. The incidence of HFMD was the highest in June, and the lowest in February.

Fig. 3 showed that the distribution of HFMD cases in different age groups. The incidence of HFMD was mainly concentrated in the age group under 5 years old, especially in the age group of 1~2 years old, which can account for 30% of all the incidence. Other age groups with more incidence were 2~3 years old (23.1%), 3~4 years old (17.5%), 4~5 years old (9.5%) and 0~1 years old (9.5%). In the age group over 5 years old, the number of cases gradually decreased with the increase of age.

The optimum temperature of HFMD in 31 provinces was presented in **Table 2**. In the age group less than 5 years old, the lowest MMT in Qinghai was 13.4°C, Hainan had the highest MMT, which was 25.8°C. In the age group 6~10 years old, Henan had the highest MMT, which was 28.0°C, and also the lowest MMT in Qinghai was 14.0°C. In the age group above 10 years old, Chongqing had the highest MMT, which was 28.9°C, the lowest MMT was still in Qinghai, which was 14.3°C. MMT increased gradually with the increase of age. MMT was mainly concentrated at 17°C to 23°C in the age group less than 5 years old, 18°C to 25°C in the age group 6~10 years old and 19°C to 27°C in the age group above 10 years old respectively (**Supplementary Fig. S2, Fig. S3, Fig. S4**).

Table 3 showed the relative risk and 95% confidence interval of high temperature on HFMD in 31 Chinese provinces. According to the age distribution of the number of HFMD cases, we calculated the relative risk of three different age groups: 0~5 years old, 6~10 years old and over 10 years old. The greatest impact of high temperature on HFMD cases in age group 0~5 years old was 2.06 (95%CI: 1.85~2.30) in Heilongjiang, and the lowest impact was 1.02 (95%CI: 1.00~1.05) in Guangdong. The greatest relative risk in age group 6~10 years old was 2.24 (95%CI: 1.72~2.91) in Guizhou, and the minimum relative risk was 1.01 (95%CI: 0.97~1.12) in Tianjin. In the age group over 10 years old, Heilongjiang and Henan had the maximum and minimum relative risk, the RR was 2.53 (95%CI: 1.66~3.87) and 1.02 (95%CI: 0.71~1.46). The effect of high temperature on HFMD at different age groups had no obvious law, but on the whole, the effect of high temperature on northern provinces was higher than that in southern provinces to a certain extent.

Discussion

Using the time series data of HFMD incidence in 31 provinces in China from 2008 to 2017, this study confirmed the correlation between temperature and hand, foot and mouth disease incidence, which is consistent with the previous research results (Xu et al., 2020; Pearson et al., 2020). However, different from other studies, we found that there are threshold differences in the impact of temperature on the incidence of HFMD in different regions and age groups, which can be used as a reference for early warning and guide the public health protection of HFMD.

The study provided evidence for health protection on HFMD attribute to heat wave. HFMD is a high incidence infectious disease in infants. It has the characteristics of high incidence rate, difficulty in diagnosis, rapid progress (Aswathyraj et al., 2016). The first outbreak of HFMD was reported the in Canada in 1957 (Chong et al., 2015). Since then, many studies on

HFMD have been widely published all over the world. Asia has the largest outbreak of HFMD in the world, which has been reported in Japan, Singapore, India and other countries (Koh et al., 2016; Gonzalez et al., 2019; Kua et al., 2020; Rao et al., 2017; Huang et al., 2018). A study from China's infectious disease surveillance system shows that has 720092 cases of HFMD from 2008 to 2012 (Xing et al., 2014). The annual incidence rate is 2010-2012 years, the highest incidence is 12-23 months. The incidence rate of HFMD in the northern region is in May, or in September and October respectively. This also suggests that the increase of temperature is an important factor in the incidence of HFMD.

Over the past 50 years, the national average high-temperature days have decreased first and then increased. The number of high-temperature days decreased from the 1950s to the early 1980s and began to increase significantly in the early 1980s. There is a linear increasing trend in the number of high temperature days in Northwest and North China, especially in North China. In midsummer, Tianjin, Jinan, Chongqing, Fuzhou, Changsha, Nanchang, Wuhan, Nanjing and other places have high temperature and hot weather under the control of the Western Pacific subtropical high. High temperature makes the human body unable to adapt to the environment, exceeding the tolerance limit of the human body, resulting in the occurrence or aggravation of diseases and even death (Liu et al., 2015).

MMT varied in different area and population, climate, geographical factors and social economic factors. Our research results show that the optimum temperature in China is mainly concentrated at 17-27°C, there are differences in MMT among different age groups, MMT increased gradually with the increase of age. Under the action of high temperature, the thermoregulation mechanism is temporarily blocked, resulting in heat storage in the body, especially in children under the age of 10, because children have poor adaptability to high temperature and high humidity weather. The adaptability of the body to meteorological conditions is limited, especially for vulnerable children. The organs and regulatory mechanisms are not fully developed. When the temperature is higher or lower than the threshold, the thermal balance regulatory mechanism is easy to be disturbed, and the burden of physiological temperature regulation will increase, resulting in physical discomfort and disease invasion (Tyler et al., 2016).

There are also differences between different provinces. MMT in different regions shows a trend of increasing from north to South and from west to East. When making relevant health policies, it should be considered to break the concept of national unity or geographical area, and to develop the policy according to local conditions. MMT in low latitude and coastal areas is higher than that in other areas. This is mainly due to the long duration of hot summer in low latitude areas, and local residents' adaptation to high temperature is affected by physiological and behavioral adaptation. When a person lives in specific climatic conditions for a long time, he will adapt to the environment (Lee et al., 2019). In addition, there is more precipitation in these areas, which will promote the spread of infectious diseases such as HFMD to a certain extent.

The incidence of children under 5 years old accounts for nearly 90% of the total incidence, resulting in serious disease burden. Therefore, we divided the study into three age groups: under 5 years old, 6-10 years old and over 10 years old. In the three age groups, the northern provinces, such as Heilongjiang and Tianjin, high temperature had a high impact on HFMD, while the southern provinces, such as Guangzhou and Guizhou, high temperature had a low impact on HFMD. There are regional differences in the impact of high temperature on the HFMD, which may be due to the large change of temperature difference in northern regions, especially non-coastal regions, under the influence of continental climate during the change of seasons, especially the alternation of spring and summer, while the temperature difference in southern regions is relatively small under the influence of marine climate. In addition, the population in the South has high adaptability to high temperature due to the population in the north.

There have some limitations in our study. Because we can't measure individual exposure dose, we use meteorological monitoring data to evaluate the impact, which inevitably has an ecological fallacy. We only considered meteorological variables. Other major environmental risk factors of HFMD were not included, such as seasonal life in cities or suburbs, accumulated ultraviolet radiation, socio-economic conditions and air pollution. These factors should be considered or adjusted in future research.

Conclusion

In summary, there are correlations and regional differences between high temperature and HFMD. Based on the study of MMT, we can formulate personalized threshold early warning for different regions and age group, and take targeted protection strategies for the population, especially children, to reduce the disease burden of HFMD.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors' contributions

Guijie Luan and Hongyan Yao conceived and designed studies; Shaonan Liu, Weiyan Zhang, Yingjie Zhang and Liang Sun collected the data; Guijie Luan analyzed the data and wrote the paper; Long Zhai revised the methods and manuscript.

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Tables

Table 1.Descriptive data on HFMD incidence and weather in 31 Chinese province.

Province	Cases	Mean temperature (°C)							Relative humidity (%)		Pressure (Kpa)	
		Min	Median	Max	75th	95th	Mean	SD	Mean	SD	Mean	SD
Anhui	920505	-0.7	17.4	30.0	24.4	28.1	16.2	9.0	72.8	7.8	1011.1	8.4
Beijing	316632	-4.8	15.0	28.6	23.6	27.4	13.7	10.9	52.2	12.6	1012.4	8.8
Chongqing	316841	2.9	17.4	28.9	23.3	28.0	17.2	7.3	77.3	5.1	955.6	7.8
Fujian	690429	9.3	22.4	29.8	26.8	29.4	21.1	6.1	73.8	6.7	1001.3	6.1
Gansu	100403	-9.3	10.2	22.8	18.6	21.1	9.1	9.2	57.1	8.8	834.1	3.4
Guangdong	2910068	9.9	23.5	29.4	27.7	28.9	22.2	5.6	77.0	6.5	1006	5.8
Guangxi	1907353	7.4	23.3	29.4	27.4	28.6	21.7	6.0	76.5	5.1	995.9	6.2
Guizhou	331396	-0.7	16.3	23.7	20.7	22.8	14.9	6.3	80.0	5.2	862.5	3.4
Hainan	373593	15.5	26.2	30.3	28.6	29.7	25.1	3.9	79.9	3.4	1007	5.1
Hebei	690042	-7.6	13.3	26.9	22.8	26.0	11.9	11.1	58.2	11.2	992.8	7.9
Heilongjiang	128934	-22.6	5.6	23.5	17.5	22.5	3.4	15.2	67.8	8.8	987.7	6.3
Henan	814822	-1.3	17.0	29.5	25.1	28.1	15.8	9.3	65.1	10.2	1003.4	8.5
Hubei	716268	1.4	17.8	29.5	24.5	28.1	16.9	8.2	76.3	5.3	993	8
Hunan	1255729	2.1	18.7	30.9	25.1	29.4	18.1	8.0	75.8	6.6	998.4	7.9
Inner Mongolia	174363	-1.7	16.9	29.9	23.9	28.3	15.6	9.2	71.5	7.5	1014	8.3
Jiangsu	1037181	2.9	20.3	30.9	26.8	30.2	19.3	8.0	75.2	5.9	1005.4	7.5
Jiangxi	379774	-18.2	8.3	24.3	18.9	23.2	6.4	13.4	64.0	9.5	987.1	6.6
Jilin	151542	-12.2	11.4	26.1	20.7	24.6	9.6	11.8	63.0	10.6	1006	7.8
Liaoning	290171	-20.2	6.2	23.7	18.3	21.9	4.4	13.8	52.8	8.5	909.5	4.7
Ningxia	61489	-11.8	11.5	25.4	20.4	23.9	10.0	10.8	50.1	11.7	877.8	4.7
Qinghai	18065	-12.1	3.1	15.7	10.6	14.1	2.6	8.5	48.0	9.8	671.1	2.5
Shaanxi	472503	-4.5	15.0	28.0	22.9	26.1	13.6	9.4	63.4	9.4	936.7	6.3
Shandong	965136	-3.7	15.7	27.8	23.5	26.8	14.2	9.7	66.4	9.9	1009.7	8.3
Shanghai	399091	1.7	19.4	32.0	24.5	30.1	17.7	8.4	70.2	6.2	1015.7	7.9
Shanxi	271522	-8.3	12.3	26.4	21.7	24.4	11.2	10.5	54.5	12.0	929.7	5.9
Sichuan	539169	1.4	13.5	21.6	18.5	20.8	12.8	6.1	64.9	8.3	815.3	2.8
Tianjin	158361	-5.6	14.8	28.1	23.9	27.2	13.5	11.0	57.6	10.9	1016.3	8.9
Tibet	10253	-11.3	6.0	17.6	14.6	17.0	5.3	9.1	52.1	6.6	719.3	2
Xinjiang	68807	-16.1	12.9	28.0	23.8	26.2	10.5	13.0	46.5	11.7	919.7	6.7
Yunnan	553768	7.6	16.7	21.2	19.7	20.5	15.9	4.1	70.6	9.6	814.4	2.1
Zhejiang	1143235	3.5	20.2	30.0	25.2	29.6	18.4	7.7	74.6	6.0	1011.7	7.4

Table 2. The Minimum Mortality Temperature of HFMD in 31 provinces.

Province	≤5 years old	6~10 years old	≥10 years old
Anhui	20.3	22.6	24.5
Beijing	24.3	24.8	26.3
Chongqing	22.3	26.7	28.9
Fujian	22.7	23.4	26.3
Gansu	15.5	16.9	19.8
Guangdong	23.8	26.5	27.8
Guangxi	22.1	23.9	25.7
Guizhou	18.7	22.0	22.8
Hainan	25.8	27.5	28.3
Hebei	19.0	22.3	23.9
Heilongjiang	17.8	20.0	20.3
Henan	23.0	28.0	28.7
Hubei	17.3	18.5	21.8
Hunan	17.5	20.6	22.7
Inner Mongolia	22.1	22.6	22.8
Jiangsu	20.5	25.2	26.6
Jiangxi	21.7	22.9	23.2
Jilin	19.1	20.2	23.5
Liaoning	18.1	19.2	20.6
Ningxia	17.3	19.6	20.6
Qinghai	13.4	14.0	14.3
Shaanxi	18.4	20.6	20.8
Shandong	21.8	23.0	24.9
Shanghai	21.4	23.3	24.5
Shanxi	20.7	22.7	22.8
Sichuan	16.1	18.3	19.9
Tianjin	21.8	22.6	24.3
Tibet	15.1	16.2	16.8
Xinjiang	18.6	19.1	20.5
Yunnan	18.6	19.6	20.5
Zhejiang	21.3	21.9	22.3

Table 3. The relative risk and 95% Confidence interval of high temperature on HFMD in 31 Chinese provinces.

Province	≤5 years old	6~10 years old	≥10 years old
Anhui	1.05(1.02,1.09)*	1.02(0.86,1.20)	1.34(1.00,1.80)*
Beijing	1.33(1.22,1.45)*	1.56(1.16,2.02)*	1.52(0.98,2.22)
Chongqing	1.10(1.06,1.14)*	1.17(0.97,1.41)	1.43(1.05,1.94)*
Fujian	1.23(1.05,1.43)*	1.25(0.71,1.96)	1.36(0.51,2.67)
Gansu	1.45(1.43,1.48)*	1.53(1.42,1.66)*	1.55(1.36,1.77)*
Guangdong	1.02(1.00,1.05)*	1.21(1.07,1.36)*	1.16(0.93,1.43)
Guangxi	1.06(1.01,1.12)*	1.13(0.86,1.48)	1.03(0.66,1.58)
Guizhou	1.96(1.88,2.05)*	2.24(1.72,2.91)*	1.68(1.12,2.52)*
Hainan	1.25(1.18,1.33)*	1.70(1.35,2.09)*	1.86(1.26,2.62)*
Hebei	1.08(1.05,1.12)*	1.28(1.03,1.59)*	1.48(1.03,2.12)*
Heilongjiang	2.06(1.85,2.30)*	2.03(1.39,2.84)*	2.53(1.66,3.87)*
Henan	1.28(1.23,1.33)*	1.19(0.96,1.48)	1.02(0.71,1.46)
Hubei	1.07(1.04,1.10)*	1.11(0.95,1.30)	1.36(1.06,1.74)*
Hunan	1.30(1.08,1.52)*	1.81(1.26,2.49)*	1.86(0.96,3.18)
Inner Mongolia	1.26(1.23,1.30)*	1.23(1.09,1.38)*	1.73(1.38,2.19)*
Jiangsu	1.04(0.99,1.10)	1.03(0.73,1.45)	1.30(0.73,2.33)
Jiangxi	1.42(1.26,1.59)*	1.08(0.50,1.75)	1.30(0.54,2.29)
Jilin	1.88(1.75,2.01)*	1.74(1.42,2.11)*	1.75(1.25,2.43)*
Liaoning	1.48(1.23,1.77)*	1.57(0.76,2.75)	1.83(1.47,2.47)*
Ningxia	1.98(1.53,2.53)*	2.08(1.07,4.03)*	1.60(0.93,3.29)
Qinghai	1.53(1.46,1.60)*	1.85(1.54,2.19)*	1.99(1.42,2.69)*
Shaanxi	1.27(1.16,1.39)*	1.69(1.20,2.28)*	1.98(1.16,3.12)*
Shandong	1.74(1.67,1.81)*	1.74(1.42,2.12)*	2.04(1.46,2.84)*
Shanghai	1.03(0.98,1.08)	1.05(0.88,1.25)	1.11(0.82,1.49)
Shanxi	1.18(1.14,1.23)*	1.39(1.10,1.75)*	1.29(0.90,1.86)
Sichuan	1.77(1.59,1.96)*	1.73(1.21,2.36)*	1.83(1.08,2.86)*
Tianjin	1.10(0.88,1.40)*	1.01(0.97,1.12)	1.40(0.44,4.41)
Tibet	1.58(1.33,1.86)*	1.69(0.94,2.74)	1.70(0.62,2.51)
Xinjiang	1.66(1.60,1.72)*	1.81(1.54,2.13)*	1.74(1.29,2.36)*
Yunnan	1.18(1.15,1.21)*	1.23(1.08,1.39)*	1.55(1.23,1.95)*
Zhejiang	1.62(1.52,1.72)*	1.67(1.19,2.36)*	1.32(0.79,2.22)

*P<0.05

Figures

Figure 1

From 2008 to 2017, the incidence of HFMD showed a gradually increasing trend in China, with less incidence in winter and a peak in summer (Fig. 1).

Figure 2

As shown in the Fig. 2, HFMD cases mainly occurred from April to July, which accounting for 58% of the total number of cases. From August to December, the incidence of HFMD was relatively stable, accounting for about 34% of the total cases.

Figure 3

Fig. 3 showed that the distribution of HFMD cases in different age groups. The incidence of HFMD was mainly concentrated in the age group under 5 years old, especially in the age group of 1~2 years old, which can account for 30% of all the incidence.

Supplementary Files

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