Original Research

Is high relative humidity associated with childhood hand, foot, and mouth disease in rural and urban areas?

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A B S T R A C T

Objective: To examine the relationship between relative humidity and childhood hand, foot and mouth disease (HFMD) in Hefei, China, and to explore whether the effect is different between urban and rural areas.
Study design: Retrospective ecological study.
Methods: A Poisson generalized linear model combined with a distributed lag non-linear model was used to examine the relationship between relative humidity and childhood HFMD in a temperate Chinese city during 2010–2012.
Results: The effect of relative humidity on childhood HFMD increased above a humidity of 84%, with a 0.34% (95% CI: 0.23%–0.45%) increase of childhood HFMD per 1% increment of relative humidity. Notably, urban children, male children, and children aged 0–4 years appeared to be more vulnerable to the effect of relative humidity on HFMD.
Conclusions: This article study indicates that high relative humidity may trigger childhood HFMD in a temperate area, Hefei, particularly for those who are young and from urban areas.

Introduction

Hand, foot, and mouth disease (HFMD) is an emerging viral infectious disease, the main clinical symptoms of which include mouth ulcers, fever, and vesicles on the hands, feet, and mouth. The disease is caused by different enteroviruses, most of which are *enterovirus 71* (EV71) and *coxsackie* A16 (CA16).[1–3] HFMD develops frequently in children, and in 2001 and 2007, a Singaporean study showed that about 90% of the reported cases were children below ten years old.[4] Some of them may develop severe neurological disorders or even die. In recent decades, epidemics of HFMD have been reported worldwide, especially in Asian-Pacific countries.[5–7] In Malaysia, about 6000 children were infected with HFMD, and 42 died during the HFMD outbreak in 1997–1998.[6] It is noteworthy that, over one million were reported in Chinese mainland, resulting in 509 deaths in 2010.[7] However, up to

now, there is no specific treatment or vaccine available for HFMD.

Many previous studies have reported that climatic factors are associated with childhood HFMD.[8,9] For instance, a previous paper showed that precipitation was associated with childhood HFMD, with a 5.12% (95% confident interval: 2.73–7.57%) increase of childhood HFMD for an extreme precipitation event versus no precipitation.[9] Extreme rainfall might affect people's behaviour, which might further increase the incidence of childhood HFMD. But extreme rainfall events occurred infrequently and the rainfall data often are unavailable. Compared to extreme precipitation, relative humidity is not only reported by the Bureau of Meteorology every day but also easy to obtain by hygrometer. In addition, a previous laboratory-based study showed that enteroviruses are resilient to the environmental conditions of the gastrointestinal tract, and viral stability in external environmental conditions is dependent on humidity, temperature, and UV radiation.[10] Based on a prior study, humidity was associated with increased HFMD at lag days 3–10, with the highest effect at lag day eight (RR = 1.009 for 1% increase in relative humidity, 95% confident interval: 1.007–1.010).[11] So the authors speculated that relative humidity might be a critical weather condition for enteroviruses' survival, reproduction and spread, which might cause HFMD epidemic.[12] The association of relative humidity with childhood HFMD in developing cities has not been known. Meanwhile, with the acceleration of urbanization over the world, providing targeted guidance assessing climate change-related human health in urban and rural area for policymakers and medical institutions to identify the focus of optimally allocate health resources and intervention strategies is urgent.[13] Here, they aimed to quantify the effects of relative humidity on childhood HFMD in both urban and rural areas in a temperate city, China.

Methods

Data sources

Hefei is the capital of Anhui. It has a population of 9.6 million people with an area of 7266 square kilometres. It has a temperate climate with four distinct seasons.

Daily cases of HFMD for the period 2010–2012 were obtained from Hefei Center for Disease Control and Prevention (CDC). HFMD is categorized as a Class C infectious disease by the Chinese Ministry of Health, which demands that all HFMD cases should be reported to CDC. HFMD case was diagnosed by clinical symptoms, according to Chinese Ministry of Health, including vesicular lesions on hands, feet, mouth (which were often ulcerated), and buttocks.[11,14] A recent research showed that the reporting completeness of CDC can reach 99.84% and the accuracy of the information reported can reach 92.76%.[15] In addition, data of daily temperature and relative humidity were retrieved from Hefei city Bureau of Meteorology.

Statistical analyses

As childhood HFMD had a high-risk period from April to July, the data of this period to analyze the effect of humidity on HFMD has been extracted. Due to the fact that daily cases of HFMD presents a Poisson distribution and DLNM model can simultaneously model non-linear exposure–response dependencies and delayed effects, a Poisson generalized linear regression model combined with a distributed lag non-linear model (DLNM) to quantify the effect of humidity on HFMD have been used.[16–18] Previous studies showed that average temperature, seasonal patterns and long-term trends, day of week may confound the relationship between relative humidity and human health.[19–21] In this paper, average temperature was controlled in the model by using a natural cubic spline with three degrees of freedom (df). Seasonal patterns and long-term trends were controlled for by using a natural cubic spline with four df per year of data. Day of week in the form of the categorical variables was adjusted. In all cases, the Akaike Information Criterion (AIC) and residual analysis to estimate the adequacy of model and choice of df have been used.

The authors found the effect of relative humidity on paediatric HFMD was negligible for lags above 21 days, so they calculated the relative risk of HFMD with lags up to 21 days. Given the incubation period (3–7 days), and also used a lag-stratified approach by examining the cumulative effects of relative humidity at lag 0–7 days. All effect estimates were presented as relative risk, using a reference humidity of 84%, which corresponded to the 75% of relative humidity level across the study period. The percent change of childhood HFMD associated with a 1% increase in humidity was used to reflect the influence of humidity on childhood HFMD. To check the robustness of the results, sensitivity analyses were performed by varying the df for time (7–15) and temperature (3–5) in the model.

The R statistical environment (version 2.15) was used to conduct all data analysis and the 'dlnm' package was used to fit the regression model.[22]

Results

Data description

There were 21,634 HFMD cases among children aged 0–14 years during the April to July from 2010 to 2012, of these, 13,771 were male, 19,285 were 0–4 years, and 14,909 were from urban areas. Table 1 shows the basic information, including meteorological parameters and childhood HFMD. Fig. 1A and B present the temporal distribution of childhood HFMD cases and humidity from 1 January 2010 to 31 December 2012 in Hefei, China, respectively, showing a strong seasonal pattern. Fig. 1C indicates that the number of HFMD cases was greater in the months of April to July than other months.

Distributed lagged effects of relative humidity on HFMD

The total influence of relative humidity on children

Fig. 2 shows that humidity was significantly associated with childhood HFMD. The relative risk increased rapidly (RR > 1.0) above a relative humidity of 84%. Table 2 reveals that the effect was the greatest at ten days lag. In particular, a 1%