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Temporal and spatial analysis of hand, foot, and mouth disease in relation to climate factors: A study in the Mekong Delta region, Vietnam

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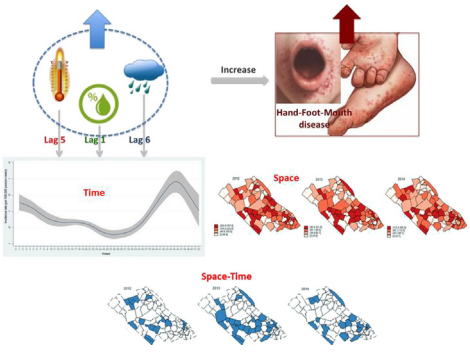
HIGHLIGHTS

- Mekong Delta region (MDR) is highly vulnerable to climate change and HFMD epidemic area.
- High temperature, humidity and rainfall associated with elevated risk of HFMD
- High-risk clusters of HFMD were found in areas with high population density and traffics.
- The findings suggest important implication on health effect of climate change in the MDR.

GRAPHICAL ABSTRACT



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ABSTRACT

This study examined the temporal and spatial patterns of hand, foot, and mouth disease (HFMD) in the Mekong Delta region in Vietnam. A time-series analysis was used to examine the temporal patterns of HFMD in relation to climate factors while a retrospective space-time scan was used to detect the high-risk space-time clusters of this disease. A 1 °C increase in average temperature was associated with 5.6% increase in HFMD rate at lag 5 days (95% CI 0.3–10.9). A 1% increase in humidity had equal influence of 1.7% increases on HFMD rate at both lag 3 days and 6 days (95% CI 0.7–2.7 and 95% CI 0.8–2.6, respectively). An increase in 1 unit of rainfall was associated with a 0.5% increase of HFMD rate on the lag 1 and 6 days (95% CI 0.2–0.9 and 95% CI 0.1–0.8, respectively). The predictive model indicated that the peak of HFMD was from October to December - the rainy season in the Mekong Delta region. Most high-risk clusters were located in areas with high population density and close to transport routes. The findings suggest that HFMD is influenced by climate factors and is likely to increase in the future due to climate change related weather events.

1. Introduction

Hand, foot, and mouth disease (HFMD) is a viral disease, whose incidence has increased significantly in Asian countries such as China, Japan and Vietnam over the last decade (WHO, 2011). HFMD is caused by a group of human enteroviruses species A, the main ones being

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Coxsackievirus A16 (CV A16) and Enterovirus 71 (EV71). This disease occurs most commonly in children under 5 years old and can be severe, even leading to death. The symptoms of HFMD range from mild symptoms of fever, skin eruptions on hand, feet and vesicles in the mouth to more severe symptoms involving the central nervous systems and/or severe respiratory symptoms (WHO, 2011). HFMD is a highly contagious disease that is transmitted from person to person by direct contact with respiratory secretions, droplets or fomites of an infected person or through fecal-oral transmission (WHO, 2011). Since there is still no specific treatment for HFMD available, and since a vaccine for EV71 has only started to be used in China since the beginning of 2016 (Knowlton et al., 2007), preventive measures such as enhanced surveillance to provide early warning of HFMD outbreaks are essential to minimize the impacts of HFMD.

Evidence of the association between HFMD and climate factors, especially temperature, has been shown in some studies elsewhere (Hii et al., 2011; Huang et al., 2013; Li et al., 2014; Onozuka & Hashizume, 2011; Urashima et al., 2003; Wang et al., 2013; Wang et al., 2016; Zhu et al., 2015). However, the relationship between HFMD incidence and the ambient temperature was inconsistent for different geographical areas (Hii et al., 2011; Huang et al., 2013; Onozuka & Hashizume, 2011; Urashima et al., 2003). A study in Singapore (Hii et al., 2011) revealed that a 1 °C increase in maximum temperature above 32 °C was significantly associated with a 36% increase of HFMD incidence. Studies in other Asian cities such as Guangzhou, China (Huang et al., 2013) and Fukuoka, Japan (Onozuka & Hashizume, 2011) have also showed positive association between increasing temperature and HFMD incidence. In contrast, a study in Shandong, China (Zhu et al., 2015) identified a negative association between temperature and HFMD when the average temperature was above 21 °C and a study in Tokyo (Urashima et al., 2003) has also detected a negative association when the average temperatures are above 25 °C. The association between ambient temperature and HFMD incidence has been shown to be non-linear in studies in Tokyo (Urashima et al., 2003), Beijing (Xu et al., 2015), and Shandong (Zhu et al., 2015). Climate factors are not alone in affecting the HFMD incidence; the difference in association between climate factors and HFMD distribution in different regions suggests that other factors such as spatial factors may modify the association. Studies in some regions in China such as Liaocheng city (Zhang & Zhao, 2015), Shandong Province (Liu et al., 2015a, b, c), Guangdong province (Deng et al., 2013), and Sichuan province (Liu et al., 2015a, b, c) have examined both spatial and temporal factors and indicated high-risk clusters of HFMD in specific periods using spatial-temporal analysis. The high-risk clusters were specific to each study region, and they tended to occur in areas that have higher population density (Deng et al., 2013; Liu et al., 2015a, b, c) and in transit hubs of highways and railways (Liu et al., 2015a, b, c). Understanding the existence of high-risk clusters in specific areas would enable public health planning to focus on these areas to maximize the prevention and control effects.

In recent decades, increased HFMD outbreaks have been reported in Vietnam (WPRO, 2016). The numbers of reported cases in 2008 and 2009 were around ten thousand, double the numbers in 2007. There was a peak of 157,654 cases in 2012 and then the incidence remained high in the following years (WPRO, 2016). Most HMFD cases in Vietnam have been reported in the South (WPRO, 2016), including the Mekong Delta Region (MDR) which is also the most vulnerable area to climate change in the South-East Asia (Yusuf & Francisco, 2009). However, no study regarding the association between HMFD and climatic factors has been conducted in this region to provide evidence for prevention measures for HFMD in the context of climate change in this highly vulnerable region. Previous studies about HFMD in Vietnam have mainly focused on virology (Khanh et al., 2012; Tan et al., 2015; Thao et al., 2010) and epidemiology characteristics of HFMD (Nguyen et al., 2014; Tu et al., 2007),

This study aims to examine the temporal and space-time clusters of HFMD in relation to climate factors in Can Tho, the central city of the MDR in Vietnam. Understanding the spatial-temporal patterns of HFMD can make a significant contribution in determining high-risk areas and periods of HFMD. The data will be useful for public health practitioners and authorities in implementing HFMD preparedness and control.

2. Methods

2.1. Research location

This study was implemented in Can Tho city, which is located in the centre of the MDR in Vietnam. Can Tho city has an area of 1409 km^2 and a population of 1,237,000 people with a population density of 878 people/km^2 which is the highest population density in the MDR (Chien, 2014). There are two seasons in Can Tho city, the dry season (December–April) and the wet season (May–November). Since it is located in a complex of intertwining rivers and a vast area of orchards and rice fields, Can Tho's residential life is highly affected by hydro-meteorological factors.

2.2. Data collection

Daily HFMD cases were collected from January 2012 to December 2014 from the disease surveillance reports of Can Tho Preventive Medicine Centre (CTPMC). In Vietnam, it has been compulsory to report all HFMD cases through the health care systems from 2011 (MOH, 2010). Once a HFMD case is confirmed by a physician in a hospital or clinic, it must be reported to the local health authority, and then be reported to the higher level within 24 h. The CTPMC is the provincial health authority responsible for collecting data of all HFMD cases in Can Tho city, and reporting them to the Ministry of Health. Thus, the data collected by CTPMC is the best available data to represent HFMD cases in Can Tho city throughout the three years from 2012 to 2014.

Daily climate factors were collected from the Southern Regional Hydro-Meteorological Centre for the period of January 2012 to December 2014. The climate factors comprise daily average temperature (°C), relative humidity (%), and cumulative rainfall (mm).

2.3. Data analysis

2.3.1. Time-series regression analysis

Time-series regression was used to examine the temporal patterns of HFMD in relation to the climate factors, comprising average temperature, humidity and cumulative rainfall. First, seasonality and long-term trends were controlled using a flexible spline function for the three years from 2012 to 2014 using 6° of freedom per year. Although there is no confirmation on how many knots are optimal, the previous study indicated that 7 knots per year can balance between providing adequate control for seasonality and other confounding factors by trend in time, while leaving sufficient information from which to estimate exposure effects (Bhaskaran et al., 2013; Dominici et al., 2000). Second, for each climate factor the lag effects of up to 6 days lag were examined using a Generalized Linear Model (GLM) using linear regression with Poisson family allowing for over-dispersion and the distributed lag model while adjusting for spline function of time, day of the week, and the offset of population (Eq. (1)). We selected 6 day lags for 2 reasons. First, the usual period from infection to onset of symptoms is 3–7 days (WHO, 2012). Second, we wished to avoid enhancing the chance of statistical significance when using many lags.

$$\mathrm{Ln}(Y) = \beta_o + \sum \beta_i T_i + \sum \beta_j H_j + \sum \beta_z R_z + s(\mathrm{time}) + \mathrm{dow} + \mathrm{Ln}(\mathrm{pop}) \quad (1)$$

where, Y is the daily count of HFMD cases, T_i is the average daily temperature at lag i day, H_j is the daily humidity at lag j day R_z is the daily cumulative rainfall at lag z day, s (time) is the flexible spline function of