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Weather Variables and Japanese Encephalitis in the Metropolitan Area of Jinan city, China

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Running title

Weather and Japanese encephalitis in a Chinese city

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Summary

Objective: To identify weather-related risk factors and their roles in Japanese encephalitis transmission and to provide policy implications for local health authorities and communities.

Methods: Data on notified cases of Japanese encephalitis and weather variables over the period 1959-1979 were collected from Jinan city, a temperate city in China. Due to seasonality of the disease, the data analysis was restricted to five months from June to October each year. Spearman correlation analysis and time-series adjusted Poisson regression analysis were performed to quantify the relationship between weather and the number of cases. The Hockey Stick model was used to detect potential threshold temperatures.

Results: Monthly mean maximum and minimum temperatures, monthly total rainfall and relative humidity were positively correlated to monthly notification of Japanese encephalitis, while monthly mean air pressure was inversely correlated. Lag times varied from one to two months. All these weather variables were significant in the adjusted Poisson regression model. Thresholds of 25.2^{o}C for maximum temperature and 21.0^{o}C for minimum temperature were also detected.

Conclusions: Weather variables could have affected the transmission of Japanese encephalitis in this urban area of China. Public health interventions should be developed at this stage to reduce future risk related to climate change.

Key words Japanese encephalitis, weather, threshold, metropolitan, China

Introduction

Japanese encephalitis (JE) is an arboviral disease, with its incidence and geographic distribution mainly in rural areas of tropical and temperate Asia and the Pacific region, including China, India, Korea, Japan, Russia, Nepal, Thailand, Vietnam, Cambodia, Laos, the Philippines, Indonesia, Malaysia and Sri Lanka. A total of about 45,000 to 50,000 clinical cases occur annually in the world. [1] Large outbreaks of Japanese encephalitis in India and Nepal have highlighted the continuing expansion of the geographic range of the disease in recent years. For instance, more than 4,255 cases were reported and 914 deaths occurred in one province of India in 2005, while the figures were 1,802 and 283 respectively in Nepal. [2]

Japanese encephalitis, or epidemic B encephalitis, is an arboviral disease, with reservoir host and the source of infection being pigs. Mosquitoes, mostly *Culex tritaeniorhynchus,* are the main vectors in China. [3] Most infections result in a mild illness, characterized by flu-like symptoms with sudden onset of fever, chills, headache, tiredness, nausea, and vomiting. The illness can progress to encephalitis with a fatality of 30%. For this, the leading cause of viral encephalitis in Asia, there is no specific therapy other than supportive care. There was an attenuated vaccine available in China in the early 1980s, with a protection rate ranging from 50-80% in epidemic areas and 33%-62% in non-epidemic areas. [4]

As a mosquito-borne disease with a seasonal distribution, external environmental factors including weather variables may play a significant role in its transmission. Studies in different rural areas of Asia have suggested that weather variables such as temperature, rainfall and relative humidity may influence the incidence of Japanese encephalitis. [5-8] The role of weather variables in such transmission may vary, given the large variations in climate type, ecological characteristics, rice-growing techniques and pig breeding methods, population immunity, public health intervention measures and socioeconomic status in the different regions. Furthermore, most of the previous studies focused on rural areas, and there has been no systematic study on the effect of weather variables on Japanese encephalitis in urban areas. To identify risk factors related to weather and their role in Japanese encephalitis transmission and to provide policy implications for local health authorities and communities, we have studied the relationship between weather variables and Japanese encephalitis in Jinan metropolitan area, a temperate city in China.

Materials and Methods

Background information

Located in eastern China, Jinan, the capital city of Shandong Province, lies 36˚N and 117˚E (Figure 1). The population in 2005 was about 3.3 million. Jinan has a temperate climate with dry winters and wet, hot summers. The annual mean temperature is about 15˚C. The mean summer temperature and mean winter temperature in Jinan are approximately 26˚C and -1˚C respectively. The annual average rainfall is between 550-950 mm.

(Figure 1 about here)

Data collection

Surveillance data: Japanese encephalitis has been a legally notifiable disease in China since the late 1950s. In this study, all Japanese encephalitis cases diagnosed by authorized hospitals in the target city are included. Monthly notified cases of Japanese encephalitis in Jinan were collected from the Jinan Municipal Centre for Disease Prevention and Control, the official organization processing notifiable disease data. According to law, medical practitioners should report Japanese encephalitis cases to the local Centre for Diseases Control and Prevention within a designated time. It is believed that the degree of compliance in disease notification over the study period was consistent.

Most notified cases are based on clinical diagnosis, which has followed the national clinical definition for Japanese encephalitis - an acute infectious disease caused by the Japanese encephalitis virus. It is spread by infected mosquitoes and can affect the central nervous system and cause severe complications and death.[9] Because of the frequent occurrence of Japanese encephalitis, local physicians were very familiar with the disease, so the accuracy of diagnosis is considered to be reliable.

According to the legislation, physicians in hospitals must report every case of Japanese encephalitis to the local health authority within 48 hours. The health authority reports these cases to the next level of the organization every month.

Meteorological data: Daily meteorological data for Jinan were extracted from the China Meteorological Administration Climatic Dataset Centre. There is only one weather station in Jinan and the monitoring system has been constant over the study period. The weather variables include daily maximum and minimum temperature, relative humidity, rainfall and air pressure.

Study period

Although data collection for Japanese encephalitis has been an ongoing process in Jinan since the late 1950s, cases were rarely occurred after 1981 due to the introduction of the vaccine in China, especially in the metropolitan areas. Therefore, the study period for this project was from 1959 to 1979. However, given the seasonal distribution of Japanese encephalitis in Jinan (most cases in summer and autumn), data analysis was restricted to the five months of June, July, August, September and October.

Data analysis

Correlation analysis: The relationship between monthly mean climatic variables and monthly incidence of the disease was examined. Spearman's correlation was used to quantify the relationship between monthly weather variables and the number of Japanese encephalitis cases with a lag of one to four months.

Regression analysis: Poisson regression adjusted for autocorrelation, secular trend and lag effects was used to quantify the relationship between weather variables and transmission of the disease. In Poisson regression, the dependent variable is assumed to follow the Poisson distribution. In general, the multiple Poisson regression model can be written as [10]:

$$\ln(Y) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots .$$

The model that adjusts for first-order autocorrelation can be written as:

$$\ln(Y_t) = \beta_0 + \beta_1 \ln(Y_{t-1}) + \beta_2 X_1 + \beta_3 X_2 + \ldots ,$$

where X stands for weather variables in this study.

Due to the high correlation among the weather variables especially between monthly mean minimum and maximum temperatures, and between relative humidity at 9am and 3pm, two models were set up with Model I having minimum temperature and humidity at 3pm, and Model II having maximum temperature and humidity at 9am. Only the lagged month with the maximum correlation coefficient was chosen for regression analysis in order to avoid multicollinearity. In order to control for a potential long-term trend in the number of cases over the study period, a year variable was included in the regression model.

Threshold detection: To detect a potential threshold of the effect of temperature, a natural cubic spline was fitted to explore the shape of the relationship. Then a Hockey Stick model was used to estimate a potential threshold temperature. [11,12] The assumption of this Hockey Stick model was that temperature has no effect on Japanese Encephalitis cases until a threshold value is reached. First-order autocorrelation of the number of cases was included in the model. Diagnosis of the model was conducted by residuals plotting to check for normality and homogeneity of variance of the residuals. The approach used the Stata-hockey (non-linear hockey) estimation program, which estimates complex linear and non-linear models by least squares. [13] Based on the Stata-hockey model, an author-written syntax-"nlhockey" were developed, with consideration of autocorrelation of the variables, to estimate whether, and if so where, a change in slope occurs in the relationship between two variables by iterative numerical methods.

Data analysis was performed by Stata (8.0). [13]

Results

Description of Japanese encephalitis in Jinan

The monthly distribution of Japanese encephalitis in Jinan between 1959 and 1979 is shown in Figure 2.

(Figure 2 about here)

There were 797 cases in total in Jinan over the study period. Figure 1 indicates that there was a seasonal distribution of the disease, with most cases occurring in summer and autumn.

Spearman's correlation analysis

Correlation analysis was conducted between monthly weather variables and monthly incidence of Japanese encephalitis in the studied months (Table 1).

(Table 1 about here)

The results in Table 1 indicate that monthly mean maximum and minimum temperatures, monthly total rainfall and relative humidity were positively related to the monthly number of Japanese encephalitis cases notified in Jinan over the study period, while monthly mean air pressure was inversely correlated with number of cases. The strongest lagged effects were from one to two months.

Regression analysis

The relationship between the most highly correlated weather variables listed above and monthly notification of the disease was examined by Poisson regression adjusted for autocorrelation, secular trend and lagged effect. The results of Model II are not presented in this paper due to the similarity of the results with those of Model I (Table 2 and Figure 3).

(Table 2 and Figure 3 about here)

The results in Table 2 and Figure 3 show that the number of cases is first-order autoregressive, indicating that the number of notified cases of Japanese encephalitis in the current month is related to the numbers of cases occurring in the previous month. The year of occurrence was included in the model as an independent variable indicating that there was a long-term decline in the number of cases notified over the study period. After controlling for this long-term trend, monthly maximum temperature (2-month lag), rainfall (2-month lag), and relative humidity (1-month lag) had a positive effect while monthly average air pressure (1-month lag) had a negative effect on Japanese encephalitis infection. Figure 3 demonstrates a goodness-of-fit with correlation between observed and expected number of cases more than 75%.

Two peaks were observed in 1967 and 1968. The numbers of cases were 158 and 83 respectively and might be attributable to weather variables. Examination of the original database revealed that the monthly minimum temperatures occurring one month prior to these peaks were over 24°C and the monthly maximum temperatures occurring two months prior were over 32°C. Additionally, substantial monthly total rainfall (more than 2300mm) and more than 30% increase in mean relative humidity occurred two months prior to the peak in number of cases.

Threshold temperature detection

Thresholds of 25.2°C for maximum and 21.0°C for minimum temperature were detected (Figure 4), above which the number of Japanese encephalitis cases could be increased with rising temperature. The temperatures preceded the two peak values were all substantially above the thresholds as stated above.

(Figure 4 about here)

Discussion

Although Japanese encephalitis is under control in China, especially after the introduction of a vaccine in the early 1980s, there are still around 5,000 to 10,000 cases being notified annually. [14] There are many risk factors in the disease transmission. These include: rainfall, temperature, population immunity, virus infection among reservoirs, the mosquito situation and its control measures and the level of social and economic development such as housing conditions. Vaccination also plays an important role in the transmission of Japanese encephalitis. However, the widespread application of Japanese encephalitis vaccination was not started until late 1981, [4] which was by design beyond the study period of this project. Therefore, the effect of the vaccination on this study was very limited. In addition to other factors, environmental conditions which affect the transmission of other mosquito-borne diseases such as malaria, dengue fever and Ross River virus infection [15-19,] may also apply to Japanese encephalitis. It is important to study the impact of weather on the transmission of Japanese encephalitis because global warming might change the patterns of temperature and precipitation, which may influence the development of the mosquitoes and the virus, as well as people's behaviour. This study found that maximum and minimum temperature, rainfall and relative humidity positively affected the transmission of Japanese encephalitis in urban areas of Jinan, a temperate city of China. This is the first attempt to develop an epidemic forecasting model for predicting Japanese encephalitis transmission in a metropolitan area, where not many pigs are raised.

Higher temperatures, within limits, lead to more rapid development of larvae, shorter times between bloodmeals, and faster incubation times for viral infections within mosquitoes. As a result, increases in temperature allow mosquito populations to reach higher levels faster, and to be maintained for longer, thereby increasing the opportunities for viral transmission. [20] For example, for Japanese encephalitis, only 14% of mosquitoes were infected when temperatures were 18-22^{o}C, but the figure reached 80% when temperatures were 26-30^{o}C. [4] In China, for locations with annual average temperatures were below 20^{o}C, there were only few cases of Japanese encephalitis; between 25-30^{o}C, there was the possibility of an epidemic of the disease; and for locations with over 30^{o}C, the epidemic peak appeared. [3] This is consistent with the threshold temperature detection in this study. Higher temperatures might also change human behaviour, i.e., more outdoor activities including fishing and swimming with exposure of more people to mosquitoes. Furthermore, a higher minimum temperature might assist larvae survival in winter. A temperature threshold was detected in this study indicating that there was an increase of cases of Japanese encephalitis in Jinan when the monthly mean maximum temperature was over 25.2°C or the minimum temperature was higher than 21.0°C.

Rainfall and relative humidity also play an important role in the transmission of Japanese encephalitis, as mosquitoes require water to support the larval and pupal stages of development. The positive association with rainfall is consistent with findings of other studies that have examined environmental factors and Japanese encephalitis disease incidence elsewhere in Asia [5-8] and other mosquito-borne diseases. [15-18] For example, summer rainfall was found to be a good predictor of increased risk of Japanese encephalitis in country areas of China, Japan and India. [5-7] In our results, relative humidity also had a positive impact on the transmission of Japanese encephalitis. Relative humidity influences longevity, mating, dispersal, feeding behaviour and oviposition of mosquitoes. [21] At higher humidity, mosquitoes generally survive for longer and disperse further. Therefore, they have a greater chance of feeding on an infected animal and surviving to transmit a virus to humans or other animals. Relative humidity also directly affects evaporation rates from mosquito breeding sites. However, the health impact of relative humidity has not been investigated in most previous studies. Our results indicate higher impact on Japanese encephalitis cases of humidity than of rainfall. It could be due to the non-linear effect on mosquito distribution and activity or the interaction with other weather variables, particularly temperatures. More studies are necessary to clarify this relationship.

The lagged effect of precipitation and temperature, at a lag of two months, on the incidence of Japanese encephalitis is important. Such delays are consistent with the development of the virus within reservoirs, the growth of mosquitoes, the external period of incubation of Japanese encephalitis virus within mosquitoes, and the incubation period of the virus in the host, and therefore are biologic plausible.

The regression models indicate that the number of new cases in a given month is related to the number of cases in the previous one. This may provide an indicator to the local communities and health authorities. Preventive public health action could be initiated by warning and educating local communities to conduct relevant health promotion/intervention campaigns, to change personal behaviour, eg cleaning living areas as soon as an increase in cases is detected by the disease notification system.

There was a long-term fluctuating incidence of Japanese encephalitis, with a declining trend over the study period in Jinan. Many factors may contribute such declination. These might include the immunity of a population, the virus titer in the blood of pigs, the density of mosquitoes that carry Japanese encephalitis virus and the virulence of the virus. Improved living condition such as net-windows and net-doors in the house and health education over the study period may have contributed to the decline in infection.

We have previously studied the relationship between weather variables and Japanese encephalitis transmission in a rural region of eastern China and received similar results. [5] It should be noted that the results from this study are from urban areas of Jinan, the capital city of Shandong Province, where no rice was grown and most of the population in the city were not farmers. The role of pigs in disease transmission for the metropolitan area is not fully understood and more studies are needed. However, weather variables do impact on the development of *Culex tritaeniorhynchus*, the main vector of Japanese encephalitis in this temperate city. The density of mosquito or some other proxy of vectorial capacity is implicitly important in the model. However, there was no routine data collection of vectorial capacity in Jinan over the study period. To establish such routine mosquito surveillance is important in mosquito control and mosquito-borne diseases prevention.

It should be acknowledged that the ecology of Japanese encephalitis is very complicated. A diverse range of environmental factors, host, animal and human susceptibility to Japanese encephalitis, and human behaviour all influence mosquito populations. The amount of contact between human beings and vectors, as well as socioeconomic status influenced the transmission of the disease. Therefore additional studies are required, which incorporate more variables such as density of mosquitoes and reservoirs such as pigs.

Climate change, particularly global warming, has already brought and will continue to bring about challenges to public health and communicable disease control and prevention. The historical climatic data from 1960 to 2000 demonstrate a significant increase trend in temperatures in Jinan city. Given the predictions for temperature increases in much of China, research outcomes from this study may be used to assist public health decision making, environmental health risk management and community health education. These would include improving vector control and personal protection.

Limitations of this study should be acknowledged. Under-reporting of infectious diseases including Japanese encephalitis in developing countries is a common challenge. The correlation between climatic variation and Japanese encephalitis may be underestimated. However, there is no evidence to suggest that there was any trend in under-reporting over the study period. Therefore it is believed that the impact of under-reporting on the results could not be significant. In addition, other factors such as vector variables and socioeconomic factors that might be expected to impact on the transmission of the disease could not be analysed in the current study. Relevant surveillance systems should be set up in future.

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Table 1. Spearman correlation between climatic variables and JE in Jinan city at the lags with maximum coefficients

	Spearman rho	*p*	Lag months
Max_Temperature	0.62	0.000	2
Min_Temperature	0.73	0.000	1
Rainfall	0.29	0.003	2
Humidity	0.65	0.000	1
Air_Pressure	-0.65	0.000	1

Table 2. Estimated coefficients by adjusted Poisson regression Model I between climatic variables and Japanese encephalitis in Jinan, 1959-79

	Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]
Case(lag1)	0.0059	0.0015	3.96	0.000	[0.0030, 0.0088]
Max_Temp (lag2)	0.0758	0.0219	3.46	0.001	[0.0328, 0.1188]
Air_Pressure (lag1)	-0.2460	0.0154	-16.02	0.000	[-0.2761, -0.2159]
Humidity (lag1)	0.0734	0.0063	11.70	0.000	[0.0611, 0.0857]

Rainfall (lag2)	0.0005	0.0001	9.09	0.000	[0.0004,	0.0007]
Year	-0.0366	0.0065	-5.60	0.000	[-0.0494,	-0.0238]
Constant	311.4213	20.3683	15.29	0.000	[271.5002,	351.3424]