The Spatial–Temporal Trend Analysis of Schistosomiasis from 1997 to 2010 in Anhui Province, Eastern China

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Abstract. Schistosomiasis is still prevalent in some parts of China. A shift in strategy from morbidity control to elimination has led to great strides in the past several decades. The objective of this study was to explore the spatial and temporal characteristics of schistosomiasis in Anhui, an eastern province of China. In this study, township-based parasitological data were collected from annual cross-sectional surveys during 1997–2010. The kernel *k*-means method was used to identify spatial clusters of schistosomiasis, and an empirical mode decomposition technique was used to analyze the temporal trend for *Schistosoma japonicum* in each clustered region. Overall, the prevalence of schistosomiasis remained at a low level except for the resurgence in 2005. According to the Caliński–Harabasz index, all the townships were classified into three different clusters (median prevalence: 3.6 per 10,100, 1.8 per 10,000 and 1.7 per 10,000), respectively representing high-, median-, and low-risk clusters. There was an increasing tendency observed for the disease over time. The prevalence increased rapidly from 2003 to 2005, peaked in 2006, and then decreased afterward in the high-risk cluster. A moderate increase was observed in the median-risk cluster from 1998 to 2006, but there was an obvious decreasing tendency in the low-risk cluster after the year 2000. The spatial and temporal patterns of schistosomiasis were nonsynchronous across the three clusters. Disease interventions may be adjusted according to the risk levels of the clusters.

INTRODUCTION

Schistosomiasis is a vector-borne tropic disease caused by the genus *Schistosoma*, which are free-swimming worms in the freshwater.^{1–3} The transmission takes place as soon as the larval worm is released by the intermediate host, snail, and penetrates the skin of human or animal reservoirs in contaminated water.¹ According to the World Health Organization, approximately 258 million people worldwide needed a preventive treatment of schistosomiasis in 2014 and 91% of them live in Africa.^{4–6} The global burden of schistosomiasis was estimated to be 3.31 (95% confidence interval: 1.70–6.26) million disable-adjusted years.⁷ Schistosomiasis has spread to 78 countries or regions,⁵ particularly to places with poor hygiene and hampered socioeconomic development. It remains an important global public health issue, ranking next to malaria among all the parasitic diseases.^{2,8}

Of the five major schistosomiasis species, *Schistosoma japonicum* is prevalent in China. With an estimated 11.6 million people infected,⁹ the 12 provinces along the Yangtze River used to be the hard-hit regions in the early period after the birth of the People's Republic of China.³ The climate and hydrology provide an ideal environment for the breeding of the intermediate host, the snail.¹⁰ The Chinese central government has made a great effort to control the epidemic of *S. japonicum* infection over the last 60 years, and Anhui was reported with a prevalence of 1.45‰ in 2005 by a recent study.¹¹ National control programs included the World Bank Loan Project (WBLP) from 1992 to 2001, which emphasized

chemical therapy, and an integrated control program implemented since 2005, which focused on the control of infection sources. Both of them have been successively implemented in the endemic provinces.¹² However, there has been a reemergence of the disease in some areas and it remains a challenge for the achieving the goal of eliminating schistosomiasis by the end of 2025.^{13–15}

The distribution of schistosomiasis has a particular spatial characteristic in China.^{16,17} It is important to delineate and define the spatial distribution and temporal trend of schistosomiasis for the sake of targeted prevention and control. Several traditional time series analytical methods, including Fourier and wavelet transform, assume linear data, which may not always agree to the actual conditions.^{18,19} An empirical mode decomposition (EMD) approach has an advantage in dealing with nonlinear and nonstationary time series. In this study, we explored the spatial and temporal characteristics of schistosomiasis based on the annual prevalence data at the township level from Anhui province from 1997 to 2010, using the methods of kernel *k*-means and EMD.

MATERIALS AND METHODS

Study area. Anhui province (29°41'–34°38'N, 114°54'–119°37'E) is located in the lower reaches of the Yangtze River basin in eastern China (Figure 1), covering an area of 139,600 km² and including 16 cities and 61 counties with a population of approximately 61.44 million residents (2015). The climate is warm and humid, with the annual temperature between 14°C and 17°C on average. There are two major rivers in Anhui—Huai River and Yangtze River, flowing through the north and south parts of the landscape, respectively.

Schistosomiasis infection data. Cross-sectional studies were conducted in epidemic administrative villages between

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FIGURE 1. The epidemic areas and sample townships in this study in Anhui province of east China. The purple points (97) represent the center of the sample townships, and the Huai River and Yangtze River flow through the north and south parts of the province, respectively. The map was created using the ArcGIS 10.0 software (ESRI Inc., Redlands, CA). This figure appears in color at www.ajtmh.org.

October and November every year during 1997–2010 with assistance from the local antischistosomiasis station. Individuals aged 5–65 years were the targeted population, and the data of infection were synthesized at the township level. All the participants were screened by using a serological test (indirect hemagglutination assay [IHA]), and then stool samples were collected from the seropositive individuals, and the Kato–Katz technique was used to determine the existence of *S. japonicum* eggs. A resident was defined as a case of *S. japonicum* infection if the resident was positive in both IHA testing and fecal examination. The human infection rate for each township was calculated by the formula: Human infection rate (%) = (positive case number of fecal testing/a total number of serological testing at the township level) $\times$ 100%. In this study, the database comprised 97 townships that met the following criteria: 1) the township was surveyed every year from 1997 to 2010 and 2) the number of the participants within the township was more than 100 (Figure 1).

Ethical statement. This study was approved by the Research Ethics Committee of Fudan University (ID: IRB #2011-03-0295), Shanghai, China. Written informed consents were provided by all the adult participants and the parents or guardians of all child participants less than the age of 18 years.

Statistical analysis. *Spatial and temporal clustering.* We used kernel *k*-means to identify different clustered risk areas of schistosomiasis. There were 97 townships, and each observation included a time series containing data of 14 yearly prevalences of schistosomiasis and their geographical locations. However, the yearly prevalence data in one township were not always higher or lower compared with those of other townships, and the observed data interwove together, which were not suitable to be separated with a linear method.^{20,21} The kernel *k*-means algorithm is generalized from the standard *k*-means algorithm,²² which has an advantage in detecting clusters that are nonlinearly separable in input (original)

space.²³ Before the clustering, data points were mapped from the input space (*X*) to a higher dimensional space (*H*) by using a kernel function *k*. This function calculates the inner product of two sample points *x_i* and *x_j* if a projection $\phi: X \rightarrow H$ is used, which highlights the differences in characteristics between samples of different categories and allows the samples to be linearly separable (or approximately linearly separable) in feature space.²⁴ In this study, we selected the Gaussian kernel function, which is a general purpose kernel and is typically used when no further earlier knowledge is available about the data.²⁵

$$k(x_i, x_j) = \exp\left(-\sigma \|x_i - x_j\|^2\right)$$

After the projection, a classical *k*-means partitioned the points ($\phi[x_i]$) in feature space. The optimal number of clusters, *k*, can be determined by the Caliński–Harabasz (CH) index²⁶ which builds statistics to make homogeneity within clusters and heterogeneity between clusters based on the principle of *F*-test. In this study, we tried to calculate the CH index by selecting different clustering numbers (*k*) from 2 to 10 to find the optimal division.

$$CH(k) = [B/(k-1)]/[W/(n-k)],$$

where *B* denotes the variance between the clusters, *W* represents the variance within the cluster, *k* value stands for the numbers of the cluster, and (*k* – 1) and (*n* – *k*) are on behalf of the free degree of within-clusters and between-clusters, respectively. Because the higher the CH index computed, the better the clustering results are, *k* value will be selected according to the corresponding maximized CH index. In this study, we use the function of kernel *k*-means in “kernlab” package of R software (version 3.3.2) for the analysis.

Temporal trend analysis. Empirical mode decomposition, a rapidly developing method for signal processing invented by Huang (1998),¹⁹ was used to analyze the temporal trend of schistosomiasis prevalence in the clustered areas during 1997–2010. The EMD approach decomposes the original data into several intrinsic mode functions (IMFs) to identify an oscillation embedded in a signal from a local time scale.²⁷ The lowest frequency of the IMF component called residual, which cannot be decomposed, usually represents the trend of the original signal. An IMF should satisfy the following two conditions: 1) the number of extrema and the number of zero crossings must be either equal or differ at most by one in the whole dataset and 2) at any point, the mean value of the envelope defined by the local maxima and the envelope defined by the local minima is zero. The prevalence series of schistosomiasis $x(t)$ can be represented by the formula:

$$x(t) = \sum_{i=1}^n h_i(t) + r_n(t),$$

where n is the number of decomposed IMF and r_n is the trend of yearly prevalence of schistosomiasis. The R software (version 3.3.2) ran the above sifting processes with the “EMD” packages written by Donghoh and Heeseok.²⁷

RESULTS

Figure 2 presents the prevalence of schistosomiasis during the study period. Overall, the prevalence increased gradually from 0 to 3.7 cases per 10,000 from 1997 to 2002. A resurgence occurred in 2005, with the prevalence being 6.64/10,000, and the prevalence decreased afterward to 1.05/10,000 in 2010. The trend of annual interquartile range of schistosomiasis was consistent with the changes of yearly medians and varied from 0–36.25/10,000 in 2001 to 0–6.44/10,000 in 2010.

As shown in Figure 3, the maximum value of the CH index was 109.1 when k was set to 3, which reached to the best sum of the square split, and therefore, the 97 towns were finally divided into three clusters. Figure 4 depicts the spatial distribution of the three clusters; the first cluster consisted of 31 townships with a median prevalence of 3.58 per 10,000; the second cluster (median risk) included 39 townships with a median prevalence of 1.785 per 10,000; and the third cluster (low risk) contained 27 townships with a median prevalence of 1.665 per 10,000.

Figure 5 represents the temporal tendency of schistosomiasis in each cluster during the study period. For the high-risk cluster, the prevalence increased modestly from 1998 to 2002 and increased rapidly from 2003 to 2005, and then decreased afterward. For the median-risk cluster, the prevalence continued to rise slowly from 1998 to 2005 and remained stable afterward. For the low-risk cluster, the prevalence of schistosomiasis increased at first and then decreased steadily to a low level after the year 2000. When comparing the trend curves, all the three clusters showed a rising tendency before 2000.

DISCUSSION

Based on the annual prevalence of schistosomiasis in 97 townships in Anhui for the period from 1997 to 2010, this study presented the spatial pattern and temporal trend of schistosomiasis over the middle and lower reaches of the Yangtze River. In this study, the median prevalence was at a low level with little change, indicating that the overall situation of schistosomiasis in Anhui province was under good control for the study period. In the past six decades, Anhui province has always been one of the high schistosomiasis epidemic areas, and the epidemic is difficult to control because of the complex landform and suitable climate for the survival of snails.¹⁷ Anhui province has a comprehensive and diverse

FIGURE 2. The annual prevalence and its trend of schistosomiasis (cases per 10,000) in 97 townships in Anhui province, east China, from 1997 to 2010. The blue points represent the medians and the red vertical line denotes the interquartile range. This figure appears in color at www.ajtmh.org.

FIGURE 3. Calculating the Caliński-Harabasz (CH) index by setting different k values from $k = 2$ to $k = 10$. The maximum value of the CH index is 109.1 when k is set to 3. This figure appears in color at www.ajtmh.org.

landscape including plains, hills, mountains, and lakes, and the endemic area is characterized by marshlands and lake regions where freshwater provides a good condition for the survival of the intermediate host of schistosomiasis.²⁸ Local residents of the regions might come in contact with contaminated water through rice cultivation, bathing, fishing, household works, and some other water-related activities.

The WBLP for schistosomiasis control had been implemented since 1992, which aims at reducing the prevalence of schistosomiasis by means of large-scale chemotherapy in humans and livestock, complemented by health education (e.g., videos for school children and relative knowledge for health workers and communities), chemical control of snails (e.g., focal Geographic Information System (GIS)/Global Position

FIGURE 4. The spatial distribution of three clusters among 97 townships according to the annual prevalence of schistosomiasis in Anhui province. The red points stand for the townships with high risk, and the yellow and green points represent the median-risk and low-risk townships for schistosomiasis, respectively. The map was created by using ArcGIS software (version 10.0; ESRI Inc.). This figure appears in color at www.ajtmh.org.

FIGURE 5. The temporal trend of schistosomiasis of the three clusters decomposed by the empirical mode decomposition method. Red solid line: high-risk cluster; orange long dashed line: median-risk cluster; green dashed line: low-risk cluster. This figure appears in color at www.ajtmh.org.

System (GPS) and chemical-based mollusciciding), and environmental modification (e.g., conduit hardening and paddy farming land rotation).^{29–31} Mass chemotherapy served as a cornerstone and covered the target populations such as school-aged children, adults at risk (e.g., fishermen, farmers, or women for their domestic work), or entire communities across the endemic areas in China.³² The stable and low level of schistosomiasis prevalence in the study area before 2000 might be attributed to the implementation of the WBLP. However, its prevalence in all the three clusters tended to increase from the year 1998, which was probably due to an extremely heavy flood³³ in 1998 and the end of the WBLP in 2001³⁴. The study found that the large-scale chemotherapy and health education of the WBLP had a far-reaching and marked effect on reducing the infection rate in humans, but it might not achieve a long-term and substantial disease interruption.³⁴ Chemotherapy may reduce disease prevalence only at the time of its implementation but does not prevent individuals from reinfection.³⁵

In addition, a severe flood occurred in 1998 along the Yangtze River, resulting in snail migration and expansion into new niches,³³ which increased the likelihood of local residents to contact contaminated water. There was a delayed effect of the flood³⁶ because an individual infected by cercaria would experience an incubation period of 2 or 3 years to become an infectious individual, which may explain the moderate rise of infection rate from 2000 in the high-risk cluster and a continuous increase in the cluster of median risk.

As shown in Figure 5, the infection rate in the high- and median-risk clusters advanced to a new level in 2005. After the end of the WBLP, schistosomiasis prevention and control was funded by local governments to continue the implementation according to the original chemotherapy strategies of the WBLP.³⁴ The WBLP strategy focused on mass drug administration and made a short-term impact on reducing the prevalence; however, flooding caused a heavy endemic of schistosomiasis reinfection in 2005.³⁵ An integrated control

strategy emphasizing on breaking off the chain of transmission of schistosomiasis was implemented since 2005.^{37,38} After that, it was observed that the temporal trend of schistosomiasis prevalence declined at various degrees in both the high-risk and median-risk clusters. Earlier studies also found that the dynamic change in schistosomiasis prevalence was related to the activities of integrated control strategies.^{39,40} Our data indicated that both WBLP and integrated control strategies had a significant impact on schistosomiasis control, although the three clusters did not present completely consistent temporal tendencies. Empirically, epidemic areas were empirically divided into different risk levels based on the human infection rate of schistosomiasis^{3,30,34}; however, this classification may not be sensible. Thus, it would be helpful to apply kernel *k*-means, a clustering method based on statistical theory, to detect and analyze different spatial clusters to take targeted and effective intervention measures.

The EMD method has been successfully applied in several fields, such as mechanical fault diagnosis⁴¹ in engineering science and stock price analyses.⁴² It is an emerging new technique for the temporal trend analysis of infectious diseases in the field of spatial epidemiology. However, there are still some limitations in our study. First, the effect of potential risk factors, such as human behavior, socioeconomic characteristics, and environmental factors, affecting schistosomiasis was not considered and adjusted in our study when using the kernel *k*-means clustering methods, which might partly explain the poor clustering effect in geography. Second, the sensitivity and specificity of the diagnostic methods need to be further evaluated. The problem of low specificity of IHA and low sensitivity of the Kato-Katz technique, approximately ranging 80–90%⁴³ and 20–70%,⁴⁴ respectively, became a crucial issue in estimating the prevalence of schistosomiasis. Uncertainties in the diagnostic method should be considered in future studies.

In summary, the overall prevalence of schistosomiasis in Anhui province had declined to a low level during the study period, and the south part of the province along the Yangtze River remained a key area for schistosomiasis control. Three different risk clusters were found in our study, and the curves of their temporal trend were nonsynchronous. Our findings suggested that the spatial and temporal dynamic changes of the disease should be monitored according to different risk clusters, and target and specific interventions can be developed and implemented to achieve the goal of eliminating schistosomiasis.

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