Environment International 73 (2014) 1–9

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

The role of environmental factors in the spatial distribution of Japanese encephalitis in mainland China

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ARTICLE INFO

Article history:
Received 14 February 2014
Accepted 8 July 2014
Available online 26 July 2014

Keywords:
Japanese encephalitis
Ecological niche model
MaxEnt
China

ABSTRACT

Japanese encephalitis (JE) is the most common cause of viral encephalitis and an important public health concern in the Asia-Pacific region, particularly in China where 50% of global cases are notified. To explore the association between environmental factors and human JE cases and identify the high risk areas for JE transmission in China, we used annual notified data on JE cases at the center of administrative township and environmental variables with a pixel resolution of 1 km × 1 km from 2005 to 2011 to construct models using ecological niche modeling (ENM) approaches based on maximum entropy. These models were then validated by overlaying reported human JE case localities from 2006 to 2012 onto each prediction map. ENMs had good discriminatory ability with the area under the curve (AUC) of the receiver operating curve (ROC) of 0.82–0.91, and low extrinsic omission rate of 5.44–7.42%. Resulting maps showed JE being presented extensively throughout southwestern and central China, with local spatial variations in probability influenced by minimum temperatures, human population density, mean temperatures, and elevation, with contribution of 17.94%–38.37%, 15.47%–21.82%, 3.86%–21.22%, and 12.05%–16.02%, respectively. Approximately 60% of JE cases occurred in predicted high risk areas, which covered less than 6% of areas in mainland China. Our findings will help inform optimal geographical allocation of the limited resources available for JE prevention and control in China, find hidden high-risk areas, and increase the effectiveness of public health interventions against JE transmission.

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1. Introduction

Japanese encephalitis (JE), a mosquito-borne disease caused by the Japanese encephalitis virus (JEV) from the Flaviviridae family, is clinically characterized by fever, nausea and vomiting, headache, lowered level of consciousness, seizures, movement disorders, and acute flaccid paralysis (Ghosh and Basu, 2009; Misra and Kalita, 2010). JEV is transmitted in an enzootic cycle among mosquitoes and vertebrate hosts, primarily domestic pigs and ardeid birds (van den Hurk et al., 2009; WHO, 2009). The primary vector species, *Culex tritaeniorhynchus*, is abundant in rural areas, where it breeds in low-lying flooded areas containing grasses or flooded rice paddies. Humans are a dead-end host and get infected when bitten by infected mosquitoes (Solomon, 2006).

JE remains an important public health concern in the Asia-Pacific region where it is the most common cause of viral encephalitis (Solomon, 2006). Some countries in the regions such as Japan and South Korea have significantly reduced the number of human JE cases through a combination of better living conditions, early diagnosis and prompt treatment, routine immunization, and effective vector control

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http://dx.doi.org/10.1016/j.envint.2014.07.004
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(WHO, 2009). However, more than three billion people still live in JE-epidemic countries (Ghosh and Basu, 2009; Le Flohic et al., 2013). It is estimated that there are about 68,000 JE cases annually in 24 Asian and Western Pacific countries and in countries such as China, India and Nepal, JE continues to be a major public health problem (Campbell et al., 2011; Wang et al., 2013a).

In China, JE has been listed as a class B notifiable infectious disease since 1951 (Zheng et al., 2012). Historically, two large human outbreaks of JE were observed in the 1960s and 1970s in China (Zheng et al., 2012). The incidence of JE has declined substantially from 20.92/100,000 in 1971 to 0.23/100,000 in 2008 following the implementation of a nationwide immunization program in the early 1970s (Gao et al., 2010; Ministry of Health, 2009). In a recent study, we reported that the spatial extent of JE dynamically changed during 2002, 2003–2005, 2006 and 2007–2010 with geographical clusters in 119, 125, 133 and 144 counties in southwestern China, respectively (Wang et al., 2013b). However, it remains unclear which factors have contributed to the observed variation in JE distribution during the last decade and which areas are at high risk for JE transmission. This information is essential to make informed decisions around preferential areas to implement targeted immunization and mosquito control.

Previous studies have shown that topography, vegetation and climate influence the spatial distribution and temporal dynamics of natural foci of JE (Solomon, 2006; WHO, 2009). Furthermore, JEV transmission to humans has been shown to be related to temperature and rainfall, which impact on abundance and stability of mosquito populations. Therefore, environmental changes could alter the locations that are suitable for JE transmission (Zhang et al., 2011).

During recent years, ecological niche modeling (ENM) approaches have been widely used in biogeography, ecology and epidemiology to characterize the geography of disease transmission (Peterson, 2006; Wei et al., 2011). For example, ENMs combined with remote sensing (RS) and geographical information system (GIS) has been applied to predict the distribution of infectious diseases, such as leishmaniasis (Gonzalez et al., 2010), Chagas disease (Mischler et al., 2012; Peterson et al., 2002), plague (Holt et al., 2009; Neerinckx et al., 2008), Marburg hemorrhagic fever (Peterson et al., 2006), and H5N1 (Bodbyl-Roels et al., 2011; Williams et al., 2008). In the case of JE, two very recent studies have used ENM to predict the distribution of *C. tritaeniorhynchus* in Asia and Korea (Masuoka et al., 2010; Miller et al., 2012). To the best of our knowledge, ENM has not been applied to forecast the distribution of JE cases in humans.

In this study, we analyzed JE surveillance data from China over the period of 2005–2011 to quantify the association between human JE cases and environmental conditions and to identify high risk areas for JE transmission in China. Our study aimed to provide an improved understanding of the factors that contribute to spatial variation in areas suitable for JEV transmission across China, thus to assist in the development of preventive and control strategies and increase the effectiveness of public health interventions against JE transmission in the country.

2. Materials and methods

2.1. Human JE presence data

Human JE cases were diagnosed according to standard diagnostic criteria issued by the National Health and Family Planning Commission (Ministry of Health, 2006). The case definition for JE has been described previously (Wang et al., 2013b). An individual was diagnosed with JE if they had lived in or traveled to an endemic area during the vector-biting season, with clinical manifestations of encephalitis and one of the following: presence of JEV-specific IgM antibody in a single sample of cerebrospinal fluid or serum; detection of JEV antigens; a 4-fold or greater rise in JEV-specific antibody; detection of JEV genome in samples by PCR; or isolation of JEV. A total of 33,193 JE cases were reported during 2005–2012. As we analyzed at township level, a township with two or more JE cases in a year was treated as one positive case. After eliminating 8798 duplicate records in the same township per year and removing 1369 records of unavailable addresses, 23,026 cases were geocoded to the administrative township center according to the patient's residential address.

2.2. Environmental data

Weather data on temperature, relative humidity and precipitation were obtained from the China Meteorological Data Sharing Service System. Annual weather data were based on monthly ground weather station measurements from 2005 to 2011. Elevation was derived from a Shuttle Radar Topography Mission database with a spatial resolution of 90 m. Land cover data were derived from European Space Agency (ESA), which were classified into 23 land cover types (Supporting Information A). Normalized Difference Vegetation Index (NDVI), generated from Free Vegetation Products with a temporal resolution of 10 days and served by VITO Belgium, was image analyzed and processed to monthly mean composite NDVI images per year from 2005–2011. Domestic pig and human population density were derived from Food and Agricultural Organization (FAO) and National Bureau of Statistics of China, respectively. All data layers (Table 1) were converted to the same geographic projection (Krasovsky_1940_Albers), and generalized to a pixel resolution of 1 km × 1 km for analysis.

2.3. Ecological niche modeling

To explore the relationship between the geographic distribution of human JE cases and environmental factors and to generate a map showing the probability of JE presence, we employed a presence-only distribution modeling technique—the MaxEnt algorithm, a Maximum Entropy approach (Hernandez et al., 2006; Li et al., 2011b). This approach has been used previously to identify areas suitable for transmission of dengue fever, Chagas disease and monkeypox based on human cases and environmental conditions (Arboleda et al., 2009; Mischler et al., 2012; Nakazawa et al., 2013). In addition, this method offered advantages compared to other modeling methods: (1) the independence of variables, which is frequently not met for environmental data, was essential for the particular Bayesian species modeling approach of Aspinall (1992), while not necessary for MaxEnt modeling; and (2) better performance has been demonstrated for MaxEnt compared to a commonly used presence-only modeling method, the Genetic Algorithm for Rule-Set Prediction (Elith et al., 2006; Phillips et al., 2006).

Table 1
Climatic-environmental and social–ecological layers used in the construction of ecological niche models in mainland China.

Variables	Description	Source
T	Minimum/maximum/mean temperature of the model year	China Meteorological Data Sharing Service System
RH	Minimum/maximum/mean relative humidity of the model year	China Meteorological Data Sharing Service System
Rain	Minimum/maximum/mean rainfall of the model year	China Meteorological Data Sharing Service System
NDVI	Minimum/maximum/mean normalized difference vegetation index of the model year	Free Vegetation Products
LC	Classification of land cover type	European Space Agency (ESA)
Dem	Elevation	Shuttle Radar Topography Mission (SRTM)
Pop_density	Population per km^2	National Bureau of Statistics of China
Pig_density	Pig per km^2	Food and Agricultural Organization (FAO)

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