Letter to the Editor

The Relationship between Japanese Encephalitis and Environmental Factors in China Explored Using National Surveillance Data*

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Japanese encephalitis (JE) is a serious public health issue. This study was undertaken to better understand the relationship between JE distribution and environmental factors in China. JE data from 2005 to 2010 were retrieved from National Notifiable Disease Report System. ArcGIS, remote sensing techniques, and *R* software was used to exhibit and explore the relationship between JE distribution and environmental factors. Our results indicated that JE cases were mostly concentrated in warm-temperate, semitropical and tropical zones with annual precipitation > 400 mm; Broad-leaved evergreen forest, shrubs, paddy field, irrigated land, dryland, evergreen coniferous forest, and shrubland were risk factors for JE occurrence, and the former five were risk factors for counties with high JE incidence. These findings will inform the effective allocation of limited health resources such as intensive vaccination, surveillance and training in areas with high environmental risk factors.

Key words: Japanese encephalitis; Environmental factors; Landscape

Japanese encephalitis (JE) is severe vector-borne encephalitis caused by JE virus (JEV) identified in about 24 countries. Available data showed an estimated 68,000 clinical JE cases occurred annually worldwide with about 30% case-fatality rate in patients with encephalitis[1]. In China, JE has been classified as a notifiable disease since the 1950s. JE case numbers peaked in 1966 with 150,000 cases (morbidity > 15/100,000) and 1971 with 174,932 cases (morbidity > 20/100,000)[2]. Although JE incidence showed a decreasing trend, JE was one of the top 10 diseases with high fatality rate of more than 30 notifiable diseases in China in recent years. By now, JE remains a considerable threat to health[3] because of its high fatality rate and protracted and severe sequelae.

As a mosquito-borne virus, circulation among pigs and mosquitoes is an important mode of JEV transmission. Humans are dead-end hosts infected by mosquito bite. More than 30 types of mosquitoes from five genera are potential JEV carriers, but *Culex tritaeniorhynchus* is the primary vector in China. Mosquito's life history as well as human abundance and activities can be affected by environmental factors. This study aimed to explore the relationship between JE distribution and environmental variables (precipitation, temperature, elevation, and landscape) using JE national surveillance data and environmental factors at county level.

JE clinical diagnosis cases and lab-confirmed cases[4] data from 2005 to 2010 for mainland China were retrieved from National Notifiable Disease Report System (NNDRS) with approval. The data extraction and use were all anonymized to protect patient privacy and confidentiality. Annual precipitation and air temperature data from 2005 to 2010 were obtained from the China Meteorological Administration. Raster maps for annual average precipitation and air temperature with a 1-km grid were generated using the inverse distance weighting method[5,6]. The annual precipitation data were

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divided into four levels: < 200, 200-400, 400-800, and > 800 mm, representing arid, semi-arid, semi-humid and humid areas, respectively. The annual average air temperature was classified into five zones: frigid-temperate, mid-temperature, warm-temperate, semitropical, and tropical. The elevation data extracted from a previously described digital elevation model (DEM) with a 1:100,000 scale were converted to a raster map with a 1-km grid[7]. Using the DEM and a map of the administrative units, the average elevation of each county was calculated. According to this, counties were divided into five levels: < 200, 200-500, 500-1,000, 1,000-4,000, and > 4,000 m. Landscape data produced based on remote sensing images in 2005 with 250-meter spatial resolution were obtained from the Institute of Remote Sensing and Digital Earth, Chinese Academy of Sciences. It was classified into six major class types, including forest, grassland, farmland, settlement, wetland and desert, and the major classes were then classified into 25 secondary class types[8]. The landscape of each county was represented by the type of land cover with the largest portion. For example, if a county was covered by 80% meadow grassland, 15% typical grassland and 5% rural settlement, the landscape was classified as meadow grassland. ArcGIS software (ESRI, USA) and remote sensing techniques was used to generate and exhibit environmental factors at county level. JE incidence was calculated according to the corresponding population. Based on six-digit county geocodes, JE cases at county level were demonstrated on the maps with different environmental factors to make geographic and spatial visualization.

R software [R Core Team (2016), Austrica. URL https://www.R.project.org/.] was used for statistical analysis. Chi-square test was used to compare JE distribution in relation to different environmental factors, including precipitation, air temperature, elevation, and landscape. To further explore the relationship between JE and landscape, counties were divided into three categories: 1) JE non-endemic counties (counties without JE cases reported), 2) JE low-endemic counties (JE cases reported in any one to four years of six years between 2005 and 2010), and 3) JE high-endemic counties (JE cases reported in any five years of six years between 2005 and 2010). The latter two combined to JE endemic counties. The comparison of endemic *vs.* non-endemic counties and high-endemic *vs.* low-endemic counties were conducted in each forest, grassland, farmland and settlement sub-factors by univariate analysis. To further explore the potential factors, variables with $P < 0.2$ in univariate analysis were included in multivariable logistic regression model with backward stepwise method. Statistical significance was set at $P < 0.05$. Odds ratio (*OR*s) and corresponding 95% confidence intervals (*CI*s) were presented.

JE case numbers and incidence decreased from 7,643 cases and 0.58 case per 100,000 population respectively, in 2006 to 2,541 and 0.19/100,000 respectively, in 2010, showing a decreasing trend with occasional fluctuation over the study period. In line with an increased national emphasis on the detection of JE, the proportion of lab-confirmed cases increased from 29.3% (in 2005) to 76.2% (in 2010). Table 1 showed the annual JE case numbers, incidence and laboratory confirmation proportion.

Average annual incidence of JE positively correlated with precipitation. The highest average yearly incidence (0.45/100,000) was observed in humid areas which was much higher than in semi-humid (0.13/100,000), semi-arid (0.02/ 100,000), and arid areas (only 0.001/100,000). The *OR* for humid areas (104.3) was also much higher than for other areas. Semitropical zones had the highest JE incidence (0.44/100,000), followed by warm-temperate (0.22/100,000), tropical (0.18/ 100,000), and mid-temperature zones (0.06/ 100,000). Few JE cases occurred in frigid-temperate

Table 1. Annual Incidence of Japanese Encephalitis from 2005 to 2010 in Mainland China

Year	Cases, *n*	Incidence, per 100,000 Population	Fatal Cases, *n*	Male, %	Female, %	Laboratory Confirmed, %*
2005	5,097	0.39	214	61.2	38.8	29.3
2006	7,643	0.58	463	62.1	37.9	48.6
2007	4,430	0.33	227	59.8	40.2	60.0
2008	2,975	0.23	142	61.0	39.0	51.5
2009	3,913	0.30	172	60.3	39.7	64.7
2010	2,541	0.19	92	59.7	40.3	76.2

Note. *The proportion of laboratory confirmed cases in the total annual JE cases.