

Climatic, reservoir and occupational variables and the transmission of haemorrhagic fever with renal syndrome in China

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Background	Being a zoonosis, the transmission of haemorrhagic fever with renal syndrome (HFRS) is influenced by climatic, reservoir and occupational factors. This paper has quantified the incidence and potential risk factors of HFRS in Yingshang County, a low-lying epidemic focus of the disease in China.
Methods	Correlation and regression analyses were conducted among climatic variables, the density of mice, autumn crop production and annual incidence of HFRS during the autumn-winter seasons in the County over the period 1980–1996.
Results	Rainfall ($r = -0.63$, $P = 0.009$), the density of mice ($r = 0.90$, $P = 0.000$) and autumn crop production ($r = 0.67$, $P = 0.01$) were statistically correlated with the incidence of HFRS. Multiple regression analysis indicated that these factors are potential predictors for HFRS transmission.
Conclusions	Rainfall, the density of mice and autumn crop production could be used as predictors of HFRS transmission in low-lying epidemic foci.
Keywords	HFRS, Hantaan virus, climate, mice, occupation
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Haemorrhagic fever with renal syndrome (HFRS) is a zoonosis caused by Hantaan or Hantaan-related virus, with characteristics of fever, haemorrhage, kidney damage and hypotension. Rodents, mostly mice, act as a reservoir and the source of infection. Humans are infected when they come into contact with excreta from infected rodents.¹

The epidemic situation of HFRS is serious in China. There were about 1.1 million HFRS cases over the period 1931–1995; more than 90% of all HFRS cases worldwide during this period. Over 46 000 people died from HFRS and the fatality rate was 3.94%.² Over the period 1950–1995, the incidence was the highest in 1986, with an average of 11.08/100 000 population nationwide.¹

The transmission of HFRS is influenced by environmental, occupational and reservoir factors.^{1,3} Environmental factors

include the amount of precipitation, the composition of the drainage system and the topography, which produce effects such as moist soil in low-lying areas. Occupational activities comprise farming, mining, railway construction, irrigation and other outdoor professional activities. Both environmental and occupational factors may impact on the transmission of the disease by influencing the ecological environment of the mice and human contact with them.^{1,3} In Anhui Province, for instance, most HFRS cases have occurred in low-lying regions along the Huai River and the Yangtze River, the third and the largest rivers in China, respectively. Most of the patients were farmers who had close contact with the mice on their farmland.¹

Vector-borne viral diseases are amongst the most sensitive of all diseases to climate change.⁴ It is important to study the impact of climatic variables on the transmission of HFRS because of the possibility of global warming and climate change, with ensuing changes in precipitation and temperatures.⁵ However, few observations have been made on the impact of climate variability on the transmission of HFRS. Hence, this study aims to assess the impact of climatic, reservoir and occupational variables on the transmission of HFRS using empirical data over the period 1980–1996 in a low-lying epidemic focus in China,^{1,6,7} and to identify potential risk factors for the transmission of the disease.

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Material and Methods

Background

There are few provinces in China with an incidence rate for HFRS as high as Anhui Province. Over the period 1980–1986, the incidence was more than 10/100 000, before falling to about 4/100 000 in 1988.¹ It reached a peak in 1991 of about 18/100 000 and then decreased smoothly. In 1995, the incidence was about 5/100 000.² Yingshang County is located in a low-lying area along the northern side of the Huai River (Figure 1), with a population of approximately 1.3 million in 1996 and a temperate climate. It has been recognized as an epidemic focus of HFRS since 1958⁶ and good records have been kept for the disease since then as it is an HFRS surveillance site of Anhui Medical University. Although *Rattus norvegicus* was found to carry the virus and is recognized as one of the reservoirs,⁸ the most important source of infection for the disease in Yingshang is *Apodemus agravius*, the dominant mouse species in the County.^{1,6,8} The seasonal incidence in autumn-winter can last from October to January.^{1,6}

Study population

All the residents in Yingshang County over the period 1980–1996 were treated as the study population.

Data collection

The data covered the period 1980–1996. Notified HFRS data were obtained from the Department of Disease Surveillance, Anhui Anti-Epidemic Station. Population data were provided by the Anhui Bureau of Statistics and meteorological data were retrieved from the Anhui Bureau of Meteorology. The meteorological data were derived from the one weather station in Yingshang County. The Southern Oscillation Index, which is related to atmospheric

pressure differences between Tahiti and Darwin and is a measure of El Niño-Southern Oscillation, is considered to be the best predictor of temperature and rainfall across the Pacific and in eastern Australia.⁹ The Australian Bureau of Meteorology provided data on the Southern Oscillation Index (SOI).

Data on the autumn density of mice were obtained from the County's Anti-Epidemic Station. This station conducts a density-of-mice survey in fields four times annually. For each survey four fields are chosen in the east, west, south and north of the County. At least 300 traps are placed at each trapping site each night, and the survey is conducted over three consecutive nights. The number of mice captured divided by the number of traps placed at a certain trapping site is that season's density of mice in that field. The average of a season's density of mice in the four different fields represents the season's density of mice for the County.

Autumn crop production data, an index reflecting local farmers' agricultural activity and their degree of indirect contact with the mice, were provided by the County's Department of Agriculture. While harvests are conducted in both spring and autumn, the autumn data were used in the analysis because this is the main harvest. The autumn crop production for each year from 1980 to 1996 was classified as 1: <0.1, 2: 0.1–0.2, 3: 0.21–0.3, 4: 0.31–0.4, 5: 0.41–0.5, 6: 0.51–0.6, 7: 0.61–0.7, and 8: \geq 0.71 million tonnes. These categories were used to represent low (1, 2), low-medium (3, 4), medium-high (5, 6) and high (7, 8) production.

Statistical methods

Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS).¹⁰ The incidence of HFRS in the autumn-winter and the mean climatic variables (temperature, precipitation, relative humidity and SOI) from July to

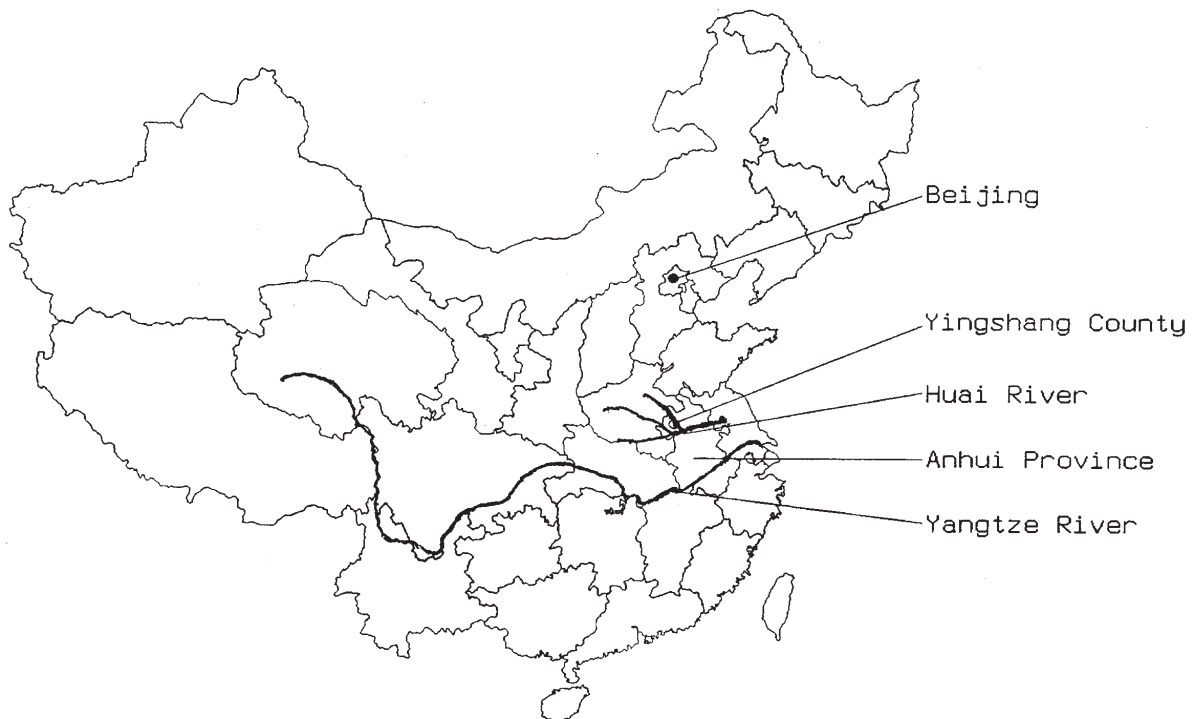


Figure 1 Geographical position of Yingshang County in China

September were calculated annually over the period 1980–1996 for Yingshang County. Spearman’s rank correlation analysis was conducted on the incidence of HFRS in autumn-winter and the seasonal climatic variables as indicated above, as well as other reservoir and occupational factors such as the autumn density of mice and the autumn crop production.

Logarithmic transformation of HFRS incidence was performed to normalize its distribution and multiple regression analysis used to assess the independent effects of climatic, reservoir and occupational variables on the transmission of HFRS over the period 1980–1996 in Yingshang County.

Results

Annual and monthly variations of HFRS incidence in Yingshang County, 1980–1996

There were two epidemic peaks over the period 1980–1996 in the County. One was in 1981–1982, and the other in 1990–1991 (Figure 2). There was a clear seasonal effect in the incidence of HFRS in Yingshang County, with most cases acquired in the autumn-winter, starting generally from October, reaching a

peak in November and December and ending in January (Figure 3).

Climate variability, autumn density of mice, autumn crop production and the incidence of HFRS in autumn-winter in Yingshang County, 1980–1996—correlation and regression analyses

Correlation analyses were conducted using (1) the incidence of HFRS in autumn-winter and the density of mice, crop production in the autumn and seasonal climatic variables such as temperature, precipitation, relative humidity, SOI and air pressure in Yingshang County, 1980–1996; and (2) the autumn density of mice and seasonal climatic variables and autumn crop production. The results are shown in Table 1.

Table 1 shows that the incidence of HFRS in autumn-winter was positively correlated with autumn crop production, the density of mice in autumn and seasonal mean minimum temperature in Yingshang County over the period of 1980–1996. Conversely, total precipitation, mean air pressure and mean SOI in autumn were inversely correlated with the autumn density of mice and the incidence of HFRS in autumn-winter.

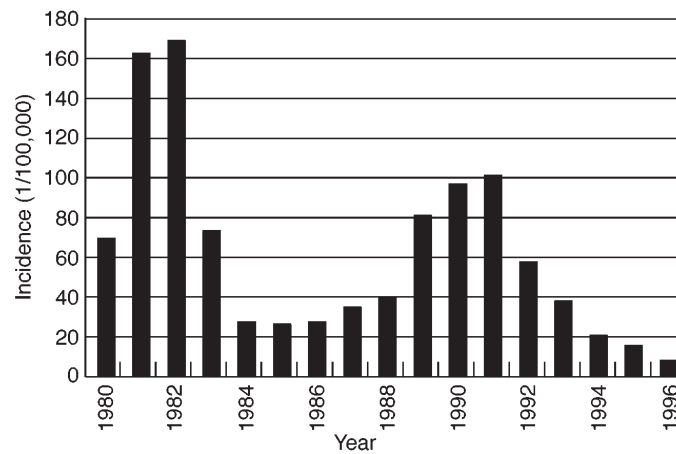


Figure 2 Annual incidence of haemorrhagic fever with renal syndrome (HFRS) in Yingshang County, 1980–1996 (1/100 000)

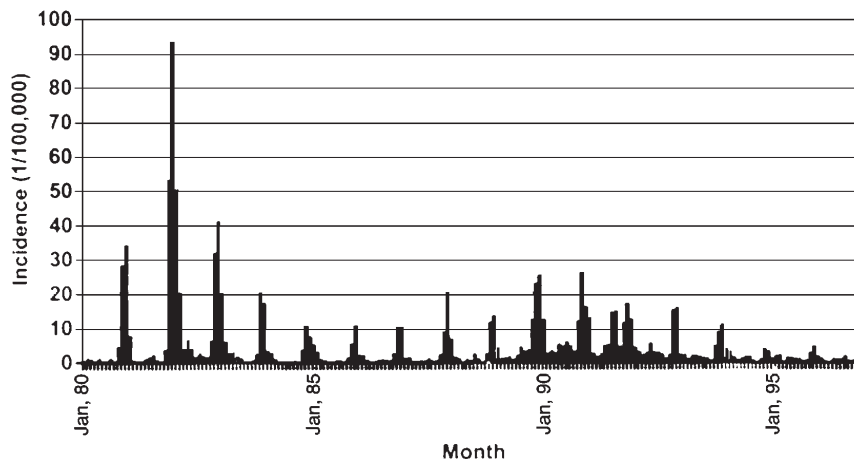


Figure 3 Monthly incidence of haemorrhagic fever with renal syndrome (HFRS) in Yingshang County, 1980–1996 (1/100 000)

Table 1 Spearman correlations among the density of mice and crop production in autumn, climatic variables and the incidence of haemorrhagic fever with renal syndrome (HFRS) in Yingshang County, 1980–1996

	Density of mice	Incidence of HFRS
Mean minimum temperature	0.53 ($P = 0.03$)	0.51 ($P = 0.04$)
Mean air pressure	-0.57 ($P = 0.01$)	-0.62 ($P = 0.01$)
Amount of precipitation	-0.69 ($P = 0.002$)	-0.63 ($P = 0.009$)
SOI ^a	-0.68 ($P = 0.003$)	-0.57 ($P = 0.02$)
Autumn crop production	0.61 ($P = 0.03$)	0.67 ($P = 0.01$)
Autumn density of mice	1.00	0.90 ($P = 0.000$)

^a Southern Oscillation Index.

Table 2 shows that the autumn density of mice and autumn crop production were positively associated with the transmission of HFRS, while the amount of rainfall showed a negative association. Together these factors explained 89% of variation in the incidence of HFRS. Therefore these factors might be treated as potential predictors of HFRS transmission in low-lying epidemic foci.

Discussion

Correlation analyses in this study showed that seasonal mean minimum temperature, the autumn density of mice and autumn crop production were positively correlated with the seasonal incidence of HFRS, while mean air pressure, rainfall and the SOI were inversely associated with it. Regression analysis indicated that the seasonal amount of precipitation, the density of mice and crop production in autumn could be used as predictors of HFRS transmission in the low-lying area of HFRS foci. The results suggested that climatic (rainfall), reservoir (the density of mice) and occupational (the autumn crop production, an indirect index) factors all played important roles in the transmission of HFRS. These findings are consistent with our previous report in which data from two local communities were analysed.³

About 90% of the HFRS epidemic foci in China are in low-lying regions with moist or semi-moist soils.¹ In Anhui Province, for example, HFRS cases usually occur in areas less than 100 m above sea level.¹ Low-lying regions with moist soil seem to provide a suitable environment for mice. The amount of precipitation could also influence the incidence of HFRS.^{1,3} For instance, the incidence of HFRS in 1980 in Anhui Province was 4.88/100 000 in the region with 400–800 mm annual precipitation, while in the region with >800 mm precipitation, the incidence was 0.43/100 000.¹ Hence, moist soil is necessary for the growth and development of the mice, but a large amount of rainfall could have a negative impact on mice by destroying their micro-environment. Also during flooding, fewer people are able to harvest crops so the number of people exposed is reduced. Moreover, because Yingshang County is located beside the Huai River, the epidemic focus of HFRS was inundated when heavy rain destroyed the banks of the Huai River. When there is heavy rain in summer, the Huai River bank on the Yingshang County side is usually destroyed and this allows floodwater to spread onto the adjoining land thus minimizing the potential damage to the industrial area on the opposite side of the Huai

Table 2 Adjusted associations of the incidence of haemorrhagic fever with renal syndrome (HFRS) in autumn-winter with climate variability, the density of mice, and autumn crop production in Yingshang County, 1980–1996

Explanatory variables	B	SE	P-value
Density ^a	0.2111	0.0110	0.005
Rain	-0.0152	0.0052	0.010
Crop ^b	0.1863	0.0096	0.003
Constant	-0.3998	0.0418	0.048
	R ² = 0.89		

^a The density of mice in autumn.

^b Autumn crop production.

River. When this strategic damage-control was implemented, the density of mice fell and thus, the incidence of HFRS decreased.¹¹

Minimum temperature is often associated with rodent survival and it may affect their numbers directly. Temperature, especially minimum temperature, could also change the behaviour of mice and people. In the harvest period, when the temperature is high, farmers in the County may sleep on their farmland because of the distance from home. Their huts may have no mice protection measures and thus they would have a high risk of exposure to the mice. However, the regression coefficient of this climatic index was not significant. This might be due to the strong cross-correlation between minimum temperature and rainfall ($r = 0.68$) and the impact of minimum temperature being swamped by the rainfall effect.

The mean values of climatic variables from July to September in Yingshang County were used to conduct the statistical analyses in our study. The reason for choosing these months is that it allows the examination of a lagged effect of climate variability to impact on the transmission of HFRS. The lag would capture the period of mice growth, virus development time within the mice and the virus incubation period within the human body. Furthermore, different mean values of climatic variables from different months and their relationship with the incidence of HFRS were quantified. It was found that the mean values of climatic variables from July to September were the most suitable indices.

Yingshang County is an epidemic focus with wild mice, mainly *Apodemus agravius*, as the main infection resource. There are two population peaks every year for *A. agravius*, one in the spring and the other in the autumn. Autumn is the main harvest season in Yingshang County, and farmers usually work on the farmland and have close contact with the mice.

Occupational factors also play an important role in the transmission of the disease. More than 95% of the population in Yingshang live in rural areas and their major occupation is agriculture. During the autumn harvest season, they work in their fields every day, and even live there. Hence, they have close contact with the mice. It is difficult to choose a direct index to reflect the degree of farmers' contact with mice, and the results of this study showed that autumn crop production might be a suitable indirect index.

Other factors, such as the mouse HFRS virus carrier rate, may also play a significant role in the transmission of HFRS. Unfortunately, such data were unavailable in Yingshang County during the study period. The density of indoor rats and their

virus carrier rate, population immunity and immigration may also impact on the transmission of the disease. In Yingshang County, however, the role of indoor rats is mainly related to sporadic cases of HFRS.^{1,8} The antibody titre of asymptomatic infection is too low to prevent the development of clinical cases.¹² Population movement may also be an important factor in the transmission of HFRS, although there was probably little population mobility in Yingshang County during the study period. These factors need to be considered in further research.

Climate change influences the emergence and re-emergence of infectious diseases including HFRS. In 1993, for example, the sudden appearance of a virulent, rodent-borne hantavirus in the arid US Southwest accompanied anomalous weather patterns.¹³ It is estimated that a rise of 2°C in global temperatures will occur by the year 2100 accompanied by irregular rainfall. Climate change would directly affect disease transmission by shifting the reservoir's geographical range and increasing reproductive rates and by shortening the pathogen's incubation period. Human migration and damage to the healthcare infrastructure from the projected increase in climate variability could indirectly contribute to disease transmission. Human susceptibility to the infection might be further facilitated by malnutrition as a result of climatic effects on agriculture and potential alterations in the human immune system caused by increased ultraviolet radiation. Therefore, increased HFRS and weather surveillance, integrated modelling, and use of geographically based data systems are necessary to monitor and prevent the disease.¹⁴

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