Analysis of Spatial Distribution Characteristics of Human Echinococcosis at the Township Level in Sichuan Province, China

Wei He
Sichuan Center for Disease Control and Prevention

Wen-jie Yu
Sichuan Center for Disease Control and Prevention

Guang-jia Zhang
Sichuan Center for Disease Control and Prevention

Sha Liao
Sichuan Center for Disease Control and Prevention

Qi Wang
Sichuan Center for Disease Control and Prevention

Rui-rui Li
Sichuan Center for Disease Control and Prevention

Bo Zhong
Sichuan Center for Disease Control and Prevention

Liu Yang
Sichuan Center for Disease Control and Prevention

Ren-xin Yao
Sichuan Center for Disease Control and Prevention

Yang Liu
Sichuan Center for Disease Control and Prevention

Dan-ba Zeli
Ganzi Center for Disease and Prevention

Sheng-chao Qin
Aba Center for Disease and Prevention

Shi-an Wang
Liangshan Center for Disease and Prevention

Yan-xia Wang
Ya-an Center for Disease and Prevention

Yan Huang
Sichuan Center for Disease Control and Prevention

Qian Wang ( wangjqian1967@163.com )
Sichuan Center for Disease Control and Prevention

Research Article

Keywords: Sichuan province, Echinococcosis, Prevalence, Spatial autocorrelation

DOI: https://doi.org/10.21203/rs.3.rs-160062/v1

License: Creative Commons Attribution 4.0 International License. Read Full License
**Abstract**

**Background**

Echinococcosis is a global zoonotic parasitic disease caused by the larvae of *Echinococcus*, which affects both humans and animals. In China, this disease is highly endemic in Sichuan Province. In this study, we investigated the prevalence and spatial distribution characteristics of human echinococcosis at the township level in Sichuan province, so as to provide a reference for the development of precise prevention and control strategies in the future.

**Methods**

We explored the prevalence of echinococcosis using the B-ultrasonography diagnostic method in Sichuan province between 2016 and 2019, where patients and transmission conditions had been identified in the past. All data were inputted using Epi-Info software, while SPSS software was used for statistical analysis. We then employed ArcGIS software to draw the spatial distribution map and perform trend surface analysis. Finally, Geoda software was used to analyze spatial autocorrelation and draw Lisa clustering map.

**Results**

A total of 2,542,135 people from 649 towns in 35 counties of Sichuan province were screened for echinococcosis, of which 11,743 echinococcosis patients were detected. The prevalence of echinococcosis in humans was 0.462%, among which the occurrence of cystic echinococcosis [CE] was 0.221%, while that of alveolar echinococcosis [AE] was 0.244%. We also observed that the predominance of echinococcosis in humans decreased gradually from west to east and from north to south based on the results of the spatial distribution map and trend surface analysis. The Global Moran's I index was 0.77 (Z = 32.07, P < 0.05), which indicated that the prevalence of echinococcosis in humans was spatially clustered, exhibiting a significant spatial positive correlation. Further, the findings of local spatial autocorrelation analysis revealed that the “high-high” concentration areas were primarily located in some townships in the northwest of Sichuan province. On the other hand, the “low-low” concentration areas were predominantly located in some townships in the southeast of Sichuan province.

**Conclusion**

Our findings demonstrated that the prevalence of echinococcosis in humans of Sichuan province is following a downward trend, implying that the current prevention and control work has achieved some substantial outcomes. However, the prevalence in humans at the township level is widely distributed and differs greatly, with a clear clustering in space. Therefore in the future, precise prevention and control strategies should be formulated for clusters, particularly strengthening the “high-high” clusters at the township level.

**Background**

Echinococcosis (also known as hydatid disease) is a zoonotic parasitic disease caused by the larvae of *Echinococcus* spp. Because of its specific manifestation and transmission mode in the hosts, it is defined to group C infectious diseases in China. It is a global public health problem due to the seriousness of the hazard [1–3]. Previous studies have established that four species of *Echinococcus* spp., namely, *echinococcus granulosus* (E.g), *echinococcus multilocularis* (E.m), *echinococcus oligarthrus* (E.o), and *echinococcus vogeli* (E.v), are responsible for echinococcosis in humans, of which E.g and E.m are the most significant [4, 5]. The larvae of these four species of *Echinococcus* spp are subjected to three types of echinococcosis in humans, including cystic echinococcosis (CE), alveolar echinococcosis (AE), and polycystic echinococcosis (PE) [6]. Infected canines and felines such as dogs, wolves, foxes, and cats are important infection sources of echinococcosis. Intermediate hosts include even-toed ungulates and small mammals, while humans are involved as incidental hosts. This disease is primarily transmitted through the fecal-oral route. It has been identified that people living in echinococcosis-endemic areas are all susceptible to echinococcosis, and high-risk groups mainly include those involved in agricultural production, livestock slaughter, fur processing, and hunting. The life cycle of *Echinococcus* spp. must be completed by canine (feline) and cloven-hoofed animal hosts/small mammals, which involves three processes including egg, metacestode, and adult worm. This disease is clinically characterized by a range of symptoms, such as cyst pressure and irritation to affected organs, pain, fever, and allergic reactions [7]. Studies have shown that the mortality rate of AE exceeds 90% in patients who have been either untreated or undertreated for 10–15 years [8].

Echinococcosis infection is widespread worldwide, showing priority in agricultural and pastoral areas. It has been demonstrated that different *Echinococcus* spp. that cause different types of echinococcosis exhibits different global distributions, resulting in differences in the prevalence of different types of echinococcosis and regions. Currently, there are only two kinds of echinococcosis in China, namely, CE and AE, which are some of the highly prevalent types in other countries in the world. In comparison, the disease burden of AE in terms of Disability Adjusted Life Years (DALY) in China accounted for 91%, while that of CE in the same country accounted for 40% of the world [9, 10]. Multiple recent reports have highlighted that echinococcosis is primarily dominant in pastoral areas and semi-agricultural and semi-pastoral areas of Inner Mongolia, Sichuan, Tibet, Gansu, Qinghai, Ningxia, Yunnan, Shaanxi, and Xinjiang in northwest China, especially in Sichuan, Tibet and Qinghai.
in Qinghai-Tibet Plateau [11, 12]. Of these regions, Sichuan is one of the provinces with the most serious prevalence of echinococcosis in China, with a mixed epidemic area of CE and AE. According to a report by the national survey conducted in 2012 in Sichuan province, echinococcosis was prevalent in 35 counties in Sichuan, mainly predominant in the whole area of Ganzi (18 counties) and Aba prefectures (13 counties), in Muli and Yuexi counties of Liangshan prefecture, and also in Tianquan and Baoxing counties of Ya'an city. Subsequently, the estimated prevalence was 1.08% [13, 14].

Presently, although the occurrence of echinococcosis in Sichuan province is clear at the county level, it remains elusive at the township level that needs further inquiry. To fully understand the current status of the human echinococcosis prevalence at the township level in Sichuan Province, we herein performed echinococcosis screening for the whole population in Sichuan province from 2016 to 2019.

Recently, the spatial statistical analysis method has been widely applied in the field of epidemiologic study of echinococcosis, particularly in evaluating the difference of prevalence in different regions and identifying disease clustering [15, 16]. For instance, in 2009, Brundu et al. analyzed the spatial scan statistics of 1029 pastures where CE of bovine was found in Sardinia and Italy, revealing two clusters existed [17]. In another report, a spatial autocorrelation analysis of the prevalence of echinococcosis in 13 counties of Aba Prefecture in Sichuan province using the global Moran's I method by Qi YF demonstrated that the incidence of echinococcosis had a significant clustering distribution, whereas the global Getis'G result elucidated that there were clusters with a high prevalence of echinococcosis [18]. In addition, a study by Zhao Y et al. used spatial scan statistics and spatial autocorrelation analysis methods to assess the detection rate of echinococcosis in 18 counties of Ganzi Prefecture in Sichuan province, concluding that there was aggregation in the spatial distribution of echinococcosis [19].

In this work, we analyzed the spatial aggregation of human echinococcosis prevalence at the township level in Sichuan province using global and local spatial autocorrelation analysis methods. We hereby aim to identify the spatial aggregation areas of echinococcosis at the township level in Sichuan province, so as to determine the areas that need to strengthen the key prevention and control in the future. We also purposed to provide a baseline reference for the formulation of precise strategies and measures for the prevention and mitigation of echinococcosis.

**Materials And Methods**

**Survey areas**

A survey conducted from 2016 to 2019 was used to investigate the prevalence of human echinococcosis in areas where many echinococcosis cases were reported previously. The scope of this study comprised of 325 townships under 18 counties in Ganzi Prefecture, 230 townships under 13 counties in Aba Prefecture, 70 townships under 2 counties in Liangshan Prefecture, and 24 townships under 2 counties in Ya'an City. Overall, 649 townships were covered to screen human echinococcosis (Fig. 1).

**Survey contents and methods**

**Taget population**

All permanent residents (including those who had a continuous residence at the surveyed areas for more than 6 months) aged 2 years and above were screened for Echinococcosis.

**Survey of prevalence**

We investigated the prevalence of human echinococcosis based on the requirements of the Technical Plan for Echinococcosis Prevention and Control. We then performed a B-ultrasound examination of the abdomen using the portable ultrasonic diagnostic instrument. Patients were diagnosed following the Diagnostic Criteria for Echinococcosis (WS257-2006)[20], while serological tests were supplemented to suspected patients. In particular, the anti-echinococcosis antibody in the serum of suspected patients was detected with ELISA. The IgG Antibody Diagnostic Kit was purchased from Shenzhen Kangbaide Biotechnology Co., Ltd.

**Trend surface analysis**

We adopted trend surface analysis to establish whether the prevalence of echinococcosis at the township level exhibits a trend in Sichuan province, as well as to understand the trend direction and degree.

**Spatial clustering analysis**

In this study, the detection rate of human echinococcosis in Sichuan Province was analyzed by global autocorrelation and local control autocorrelation, in order to understand the aggregation degree and scope of echinococcosis.

**Data processing and statistical analysis**
In this study, all data (consisting of name, sex, age, lesion type, lesion size, and location) were inputted using Epi-info software version 7.2.4. We subsequently combined the data of 35 counties. The error and duplicate data were eliminated, whereby the error was corrected via the double-entry comparison method, and error corrections were made using the two-item comparison method, and finally a human echinococcosis screening database was created.

Statistical data analyses were executed using SPSS version 21.0 software. We also calculated the prevalence of human echinococcosis in each township.

Prevalence of human echinococcosis was calculated as per the following formula:

\[ P = \frac{n}{N} \times 100\% \]

where P is the prevalence of the population in the surveyed area, n refers to the number of patients detected, and N denotes the number of examined people.

We further used the ArcGIS 10.2 software to map the spatial distribution map of the human echinococcosis prevalence at the township level and to analyze the trend surface, while GeoDa 1.6.7 software was employed to analyze the prevalence of human echinococcosis in townships for global and local spatial autocorrelations. Then, the spatial autocorrelation indexes were respectively adopted as Global Moran's I index and Anselin's Local Moran's I index, and the related results were displayed visually. A level of \( P < 0.05 \) was considered statistically significant.

**Results**

**Basic information**

In total, 649 townships from 35 endemic counties in 4 prefectures (cities) of Sichuan province were included to carry out this survey. A total of 2 758 525 people were examined, and 11 743 patients were detected. Notably, we found the distribution of patients in 426 townships, including 405 townships with CE patients, 167 townships with AE patients, and 146 townships with both kinds of echinococcosis patients (Table 1).

| City          | No. of townships surveyed | No. of CE epidemic townships | No. of AE epidemic townships | No. of total epidemic townships |
|---------------|---------------------------|-------------------------------|-------------------------------|--------------------------------|
| Aba Prefecture| 230                       | 134                           | 40                            | 146                            |
| Ganzi Prefecture| 325                      | 255                           | 125                           | 262                            |
| Liangshan Prefecture| 70              | 12                            | 0                             | 12                             |
| Ya’an City    | 24                        | 4                             | 2                             | 6                              |
| Total         | 649                       | 405                           | 167                           | 426                            |

**Geographical distribution**

Here, we found that the prevalence of echinococcosis in Sichuan province was 0.462%. Noticeably, 5 out of the 35 endemic counties exhibited a predominance of more than 1%, namely, Shiqu (6.512%), Seda (3.056%), Baiyu (1.237%), Dege (1.180%), and Ganzi (1.171%) counties (Table 2).
Table 2 The prevalence of human echinococcosis of epidemic counties in Sichuan province

| City          | County | Total no. of township | Pop. in endemic areas | No. exam’d | Total no. of patients | Total prevalence (%) | CE No. patients | Prevalence (%) | AE No. patients | Prevalence (%) |
|---------------|--------|-----------------------|-----------------------|------------|-----------------------|----------------------|----------------|----------------|----------------|----------------|
| Aba Prefecture| Aba    | 21                    | 84 299                | 75 150     | 109                   | 0.145                | 83             | 0.110          | 26             | 0.035          |
|               | Heishui| 17                    | 63 700                | 57 226     | 46                    | 0.080                | 39             | 0.068          | 7              | 0.012          |
|               | Hongyuan| 11                    | 47 186                | 45 751     | 90                    | 0.197                | 83             | 0.181          | 7              | 0.015          |
|               | Jinchuan| 23                    | 86 657                | 79 499     | 95                    | 0.119                | 91             | 0.114          | 4              | 0.005          |
|               | Jiuzhaigou| 19                    | 80 701                | 77 204     | 8                     | 0.010                | 8              | 0.010          | 0              | 0.000          |
|               | Li      | 13                    | 50 235                | 45 405     | 17                    | 0.037                | 17             | 0.037          | 0              | 0.000          |
|               | Maerkang| 14                    | 55 459                | 50 378     | 160                   | 0.318                | 160            | 0.318          | 0              | 0.000          |
|               | Mao     | 21                    | 111 578              | 106 125    | 5                     | 0.005                | 5              | 0.005          | 0              | 0.000          |
|               | Rangtang| 12                    | 44 525                | 39 564     | 207                   | 0.523                | 3              | 0.008          | 204            | 0.516          |
|               | Ruoergai| 19                    | 80 931                | 71 028     | 380                   | 0.535                | 380            | 0.535          | 0              | 0.000          |
|               | Songpan | 26                    | 70 087                | 65 888     | 2                     | 0.003                | 2              | 0.003          | 0              | 0.000          |
|               | Wenchuan| 13                    | 100 093               | 96 302     | 2                     | 0.002                | 2              | 0.002          | 0              | 0.000          |
|               | Xiaojin | 21                    | 82 243                | 76 227     | 30                    | 0.039                | 25             | 0.033          | 5              | 0.007          |
| Ganzi Prefecture| Batang| 19                    | 52 232                | 48 108     | 52                    | 0.108                | 52             | 0.108          | 0              | 0.000          |
|               | Baiyu   | 17                    | 59 118                | 55 382     | 685                   | 1.237                | 423            | 0.764          | 264            | 0.477          |
|               | Danba   | 15                    | 54 842                | 53 538     | 25                    | 0.047                | 24             | 0.045          | 1              | 0.002          |
|               | Daofu   | 22                    | 44 549                | 40 588     | 109                   | 0.269                | 109            | 0.269          | 0              | 0.000          |
|               | Daocheng| 14                    | 35 393                | 28 206     | 16                    | 0.057                | 15             | 0.053          | 1              | 0.004          |
|               | Derong  | 12                    | 28 785                | 26 490     | 3                     | 0.011                | 4              | 0.015          | 0              | 0.000          |
|               | Dege    | 26                    | 90 523                | 81 810     | 965                   | 1.180                | 698            | 0.853          | 269            | 0.329          |
|               | Ganzi   | 22                    | 66 501                | 62 016     | 726                   | 1.171                | 283            | 0.456          | 450            | 0.726          |
|               | Jiulong | 18                    | 53 471                | 52 770     | 13                    | 0.025                | 13             | 0.025          | 0              | 0.000          |
|               | Kangding| 21                    | 117 695              | 112 059    | 68                    | 0.061                | 42             | 0.037          | 27             | 0.024          |
|               | Litang  | 24                    | 72 344                | 68 346     | 265                   | 0.388                | 265            | 0.388          | 0              | 0.000          |
|               | Luhuo   | 16                    | 39 890                | 39 768     | 108                   | 0.272                | 103            | 0.259          | 5              | 0.013          |
|               | Luding  | 12                    | 87 961                | 85 978     | 18                    | 0.021                | 13             | 0.015          | 5              | 0.006          |
|               | Seda    | 17                    | 56 777                | 51 403     | 1 571                  | 3.056                | 739            | 1.438          | 840            | 1.634          |
|               | Shiqu   | 22                    | 89 367                | 88 116     | 5 738                  | 6.512                | 1 731          | 1.964          | 4 061          | 4.609          |
|               | Xiangcheng| 12                    | 29 839                | 26 936     | 9                     | 0.033                | 9              | 0.033          | 0              | 0.000          |
|               | Xinlong | 19                    | 51 970                | 46 209     | 166                   | 0.359                | 147            | 0.318          | 19             | 0.041          |
|               | Yajiang | 17                    | 42 034                | 38 577     | 30                    | 0.078                | 30             | 0.078          | 0              | 0.000          |
| Liangshan Prefecture| Muli| 29                    | 138 555              | 121 198    | 12                    | 0.010                | 12             | 0.010          | 0              | 0.000          |
|               | Yuexi   | 41                    | 378 425              | 349 851    | 7                     | 0.002                | 7              | 0.002          | 0              | 0.000          |
| Ya'an City    | Baxing  | 9                     | 51 725                | 43 940     | 2                     | 0.005                | 1              | 0.002          | 1              | 0.002          |
| City | County | Total no. of townships | Pop. in endemic areas | No. exam'd | Total no. of patients | Total prevalence (%) | CE | No. patients | Prevalence (%) | AE | No. patients | Prevalence (%) |
|------|--------|------------------------|-----------------------|------------|----------------------|---------------------|----|-------------|----------------|----|-------------|----------------|
| Tianquan | 15 | 158 835 | 135 099 | 4 | 0.003 | 3 | 0.002 | 1 | 0.001 |
| Total | 649 | 2 758 525 | 2 542 135 | 11 743 | 0.462 | 5 621 | 0.221 | 6 197 | 0.244 |

Based on the analysis at the township level, we observed that the top three overall prevalences were all under the jurisdiction of Shiqu county, they were Changsha Gongma (14.961%), Gemeng (12.065%), and Sexu (10.588%) townships. In particular, the top three occurrences of CE were Gayi (3.243%) and Changxu Gongma (3.21%) townships in Shiqu county, and Suoba (3.22%) township in Dege county. Conversely, the top three incidences of AE were Changsha-Gongma (12.986%), Gemeng (10.462%), and Mengyi (10.363%) townships in Shiqu county. The number of townships with human prevalence 0–0.1%, 0.1–1%, and 1% or above were 153, 209, and 64, respectively (Table 3).

Table 3 The prevalence of different types of echinococcosis in Sichuan province

| Human prevalence(%) | No. of CE epidemic townships | No. of AE epidemic townships | No. of total epidemic townships |
|---------------------|------------------------------|-----------------------------|--------------------------------|
| P ≤ 1               | 47                           | 36                          | 64                             |
| 0.1 ≤ P < 1        | 197                          | 71                          | 209                            |
| P < 0.1            | 161                          | 60                          | 153                            |
| Total               | 405                          | 167                         | 426                            |

Comparison with previous results

Overall, the survey results in 2016–2019 demonstrated that the prevalence of CE was 0.31%, while AE was 0.35%. In comparison, the prevalence of AE was significantly higher than that of CE ($\chi^2 = 28.166, P < 0.05$). On the other hand, the survey findings of 2012 showed that the predominance of CE was 0.88%, whereas that of AE was 0.27% [14]. In contrast, the prevalence of CE was significantly higher than that of AE ($\chi^2 = 372.204, P < 0.05$) (Fig. 2).

Description of spatial distribution characteristics

The spatial distribution map of Sichuan province displayed that the high prevalence of echinococcosis was primarily distributed in the west, northwest, and north, while the low prevalence was predominantly distributed in the south and east. The prevalence of echinococcosis in Sichuan province exhibited spatial clustering characteristics, indicating that areas with high or low prevalence tended to aggregate into pieces. However, the judgment of this aggregation was not statistically significant, and therefore we adopted spatial autocorrelation analysis and other methods for further inference (Fig. 3).

Trend surface analysis

To make a three-dimensional trend analysis chart, we used the trend analysis function of ArcGIS 10.1 software. The x- and y-axes represented longitude and latitude, respectively, while the z-axis denoted the human prevalence in townships. Additionally, the blue line represented the change of prevalence from south to north, whereas the green line indicated the change of prevalence from east to west. Remarkably, the findings illustrated that the prevalence of echinococcosis at the township level in Sichuan province followed a decreasing trend from north to south and from west to east, which agreed with the results based on regional distribution characteristics (Fig. 4).

Spatial clustering analysis

Global spatial autocorrelation analysis

The results of global spatial autocorrelation analysis of the prevalence of echinococcosis at the township level in Sichuan province indicated that there were positive spatial autocorrelation and aggregation distribution rather than random distribution (Table 4).

Table 4 Spatial autocorrelation global Moran’s I analysis on the prevalence of echinococcosis

| Rate type         | Moran’s I | Z-value | P-value | Expected value | Standard deviation |
|-------------------|-----------|---------|---------|----------------|-------------------|
| Total prevalence  | 0.77      | 22.07   | <0.01   | -0.0015        | 0.02              |
| Prevalence of CE  | 0.70      | 29.67   | <0.01   | -0.0015        | 0.02              |
| Prevalence of AE  | 0.71      | 30.52   | <0.01   | -0.0015        | 0.02              |
Local spatial autocorrelation analysis

In this subsection, the outcomes of local spatial autocorrelation analysis showed that the “high-high” gathering areas of overall prevalence were mainly located in the townships of Shiqi, Seda, Ganzi, Dege, and Baiyu counties, totaling 41. The “high-high” gathering areas of CE prevalence were dominantly located in townships of Shiqi, Seda, Ganzi, Dege, Baiyu, Rangtang, Xinlong, and Litang counties, totaling 48. The “high-high” gathering areas of AE prevalence were predominantly located in town of Shiqi, Dege, Seda, Ganzi, and Rangtang counties, totaling 31.

The “low-low” gathering areas of the overall prevalence were primarily located in towns of Jiuzhaigou, Songpan, Heishui, Mao, Li, Wenchuan, Xiaojin, Baoxing, Tianquan, Kangding, Luding, Muli, Daocheng, Xiangcheng, and Yuexi county, totaling 193. The “low-low” gathering areas of the predominance of CE were largely located in towns of Jiuzhaigou, Songpan, Heishui, Mao, Li, Wenchuan, Xiaojin, Baoxing, Tianquan, Kangding, Luding, Muli, Daocheng, Xiangcheng, and Yuexi county, totaling 165. Finally, the “low-low” gathering areas of the occurrence of AE were generally in the townships of Jiuzhaigou, Songpan, and Kangding, totaling 4 (Fig. 5).

Discussion

Echinococcosis is a worldwide zoonotic parasitic disease that seriously endangers the health and life safety of people. It also affects social and economic development, brings heavy economic burdens to the families of patients, and is one of the major reasons that lead people in endemic areas of China to become poor and live in poverty due to illness [21]. To deeply understand the prevalence of human echinococcosis in Sichuan province, we herein performed a survey in 35 epidemic counties previously identified in 2012 from 2016 to 2019. We specifically investigated the epidemic areas and human echinococcosis at the town level in Sichuan province. Our results revealed that the echinococcosis patients were distributed in 426 townships, which were primarily located in the northwestern part of Sichuan province and concentrated in high mountain meadows, pastoral areas with a cold, arid climate and little rainfall, and semi-agricultural and semi-pastoral areas. A major reason for this is that Echinococcus eggs are well adapted for cold, dry, and rainless natural environments. In addition, there were abundant animal resources in these environments, which form a relatively suitable food chain for predation and prey, thus enabling Echinococcus spp. to form a complete life history, resulting in the prevalence of echinococcosis [22, 23]. We also found that CE and AE were prevalent in 405 and 167 townships, CE epidemic areas were more widespread compared with AE. This observation may be attributed to the fact that CE is mainly spread in the biological circulation chain composed of domestic dogs as the main definitive host and domestic animals as the main intermediate hosts, while AE is primarily spread in the biological circulation chain composed of foxes and dogs as the main definitive host and small mammals as the main intermediate hosts. In comparison, the distribution range of small mammals is smaller than that of domestic animals [24–27].

Among the 426 townships where patients were distributed, we noted that there were 64 townships with a human population prevalence of ≥1.00%, which were predominantly distributed in some townships of Shiqi, Seda, Ganzi, Dege, and Baiyu counties in the northwest part of Sichuan province. Similarly, the spatial distribution of human echinococcosis prevalence map elucidated that echinococcosis was largely spread in Sichuan province, particularly with a high prevalence in the northwest.

Trend surface analysis is a commonly used spatial statistical analysis method for evaluating the trend and gradual change of spatial geographical position on a regional scale. It often establishes a polynomial regression mathematical model and carries out interpolation analysis according to the observed values of observed variables and the polynomial regression results of their sampling locations, so as to obtain one-dimensional, two-dimensional, or three-dimensional continuous line segments, planes, or solid surfaces [28]. Based on the results of the trend analysis, we demonstrated that the predominance of human echinococcosis in Sichuan province followed a trend in both the east-west and north-south directions for most of the years, gradually decreasing from west to east and from north to south. These findings were concurred with the results of trend surface analysis of echinococcosis conducted by Qi Yanfeng in Aba Prefecture in 2013 and also with the spatial and temporal distribution characteristics of the new human echinococcosis prevalence in Sichuan province between 2007 and 2017 by He Wei et al. The true explanations why the areas with high prevalence were essentially distributed in the northwest of Sichuan may be as follows. First, the climatic conditions of high altitude and low temperature favored the Echinococcus eggs to survive for a long time to exacerbate the spread of echinococcosis. Second, the existence of a large number of intermediate hosts increased the spread of diseases, developed animal husbandry was brought a large number of intermediate hosts of CE, and grassland was also a favorable environment for the intermediate hosts of AE (small mammals). Previous findings have shown that most of the areas with high prevalence had developed animal husbandry. Third, close contact with dogs, feeding diseased organs to dogs, not washing hands before eating or preparing food, and lack of safe drinking water sources significantly increased the risk of infection [29–34].

According to the results of the 2012 national echinococcosis prevalence survey, the number of patients with CE in Sichuan province was distinctively higher than those with AE, while the findings of the 2016–2019 survey showed that AE patients accounted for 52.77% of the total number of patients. The major reasons for this discrepancy may be as follows. First, the infectious source of CE was primarily dogs, and since the implementation of the Echinococcosis Prevention and Control Project, Sichuan province had standardized the management and deworming...
of dogs, and reduced the number of stray dogs, the infectious source had been effectively controlled, so the number of newly found patients had decreased. Second, the surgical operation difficulty of CE was less compared to that of AE, and more CE patients were effectively cured [35, 36]. Third, the experience and diagnostic techniques of ultrasonographers differ from one region to another, and there may be caused inaccurate diagnosis.

Numerous reports have concluded that the prevalence and transmission of echinococcosis are influenced by natural, biological, and social factors, and were also restricted by the imago in the definitive host segments and eggs in the external environment, larvae in intermediate hosts and stability of parasites, and had spatial autocorrelation [37–42]. According to the literature, spatial autocorrelation can accurately reflect the aggregation degree of an indicator in a spatial unit. For example, if an indicator shows the same distribution between its center and its surroundings in space, it is referred to as a spatial positive correlation, if an indicator is spatially opposite, it is called spatial negative correlation, and ultimately if an indicator is randomly spatial, it indicates that the spatial correlation is not significant. In addition, spatial autocorrelation is categorized into global and local spatial autocorrelations. Specifically, the global spatial autocorrelation analysis is used to explore the spatial aggregation of an indicator over the entire study area, using a single value to reflect the autocorrelation of the whole region. Subsequently, the common indicators of analysis included Global Moran's I index, Getis-Ord General G coefficient, and the Geary C coefficient. On the other hand, the local spatial autocorrelation analysis is used to investigate the degree of correlation between an indicator in each spatial unit and neighboring units. To test whether its spatial autocorrelation is significant for the whole survey area, thus indicating the spatial distribution pattern of the index with high and low and low, the common analysis indexes include local Moran's I index and local Getis-Ord G coefficient [43, 44]. Therefore, spatial autocorrelation analysis can be employed in medicine and related fields, which can improve the understanding of researchers of the spatial distribution law of disease prevalence, hence providing a reliable basis for formulating disease prevention and control strategies. Here, we employed spatial autocorrelation statistical analysis to explore the spatial distribution characteristics of echinococcosis at the township level in Sichuan province. Through the global autocorrelation analysis of the total prevalence of echinococcosis, and the prevalence of populations CE and AE, we found that the predominance of different types of echinococcosis exhibited a positive spatial correlation, with an aggregated distribution.

Moreover, the results of global spatial autocorrelation analysis showed that the prevalence of echinococcosis was clustered in space with a positive spatial correlation, that is, the prevalence of neighboring areas of the townships with high prevalence was also high, while that of neighboring areas of the townships with low prevalence was also low, which was spatially diffuse. On the other hand, in the local spatial autocorrelation analysis, the LISA aggregation map clearly showed the "high-high" and "low-low" clusters of human echinococcosis prevalence at the township level. Of note, the “high-high” clusters were dominantly distributed in most of the townships of Shiqu, Seda, Ganzi, Dege, and Baiyu counties near the northwest of Sichuan province. The areas with high prevalence might be associated with special natural environmental and socio-geographical factors influenced by the high altitude. Meanwhile, the unhealthy production lifestyle of local Tibetans might have a great similarity due to the close geographical location, thus forming a high-risk behavior of echinococcosis. Additionally, the "low-low" gathering areas were mostly located in some townships of Jiuzhaigou, Songpan, Heishui, Mao, Li, Wenchuan, Xiaojin, Baoxing, Tianquan, Kangding, Luding, Muli, Daocheng, Xiangcheng, and Yuexi county near the southeast in Sichuan province. These areas did not belong to the Qinghai-Tibet plateau, and their altitude was relatively low, and the natural conditions were superior to those of high prevalence areas, production and lifestyle were relatively healthy, thus these risks were relatively small. These findings suggest that we need to strengthen the comprehensive prevention and control of echinococcosis in “high-high” gathering areas, at the same time, we should actively explore the favorable factors for the low prevalence of echinococcosis in “low-low” gathering areas to provide a baseline reference for the prevention and control of echinococcosis in “high-high” gathering areas. In this regard, we thus recommend the following suggestions. First, based on previous screening results, "high-high" gathering areas should carry out herd screening in endemic villages, especially in remote agricultural and pastoral areas, nomadic and migratory groups; “low-low” congregation areas should strengthen screening in pastoral areas, temples, and other key areas. Second, "high-high" gathering towns should perform standardized management on dogs, bring dogs into legal management, establish a standardized management and control mechanism for dogs, manage household registration of domestic dogs, establish a regular deworming system for domestic dogs in combination with local conditions, establish the deworming day and conduct its regularly. Conversely, “low-low” gathering towns should prohibit the import of wild dogs and prevent the introduction of infection sources. Third, according to local conditions, "high-high" clustering towns should explore a centralized slaughter management mechanism for cattle and sheep. All endemic towns should strictly implement the quarantine system of cattle and sheep origin, take harmless treatment of diseased organs, immunize sheep in stock, ensure good immunization registration, and carry out small mammals in settlements and the surrounding 1 km radius in the epidemic areas of alveolar echinococcosis. Fourth, "high-high" gathering towns should actively organize and publicize echinococcosis prevention policies and knowledge, mobilize patients who meet the treatment conditions to carry out the treatment in medical institutions, make full use of various media to disseminate health knowledge, strengthen publicity and education to the masses in towns where echinococcosis was prevalent, guide key populations such as monks and nuns to support participation in echinococcosis prevention and control, and compile echinococcosis prevention and control materials parallel with local customs. Health education materials containing the core information of echinococcosis prevention and control are produced, farmers and herdsmen are guided to develop good health habits, and the knowledge of echinococcosis prevention and control is included in the health education content of schools in epidemic areas. Students are
regularly guided to spread the knowledge of echinococcosis prevention and control to parents and society through “small hands pull big hands” activities. Finally, “low-low” gathering townships should strengthen the publicity of the knowledge of prevention and treatment of echinococcosis among the migrant population, in order to prevent infection from outside [45].

Conclusion

In summary, this study is the first to examine the echinococcosis prevalence and spatial distribution characteristics of the population in Sichuan province at the township level, to define the specific spatial distribution of the aggregated areas, and to propose the key prevention and control in the “high-high” aggregated areas in the future. However, despite these promising results, this study did not further analyze the specific reasons for the formation of spatial gathering areas in combination with the prevention and control measures implemented in the local gathering and non-gathering areas, as well as the biological, socio-geographical, and natural environmental factors. In this respect, this work has certain limitations, especially in formulating specific prevention and control measures. Therefore, we recommend that specific prevention and control work should be explored and studied in depth in the future.

References

1. Eckert J, Gemmell MA, Meslin FX, Pawlowski ZS. WHO/OIE manual on Echinococcosis in humans and animals: a public health problem of global concern. Vet Parasitol. 2001;31(14):1717-8.
2. Lei ZL, Wang LY. Control Situation and Primary Task of Key Parasitic Diseases in China. Chin J Parasitol Parasit Dis. 2012;30(1):1-5.
3. Jenkins DJ, Romig T, Thompson RCA. Emergence/re-emergence of Echinococcus spp.: a global update. Int J Parasitol. 2005;35(11-12):1205-11.
4. Thompson RC, McManus DP. Towards a Taxonomic Revision of the Genus Echinococcus. Trend Parasitol. 2002;18(10):452-7.
5. Xiao N, Qiu JM, NaKao M, Li TY, Chen XW, et al. Biological features of a new Echinococcus species (Echinococcus shiquicus) in the east of Qinghai-Tibet Plateau. Chin J Parasitol Parasit Dis. 2008;26(4):307-12.
6. Budke CM, Casulli A, Kern P, Vuitton DA. Cystic and alveolar echinococcosis: successes and continuing challenges. PLoS Neglect Trop Dis. 2017;11(4):54-77.
7. Wen H. Beijing: People's Medical Publishing House; 2015.
8. Brunetti E, Kern P, Vuitton DA. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. Acta Trop. 2010;114(1):1-16.
9. Budke CM, Deplazes P, Torgerson PR. Global Socioeconomic Impact of Cystic Echinococcosis. Emerg Infect Dis. 2006;12(2):296-303.
10. Torgerson PR, Macpherson CN. The socioeconomic burden of parasitic zoonoses: Global trends. Vet Parasitol. 2011;182(1):79-95.
11. Shi DZ. Geographical distribution of echinococcosis in China. Bulletin Endemic Dis. 2000;5(1):74-5.
12. Yang YR, Ellis M, Sun T, Li ZZ, Liu XZ, Vuitton DA, et al. Unique family clustering of human echinococcosis cases in a Chinese community. Am J Trop Med Hyg. 2006;74(3):487-91.
13. Yang W. Epidemic situation and control measures of echinococcosis in Tibetan areas of Sichuan. Proceedings of the National Symposium on Zoonosis. Chinese Association for Science and Technology, Ministry of Health of the People's Republic of China, 2006;2:319-20.
14. Wang GQ. Epidemiological survey on echinococcosis in China. Shanghai: Shanghai Science and Technology Press; 2016.
15. Waller LA, Gotway CA. Applied spatial statistics for public health data. John Wiley & Sons;2004.
16. Liu L, Guo B, Li W, Zhong B, Yang W, Li SC, et al. Geographic distribution of echinococcosis in Tibetan region of Sichuan Province, China. Infect Dis Poverty. 2018;7(1):104-12.
17. Brundu DiAloisio D, Rolesu SiPiseddu T, Masala G, et al: Cystic echinococcosis in slaughtered cattle in Sardinia: a retrospective epidemiological study and spatial analysis. Geospat Health. 2012;6(2):285-91.
18. Qi YF. Study on the distribution characteristics and influencing factors of echinococcosis in Aba Prefecture, Sichuan Province. China CDC; 2013.
19. Zhao Y, Wu WP, Li W, Xu KJ, Wang LY, Wang Y. Spatial clustering analysis of echinococcosis in Ganzi Tibetan Autonomous Prefecture, Sichuan Province. Int J Med Parasit Dis. 2015;42(3):164-9.
20. Ministry of Health of the People's Republic of China. Diagnostic criteria for Hydatid Disease (WS 257-2006);2006.
21. Wang Q, Francis R, Christine B, Philip SC, Xiao YF, Dominique A, et al. Grass height and transmission ecology of Echinococcus multilocularis in Tibetan communities. Chin Med J. 2010;123(1):61-7.
22. Zeng XM, Guan YY, Wu WP. Epidemiological distribution characteristics of echinococcosis. Chin J Z 2014;30(4):413-7.
23. Yang YR, Clements ACA, Gray DJ, Atkinson JAM, Williams GM, Barnes TS, et al. Impact of anthropogenic and natural environmental changes on Echinococcus transmission in Ningxia Hui Autonomous Region, the People’s Republic of China. Parasit & Vect. 2012;5(1):146-
54. Ziaei H, Fakhar M, Armat S. Epidemiological aspects of cystic echinococcosis in slaughtered herbivores in Sari abattoir, North of Iran. J Parasit Dis. 2011;35(2):215-8.
55. Fang Q. Analysis of epidemic situation and influencing factors of echinococcosis in Qinghai-Tibet Plateau. China CDC; 2014.
56. Craig PS, Larrieu Control of Cystic Echinococcosis/Hydatidosis: 1863–2002. Advances Parasitol. 2006;61:443-508.
57. Wang Q, Vuitton D A, Xiao YF, Budke CM, Ponce MC, Schantz PM, et al. Pasture types and Echinococcus multilocularis, Tibetan communities. Emerg Infect Dis. 2006;12(6):1008-10.
58. Qi XS, Wang XM, Zhang YF. Research Method and Its Application of Distributing Rule of Environmental Data in Space: Trend-curve Analysis Method. Environmental Protection. 2000;10(7):20-2.
59. Fromsa A, Jobre Y. Infection prevalence of hydatidosis (Echinococcus granulosus, Batsch, 1786) in domestic animals in Ethiopia: a synthesis report of previous surveys. Vet Journal. 2011;15(2):11-33.
60. Ibrahim MM. Study of cystic echinococcosis in slaughtered animals in Al Baha region, Saudi Arabia: interaction between some biotic and abiotic factors. Acta Trop. 2010;113(1):26-33.
61. Wang Q, Xiao YF, Dominique AV, Peter MS, Francis R, Christine B, et al. Impact of overgrazing on the transmission of Echinococcus multilocularis in Tibetan pastoral communities of Sichuan Province, China. Chin Med J. 2007;120(3):237-42.
62. Wang H. Analysis of human hydatid disease risk factors in Qinghai province. Chin J Parasitol Parasit Dis. 2004;17(4):214-6.
63. He W, Shang JY, Yu WJ, Zhang GJ, Wang Q, Huang Y, et al. Epidemiological investigation of echinococcosis in shiqi county, Sichuan province. J Preventive Med Information. 2017;33(9):850-4.
64. Qi XW, Feng KH, Freya VK, Li HT, Song T, Duan XY, et al. Epidemic status of Echinococcus granulosus and risk of human cystic echinococcosis in Hoboksar Mongolian Autonomous County of Xinjiang. Chin J Endemiol. 2010;31(3):297-9.
65. Wu WP, Wang H, Wang Q, Zhou XN, Wang LY, Zheng CJ, et al. A nationwide sampling survey on echinococcosis in China during 2012-2016. Chin J Parasitol Parasit Dis. 2018;36(1):1-14.
66. Aini ABDSLM, Shao YM, Aji TEGAL, Zhang WB, Lin RY, Hou YY et al. Establishment and innovative practice of Integrative System of Prevention, Diagnosis and Management for echinococcosis in China. Chin J Parasitol Parasit Dis. 2019;37(4):388-94.
67. Mitterpáková M, Humiková Z, Antolová D, Dubinský P. Endoparasites of red Fox (Vulpes vulpes) in the Slovak Republic with the emphasis on zoonotic species Echinococcus multilocularis and Trichinella spp. Helminthologia. 2009;46(2):73-9.
68. Gudewar J, Pand D, Bera K, Das K, Konar J, Rao A, et al. Molecular characterization of Echinococcus granulosus of Indian animal isolates on the basis of nuclear and mitochondrial genotype. Mol Biol Rep. 2009;36(1):1381-5.
69. Let H, Pearson MS, Blair D. Complete mitochondrial genomes confirm the distinctiveness of the horse-dog and sheep-dog strains of Echinococcus granulosus us. Parasitol. 2002;124(1):97-112.
70. Capuano F, Rinaldi L, Maurelli MP, Perugini AG, Vania G, Garippa G, et al. Cystic echinococcosis in water buffaloes: Epidemiological survey and molecular evidence of ovine (G1) and Buffalo (G3) strains. Vet Parasitol. 2006;137(3-4):262-8.
71. Yamamoto N, Kishi R, Katakura Y, Miyake H. Risk factors for human alveolar echinococcosis: a case-control study in Hokkaido, Japan. Annals Trop Med & Parasitol. 2001;95(7):689-96.
72. Zhao Y, Wu WP. Application of spatial statistics on echinococcosis. Studies. Chin J Zoonos. 2015;31(3):272-6.
73. Li XY, Chen K. The theory of scanning statistics and its application in spatial epidemiology. Chin J Epide 2008;29 (8): 828-31.
74. Zhou XN. Spatial Epidemiology. Beijing: Science Press; 2009.
75. Wen H, Aji TEGAL, Shao YM, Lin RY, Li HT, Tuxun TEHJ, et al. Research Achievements and Challenges for Echinococcosis Control. Chin J Parasitol Parasit Dis. 2015;33(6):466-71.