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Seasonal Rainfall Variability, the Incidence of Hemorrhagic Fever with Renal Syndrome, and Prediction of the Disease in Low-lying Areas of China

Peng Bi,[1,2] Xike Wu,[2] Fangzhen Zhang,[2] Kevin A. Parton,[3] and Shilu Tong[4]

To investigate determinants of hemorrhagic fever with renal syndrome (HFRS) in low-lying areas of China, the authors studied Chuigang and Wanggang communities in Anhui Province. These adjacent farming communities have a population of about 100,000. Data were collected from the two communities in 1961–1977 and from Yingshang County in 1983–1995; information covered the incidence of HFRS, amount of precipitation, differences in the water level of the Huai River, density of *Apodemus agrarius*, autumn crop production, and areas of inundated farmland. Correlation and multiple linear regression analyses were used to estimate the relation between seasonal rainfall, density of mice, occupational factors, and occurrence of the disease. Associations were observed between the incidence of HFRS and the amount of precipitation, the water level of the Huai River, and the areas of inundated farmland in Chuigang community. The smaller the water-level difference, the less farmland was inundated and the higher the incidence of HFRS. In Wanggang community, the density of *A. agrarius* ($r_1 = 0.63$, $p = 0.02$), the water-level difference in the Huai River ($r_2 = -0.81$, $p = 0.007$), and crop production ($r_3 = 0.96$, $p = 0.005$) were correlated with the incidence of HFRS. The regression analyses based on Wanggang community suggested that these indexes could be used as predictive variables, and the results from the model were well calibrated with the actual incidence of HFRS in that community ($R^2 = 0.88$, $p < 0.01$) and Yingshang County ($R^2 = 0.91$, $p < 0.01$). *Am J Epidemiol* 1998;148:276–81.

forecasting; hemorrhagic fever with renal syndrome; precipitation; topography, medical

The occurrence and epidemics of hemorrhagic fever with renal syndrome (HFRS) are influenced by both natural and occupational factors (1). Natural factors, such as low-lying and wet lands, level of precipitation, soil moisture, and state of the river system (the level of the water in the rivers and the amount of surrounding land), influence the ecologic environment of rodents (mainly mice), the host of the disease. Occupational activities, such as farming, mining, railway construction, and irrigation, might also affect the incidence of HFRS because they affect people's contact with rodents.

China has the highest incidence of HFRS in the world, and the country had more than 600,000 cases of the disease from 1958 to 1988. The incidence rate was highest in 1986, at 11.08 per 100,000 (1). Located in eastern China with a population of nearly 60 million, Anhui Province has one of the highest average incidence rates of HFRS in the country, at 10 per 100,000 (1). Most of the cases in Anhui Province occurred on low-lying lands along the Huai River. The incidence of HFRS seems to be associated with year-to-year variations in seasonal conditions in that province. Furthermore, over time, changes in natural and occupational conditions have affected the occurrence of the disease. Since the Industrial Revolution, emissions of greenhouse gases in the world have changed and will continue to change the global climate, which may have a significant impact on the distribution and amount of precipitation. These changes may have influenced and will continue to influence the incidence and distribution of communicable diseases (2).

This paper examines the relation between several key climatic and occupational variables (e.g., precipitation, water level of the Huai River, and crop production) and the occurrence of HFRS on low-lying land in Anhui Province, China. It also assesses potential determinants of the occurrence of the disease and predicts its incidence by using several indices.

MATERIALS AND METHODS

Study sites and population

Yingshang County is located on low-lying land along the Huai River, north of Anhui Province. It has

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Abbreviation: HFRS, hemorrhagic fever with renal syndrome.

[1] Department of Social and Preventive Medicine, University of Queensland, Brisbane, Australia.
[2] Department of Epidemiology, Anhui Medical University, Hefei, People's Republic of China.
[3] Department of Health Studies, University of New England, Armidale, Australia.
[4] School of Public Health, Queensland University of Technology, Kelvin Grove, Australia.

had epidemics of HFRS since 1958 (3). Chuigang and Wanggang are two county communities that have had consistently high incidence rates of HFRS; therefore, they were selected as research sites.

The two communities, with sea levels of 18.5–25.5 m, are located in southeast Yingshang County beside the Huai River (the third largest river in China). Tangduohu Lake lies to the southeast of the two communities, and the water level of the lake depends on the amount of precipitation and the water level of the Huai River. The water level of Tangduohu Lake usually increases in summer and autumn and decreases in winter and spring. The lake margins are used as farmland, even though they are inundated during flood years. The center of the lake is sometimes used as farmland when the water level is low, e.g., during drought years.

In the area around Tangdouhu Lake, about half of the farmland is on low-lying land, and the rest is located in more upland regions. The harvest season in the communities is between August and November. Farmers typically live in the fields during this season because their homes are at a distance, many as far as 10 km from the fields.

Data collection

For various reasons, including data availability, more information was obtained from Wanggang than from Chuigang community. Incidence rates of HFRS were collected from 1961 to 1963 in Chuigang community and from 1964 to 1977 in Wanggang community. Because of the frequent occurrence of HFRS, local physicians were very familiar with the disease, so the accuracy of diagnosis was high. Moreover, all reported cases were reexamined by physicians in the county hospital for confirmation.

Data on precipitation and differences in water levels of the Huai River between July and September in relevant years were collected from the county meteorologic and hydrologic stations. It was expected that changes in these variables during these months might affect the density of mice and thus the incidence of HFRS. These data were relevant to both Wanggang and Chuigang. Data on the density of *Apodemus agrarius* from 1964 to 1977 in Wanggang community were obtained from the county antiepidemic station. However, vector information was unavailable from Chuigang community.

Because most cases of HFRS occurred during the autumn and winter, data on crop production during the autumn harvest season in Wanggang community were used as an index of occupational factors to reflect local farmers' agricultural activity and their consequent degree of contact with the rodents. Crop production data were provided by the county department of agriculture. Because it is difficult to judge the accuracy of the crop production data, a Spearman's rank correlation analysis was used. The autumn crop production for each year from 1964 to 1977 was ranked as 1) less than 0.5 million kg, 2) 0.5 to less than 0.7 million kg, 3) 0.7 to less than 0.9 million kg, 4) 0.9 to less than 1.1 million kg, or 5) 1.1 million kg or more.

Information was also collected on the incidence of HFRS, density of *A. agrarius* (the number of captured mice divided by the number of mousetraps placed in a certain area), differences in the water level of the Huai River, and autumn crop production in Yingshang County between 1983 and 1995. The aim was to validate the predictive models.

Data analysis

In Chuigang community, associations of the occurrence of HFRS with the amount of precipitation, the water level, and the areas of inundated farmland were assessed by using correlation analyses. In Wanggang community, correlation analyses were conducted first, and then multiple linear regression analyses were used to relate the impact of the difference in the water level of the Huai River, the amount of precipitation, the density of *A. agrarius,* and crop production on the occurrence of HFRS.

In the regression model, the explanatory variables were the density of *A. agrarius,* the difference in the water level of the Huai River between July and September (because it can reflect variations in the water level of the river and the amount of precipitation as well as affect the water level of Tangduohu Lake), and crop production. The logarithm of the incidence rate of HFRS was used as the dependent variable because there was a strong exponential correlation between HFRS and the explanatory variables. The analysis covered the years 1964–1977, except for 1966 and 1969, when complete data on the density of *A. agrarius* were unavailable.

Standard partial regression coefficients were also calculated to determine the relative contribution of the explanatory variables (4). (A standard partial regression coefficient is a regressor of the following: (individual value − mean)/standard deviation, after adjustment for covariates.) Finally, predicted models were calibrated with the data on the actual incidence of HFRS in Wanggang community and Yingshang County.

RESULTS

Precipitation amount, water level, and the occurrence of HFRS

Data were examined for the three epidemic years from August 1961 to July 1964 in Chuigang community. It was found that higher incidence rates of HFRS were associated with lower levels of precipitation, a smaller difference in the water level of the Huai River (maximum minus minimum water level between July and September annually), and less inundation of farmland around Tangduohu Lake (table 1).

Clearly, these results from Chuigang simplify a complex situation considerably. The 1961 HFRS outbreak, which occurred when the lake was dry and exceptional crop production resulted, is well known, and most experts agree that it was far from normal. Hence, the results shown in table 1 suggest possible risk factors for the HFRS outbreak.

Correlation analysis

These potential risk factors were examined further using correlation analysis in Wanggang community. The results showed that the density of *A. agrarius,* the difference in the water level of the Huai River, and crop production were significantly associated with the incidence rate of HFRS ($r_1 = 0.63$, $p < 0.05$; $r_2 = -0.81$, $p < 0.01$; $r_3 = 0.96$, $p < 0.01$) (tables 2 and 3).

Multiple regression analysis

A multiple regression analysis was also conducted, using the difference in the water level of the Huai River and crop production in Wanggang community as explanatory variables and the logarithm of the incidence of HFRS in Wanggang community as the dependent variable. The results are shown in table 4 (model 1). To examine further the possible influence of the density of *A. agrarius,* this factor was included as an additional explanatory variable (table 4, model 2).

It was found that model 2 was better able to explain the incidence of hemorrhagic fever than model 1. Density of *A. agrarius* and autumn crop production were statistically significant. To determine the relative contribution of different explanatory variables, the standard partial regression coefficients were calculated as shown in table 4. These coefficients show that the relative contribution of autumn crop production to the occurrence of HFRS was almost three times greater than that of the other variables combined.

TABLE 1. Seasonal rainfall variability and incidence rate of hemorrhagic fever with renal syndrome, Chuigang community, Anhui Province, China, 1961–1964

Year	Autumn rainfall (mm)	Difference in water level* (m)	Inundated areas	Incidence rate (per 100,000)
August 1961–July 1962	297.4	2.87	No	1,505.90
August 1962–July 1963	452.5	5.39	Partly	251.10
August 1963–July 1964	864.9	9.30	All	16.10

* Maximum minus minimum difference in the level of water in the Huai River between July and September each year.

TABLE 2. Incidence rate of hemorrhagic fever with renal syndrome and predictive indexes, Wanggang community, Anhui Province, China, 1964–1977

Year	Incidence rate (per 100,000)	Predictive indexes: Density of *Apodemus agrarius* (%)*	Difference in water level (m)†	Crop production rank‡
1964	16.3	1.0	3.21	3
1965	99.8	3.2	7.76	5
1966	25.7	—§	2.25	—
1967	135.7	—	3.50	5
1968	2.5	—	8.81	1
1969	—	—	9.12	1
1970	44.9	1.5	4.74	4
1971	8.2	2.5	5.72	1
1972	4.1	5.4	7.13	1
1973	66.0	21.8	3.97	4
1974	246.1	26.1	3.01	5
1975	5.8	3.2	7.34	1
1976	107.8	7.8	3.60	4
1977	40.5	1.7	5.46	3

* Mousetraps were placed in the same field location for three consecutive nights. The number of captured mice divided by the total number of traps yielded the density of mice in that location.
† Maximum minus minimum difference in the level of water in the Huai River between July and September each year.
‡ Rank value is defined in the text.
§ Data unavailable.

TABLE 3. Comparison of exponential correlation coefficients between explanatory and dependent variables,* Wanggang community, Anhui Province, China, 1964–1977

Explanatory variable	Dependent variable	*p* value
Density of *Apodemus agrarius* (no. of mice/trap)	$r_1 = 0.6335$	<0.05
Difference in water level† (m)	$r_2 = -0.8075$	<0.01
Crop production (kg)	$r_3 = 0.9559$	<0.01

* Logarithm incidence of hemorrhagic fever with renal syndrome per 100,000.
† Maximum minus minimum difference in the level of water in the Huai River between July and September each year.

Test of predictive models

Using models 1 and 2 in table 4, predicted incidences of HFRS were obtained and compared with actual incidences from 1964 to 1977 in Wanggang community. The multiple correlation coefficients (R^2) were 0.89 ($p < 0.01$) and 0.88 ($p < 0.01$), respectively, which indicates that the regression equations were able to provide good explanations for the incidence of hemorrhagic fever and that the predicted incidence rate reflected the actual incidence rates of

TABLE 4. Two linear regression models of the incidence of hemorrhagic fever with renal syndrome,* Wanggang community, Anhui Province, China, 1964–1977

	Model 1		Model 2		
	β†	SE† (β)	β	SE (β)	Standard partial regression coefficient
Density of *Apodemus agrarius* (no. of mice/trap)			0.0113	0.0084	0.0013
Difference in water level‡	−0.0599	0.0350	−0.0416	0.0433	0.0013
Crop production (kg)	0.3297	0.0417	0.3436	0.0459	0.0077
Constant	−0.2237		−0.4210		
R^2	0.88		0.91		

* Dependent variable: logarithm of incidence per 100,000.
† β, linear regression coefficient; SE, standard error.
‡ Maximum minus minimum difference in the level of water in the Huai River between July and September each year.

HFRS on the low-lying land of the epidemic foci (figures 1 and 2).

An attempt was made with the same models to predict HFRS incidence rates from 1983 to 1995 in Yingshang County and to compare them with actual rates to test the model in another temporal and spatial context, although still one of low-lying land of HFRS foci. The results were similar to those obtained for Wanggang community ($R^2 = 0.91, p < 0.01$ for both models) (figures 3 and 4).

DISCUSSION

Potential risk factors for HFRS

The study in Chuigang community showed an inverse relation between the amount of precipitation, the water level of the Huai River, areas of inundated farmland (an index reflecting people's contact with rodents), and the incidence rate of HFRS on low-lying land. The same relation was also found in Wanggang community.

In the years with less-than-normal precipitation, the low-lying land around Tangduohu Lake provided more farmland to be planted. Thus, people worked more and spent more time on the low-lying land; more vegetation created a favorable microenvironment for mice; and more arable farmland provided more food for mice, which increased their number. All of these factors provided people with more opportunities for exposure to mice; therefore, the incidence rate of HFRS was expected to increase. In contrast, in the years with more precipitation than usual, the water level of the Huai River rose. As a result, the low-lying land, such as that around Tangduohu Lake, was inundated, the mice habitat was destroyed because of heavy rain and higher levels of water in the river, the density of mice was reduced, people had fewer chances for exposure to mice, and the incidence rate of HFRS decreased. For instance, in 1961–1962, when there was lower-than-normal precipitation, the local density of mice was 10 percent; in 1963–1964, when there was more precipitation, the density was 2 percent. Therefore, precipitation influences the density of mice and thus the incidence rate of HFRS. Hence, both the amount of precipitation and differences in the water level of the Huai River, as well as the areas of inundated farmland or the autumn crop production,

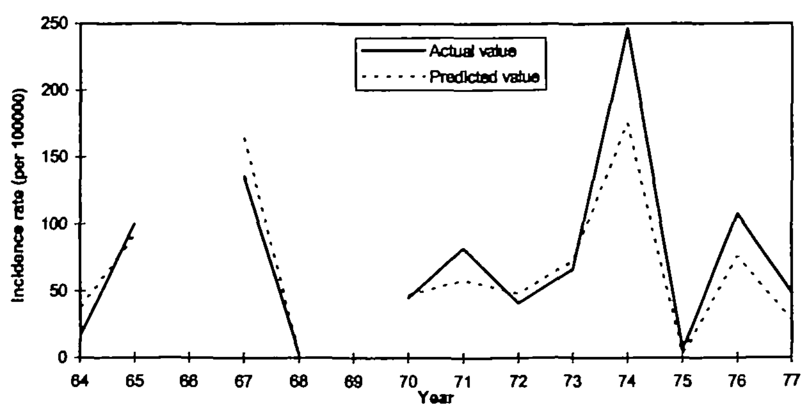

FIGURE 1. Comparison between actual and predicted incidence rates of HFRS in Wanggang community, 1964–1977 (using water-level difference of the Huai River and crop production as explanatory variables, as model 1 in table 4) (data missing in 1966 and 1969).

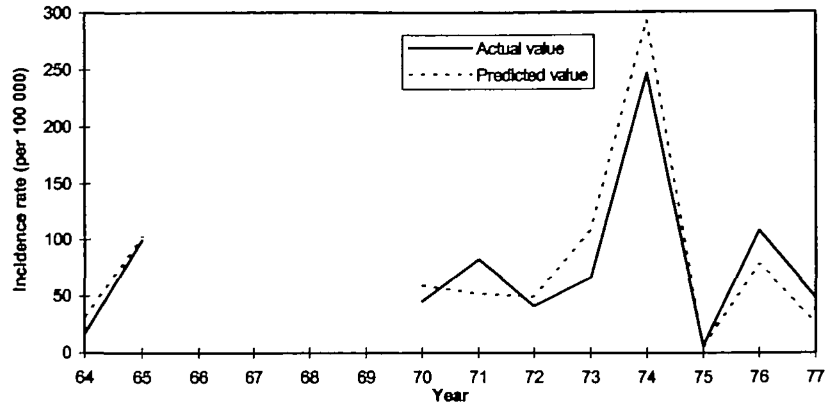

FIGURE 2. Comparison between actual and predicted incidence rates of HFRS in Wanggang community, 1964–1977 (using water-level difference of the Huai River, density of *Apodemus agrarius*, and crop production as explanatory variables, as model 2 in table 4) (data missing from 1966 to 1969).

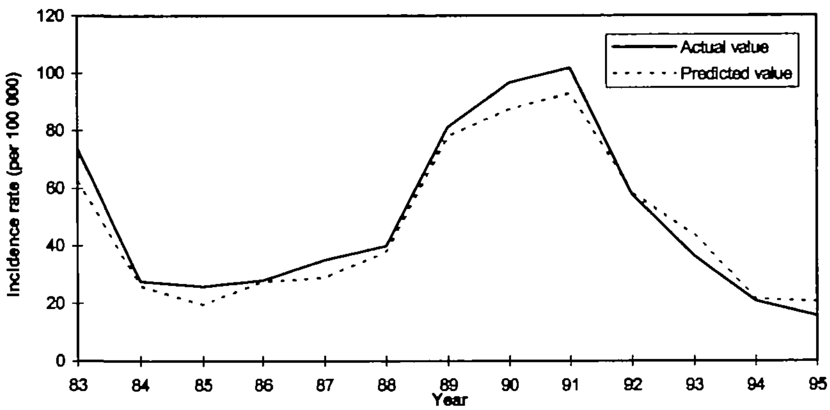

FIGURE 3. Comparison between actual and predicted incidence rates of HFRS in Yingshang County, 1983–1995 (using water-level difference of the Huai River and crop production as explanatory variables, as model 1 in table 4).

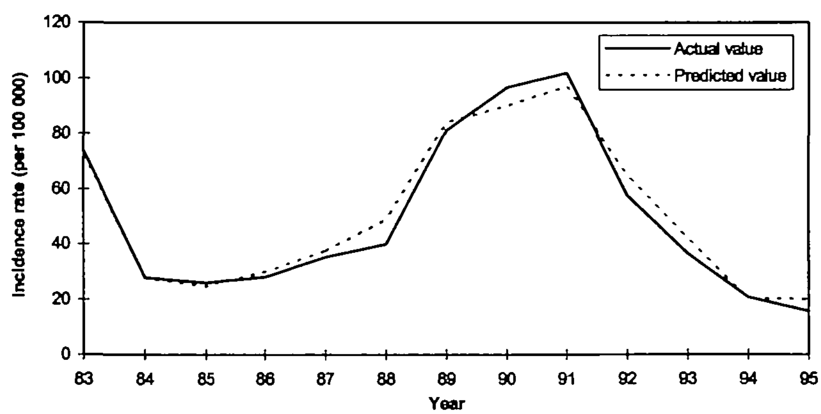

FIGURE 4. Comparison between actual and predicted incidence rates of HFRS in Yingshang County, 1983–1995 (using water-level difference of the Huai River, density of *Apodemus agrarius*, and crop production as explanatory variables, as model 2 in table 4).

might be predictive indices of HFRS for the low-lying land that was the focus of the epidemic.

A study in the former Soviet Union found that flooding forced mice to move to high land and caused a higher incidence of HFRS in the population there (5). Our study also found that during a period of higher-than-normal precipitation, the incidence rate of HFRS in some villages on high land was slightly higher than their usual incidence rate. However, the higher number of cases in these upland villages did not outweigh the lower number of cases elsewhere, so that the overall incidence of HFRS decreased.

Prediction of the occurrence of HFRS

HFRS comprises a group of serious infectious diseases that have been endemic in Asia, Europe, and the United States for a long time. It is important to study the determinants of epidemics and to look for possible indices to predict their occurrence.

The distribution of HFRS in China is related to topography, precipitation, and the river system (1). Most of the epidemic foci are low-lying and wet lands, within 100 m above sea level. Our previous study indicated an association between the amount of precipitation and the incidence rate of HFRS (1). In Anhui Province in 1980, for example, the rates per 100,000 were 4.88 in those areas with annual precipitation of 400–800 mm and 0.43 in areas with annual precipitation of more than 800 mm. Most of the HFRS cases were distributed along river systems such as the Yangtze and the Huai in Anhui Province, where the most suitable habitats for *A. agrarius* are located.

On the low-lying land of Anhui Province, the density of mice and people's agricultural activities were influenced by the amount of precipitation and differences in the water level of the nearby Huai River. The results of this study suggest that differences in water level are an important predictive index.

Another predictive index was agricultural activity, which reflected the frequency of people's contact with rodents. In Anhui Province, the main epidemic peak of HFRS occurred in autumn and winter, and agricultural activities such as sleeping in the fields, irrigating, and working on the farmland during the autumn harvest season might have played a significant role in the occurrence of HFRS. In the survey, however, it was difficult to collect such detailed data, so it was appropriate to choose crop production during the autumn harvest season as an index, which could indirectly reflect farmers' agricultural activities; this index could also be used in rank correlation analyses and was convenient to analyze.

A previous study showed that density of *A. agrarius,* the main host of the disease, was important to the development of HFRS (6). Most cases of the disease occur during the autumn and winter seasons, so the density of *A. agrarius* in September was selected as another predictive index.

The other factor that might be treated as a predictive index is the HFRS virus carrier rate of mice. Unfortunately, no detailed data were available for our study, because a method for detecting the virus was not invented until 1976 (6), only 1 year before data collection ended. This index should be used in future studies, however.

Many factors could affect the occurrence of HFRS, and it is difficult and unnecessary to consider all of them in predicting the disease. It is essential, however, to consider typical natural and occupational factors that have the most impact on the epidemic process of the diseases in this type of foci. In this case, the density of *A. agrarius,* differences in the water level of the Huai River, and crop production during the autumn season were selected as predictive indices. Results from the models that were estimated were well calibrated with the actual incidence rate of HFRS.

It is appropriate to use regression analysis to explain the incidence rates of communicable diseases (e.g., HFRS) when using data available on major indices. However, predictive results may not be accurate if the observation period is too short or if unusual events occur, such as disease control programs, population movement, or both. The results of this study should be interpreted cautiously, since the dynamics of HFRS transmission may be different in different types of epidemic foci. Multifactorial influences, such as occupational and environmental factors, climate variability, observation period, and quality of data, should be considered in the prediction of communicable diseases such as HFRS.

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