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Research Article

Spatial-Temporal Epidemiological Characteristics of Tuberculosis in Shandong Province, China in 2011-2015

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Abstract

Objectives: To explore spatial-temporal epidemiological characteristics of tuberculosis in Shandong province, China in 2011 - 2015, and to provide technical suggestions to improve future control interventions.

Methods: Notification Statistics of active TB and smear positive TB in Shandong in 2011 - 2015 were collected and imported into Geographic Information System (GIS), and global autocorrelation statistics (Moran's I) and local autocorrelation statistics (Getis-Ord G) were employed to analyze the spatial aggregation of TB notification. Then SaTScan was used to explore spatial-temporal aggregation of TB notification at county level.

Results: Notification data of active TB and smear positive TB both showed a declining trend in 2011 - 2015, and both had a spatial aggregation ($P < 0.05$). Hot spots of active TB were mainly in northwest (Liaocheng prefecture), south central (Linyi prefecture), and southeast (Qingdao prefecture) of Shandong; while hot spots of smear positive TB were mainly in northwest (Liaocheng prefecture), north central (Dezhou prefecture) , and southeast (Qingdao prefecture). The hot spots of spatial aggregation coincided with the primary and secondary spatial- temporal aggregation areas.

Conclusion: Notification data of active TB and smear positive TB in 2011 - 2015 had a spatial aggregation. Northwest and southeast parts of Shandong had higher TB burden as well as higher risks for TB transmission, while south central part of Shandong had higher TB burden only.

Keywords: *Tuberculosis; Notification; Spatial-Temporal; Aggregation; China*

Abbreviations

TB: Tuberculosis; MDR-TB: Multi-Drug Resistant Tuberculosis; GIS: Geographic Information System; WHO: World Health Organization

Introduction

Geographic Information System (GIS), an information technology that combines spatial data management and spatial information analysis, could be utilized for analyzing geographical distribution of infectious diseases, projecting disease developmental trend, and establishing disease early-warning and monitoring system [1]. Using GIS for spatial analysis has become a popular approach to determine the hot spots of public health hazards in the studies of nosogeography domestically and internationally [2]. Nowadays, GIS has been used more frequently in the study of TB control, and multiple studies have demonstrated that incidence of TB has evident spatial structures and heterogeneity [3].

World Health Organization (WHO) reports that China is one to 22 high TB burden countries with the third largest number of cases in the world [4]. China has adopted DOTS strategy and free first line medicines policy for active TB patients. The epidemic of TB in China is declining, with the prevalence of TB in 2010 eight percent lower than that in 2000 [5].

Shandong situating at east coast of China, is the second most populous province in China with a population of 97 million. The 2010 prevalence survey in Shandong showed that the active TB prevalence was 271 per 100 000 among the group older than 15 years, which was at average level of all the provinces; the prevalence of TB in urban areas was lower than that of rural areas. However, prevalence data in different geographical areas in Shandong have not been available [6]. The spatial-temporal epidemiological characteristics of tuberculosis in Shandong have not been reported. This study aims to using the GIS and TB incidence data, revealing spatial distribution and aggregation of TB incidence, determining the priority control areas, and providing evidences for TB control strategies.

Data and Methods

Data Source

Case notification data were from the National TB Information Management System, population sizes were from provincial statistical year book 2015. Geographical data were drawn from administrative units' boundary vector map (1:1000000). The basic unit for spatial analysis was county (district in urban areas).

Methods

Global spatial auto-correlation

Notification data of active and smear positive cases were imported into electronical map of Shandong province that features county boundaries, then GIS database of TB notification rates were established. Maps featuring notification rates were drawn with ArcMap. When conducting spatial auto-correlation analysis, we assumed the incident risks were at same level across all the counties, which conforms Poisson distribution. We used global spatial auto-correlation Moran's I to test if the TB notification has global aggregation [7]. The test results were judged according to the Z value, if $-1.96 \le Z \le 1.96$, the it has no statistical significance, and the notification was conforming Poisson distribution and no global aggregation is detected; if $Z > 1.96$, we can assume that the notification has aggregation; if $Z < -1.96$, then the notification was sporadic.

Local spatial auto-correlation

At county level, local Getis-Ord G was adopted to conduct local spatial auto-correlation, so as to acquire specific locations and types of TB incidence aggregation. G value was the local spatial auto-correlation indicator indicating the extent of aggregation, and detecting hot spots and cold spots. Standard statistical Z value (Gi) was used to test statistical significance.

Temporal-spatial scanning

Temporal-spatial scanning was conducted with software SaTScan 9.1 to detect aggregation center and aggregation radius. SaTScan was based on dynamic space window scanning statistics. Log likelihood Ratio (LLR) of space units of intra and extra areas with different center and radiuses was used for statistical inference, and Monte Carlo Simulation was used for evaluating the statistical significance and largest possible aggregation areas. For each possible temporal-spatial aggregation area, when $P < 0.05$, the bigger the LLR is, the bigger the capability of aggregation in areas covered by the scanned dynamic window is. The window with biggest LLR value was regarded as category I aggregation area, and other windows with statistical significance were category II aggregation areas. The study was retrospective spatial analysis, and Poisson distribution modules of SaTScan were used to analyze the high space value aggregation. The biggest scanned area was set to 50% of the total population of Shandong, and the longest scan time was 50% of the total study time.

Statistical Analysis

Excel 2010 was used to conduct data cleansing and descriptive analysis. Arcgis 9.3 was used for statistical analysis and visualization of analysis results with mapping.

Global Moran's I was used for global spatial auto-correlation analysis. Local Getis-Ord G was used for local spatial auto-correlation analysis, and SaTScan9.1 was used to conduct time-spatial scan, with all tests' significant level at $\alpha = 0.05$.

Results

TB epidemic in Shandong

There were 174143 active TB cases reported in Shandong from 2011 to 2015, among which 65256 cases were smear positive, making 37.47% of the total active cases; the rest 108887 (62.53%) cases were smear negative. Both the notified active TB cases and smear positive cases showed decreasing trends by year. The five-year average notification rate of active cases was 35.96/100 000, with the highest of 38.05/100 000 in 2011, and the lowest of 32.46/100 000 in 2015. Liaocheng prefecture had the highest active TB average notification of 49.06/100 000 and Laiwu prefecture had the lowest active TB notification of 22.03/100 000. The five-year notification smear positive cases on average was 13.48/100 000, with the highest of 19.99/100 000 in 2011, and lowest of 8.99/100 000 in 2015; Liaocheng prefecture had the highest average rate of 23.52/100 000, Dongying prefecture had the lowest of 11.12/100 000. Please see table 1 for further details.

Year	Population (Million)	No. of patients		Notification rate (1/100 000)	
		Smear positive	Active	Smear positive	Active
2011	95.79	19201	36444	19.99	38.05
2012	96.37	14861	36078	15.48	37.44
2013	96.85	12947	35674	13.48	36.83
2014	97.33	9616	34171	10.01	35.11
2015	97.89	8631	31776	8.99	32.46
Total	48423	65256	174143	13.48	35.96

***Table 1:** Notification active cases and smear positive cases in 2011 - 2015.*

Global spatial autocorrelation analysis

Active tuberculosis

Global Moran's I was employed to conduct global spatial autocorrelation test, and which revealed that the spatial distribution difference among counties from 2011 to 2015 had statistical significance (Moran's I > 0.258, P < 0.01), indicating there was spatial aggregation in Shandong in 2011-2015, see table 2.

Smear positive tuberculosis

Global Moran's I was used to have a global spatial auto correlation test, and the test revealed that the spatial distribution difference among counties from 2011 to 2015 had statistical significance (Moran's I > 0.133, P < 0.05), implying notification of sputum smear positive (SS+) cases had spatial aggregation in Shandong in 2011 - 2015, see table 2.

Indicators	Year	Moran's I	Z-score	P-value
Active TB notification rate	2011	0.258	4.023	< 0.001
	2012	0.492	7.664	< 0.001
	2013	0.648	9.898	< 0.001
	2014	1.041	16.109	< 0.001
	2015	1.191	18.418	< 0.001
Smear positive notification rate	2011	0.188	2.859	0.004
	2012	0.133	2.133	0.033
	2013	0.154	2.414	0.016
	2014	0.214	3.328	0.0009
	2015	0.227	3.53	0.0004

***Table 2:** Global auto correlation analysis of TB case notification in Shandong in 2011 - 2015.*

Local spatial autocorrelation analysis

Active tuberculosis

To acquire specific locations and notification hot spots and cold spots, Getis-Ord G was used to analyze the local spatial autocorrelation. The results showed that notification of active cases in 2011 - 2015 had hot spots in Liaocheng prefecture, northwest of Shandong, and some counties in Linyi prefecture, south central part of Shandong province. The hot spots and cold spots showed a pattern with minor varieties in different years, see figure 1.

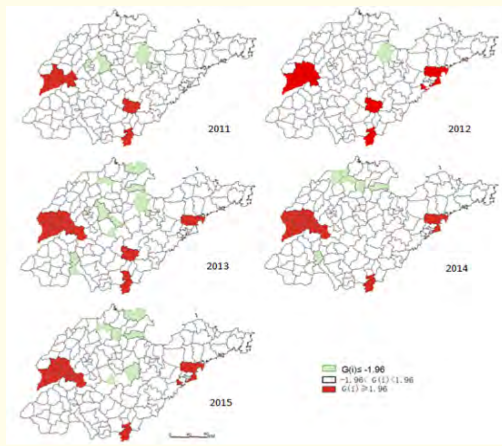

Figure 1: *Active TB notification hot spot and cold spot distribution in 2011 - 2015 in Shandong.*

Smear positive cases

Getis-Ord G was used to run a local spatial autocorrelation analysis to detect hot spots and cold spots in notification of smear positive cases. Hot spots were found mainly in Liaocheng prefecture, northwest of Shandong, Dezhou prefecture, north central part of Shandong, and some counties in Qingdao prefecture. There were small variations in the distributions in different years, with majority of the spots remaining relatively stable. See figure 2.

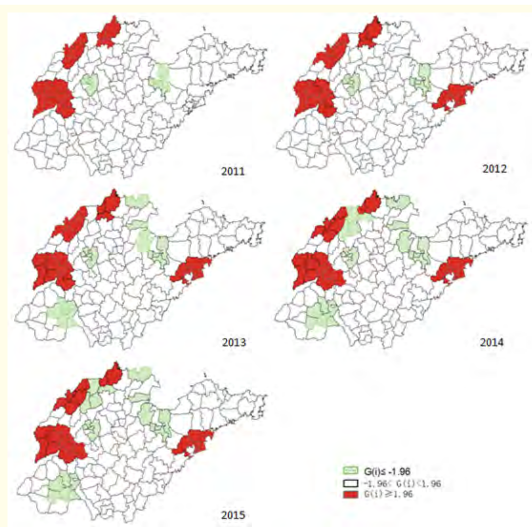

Figure 2: *Hot spots and cold spots in smear positive cases in Shandong in 2011 - 2015.*

Spatial-temporal analysis

Notification of active TB

Four spatial-temporal aggregation areas were detected in the notification of active TB in 2011 - 2015. The biggest aggregation area centered at Donge county in Liaocheng prefecture covering 9 counties from second quarter in 2014 to the fourth quarter of 2015. The actual notification in the area was 6328 cases with the expected number was 4798 cases (RR = 1.33, LLR = 228.38, P < 0.001). There were three secondary aggregation areas that were south central aggregation area centered at Hedong county, southeast aggregation area centered at Laoshan country, and north central aggregation area centered at Huantai county. Please see figure 3 and table 3.

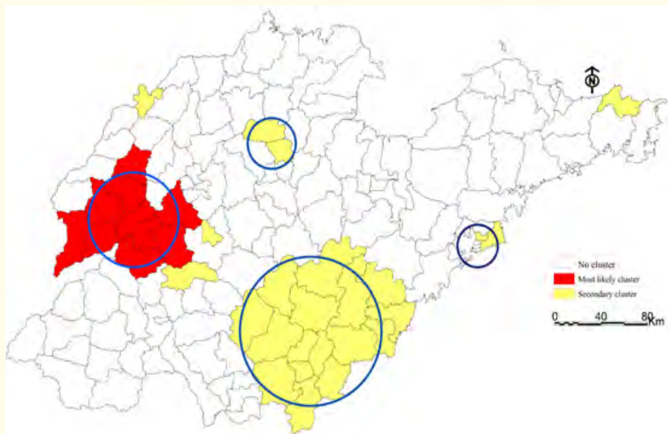

Figure 3: *Spatial and temporal scan of notification of active TB in 2011 - 2015.*

Notification of smear positive TB

Two aggregation areas were spotted, and the most possible area was centered at Licheng county covering north central part of Shandong province in 2011 - 2012. The actual notification was 17713 cases and the expected notification was 11435 cases, RR = 1.75, LLR = 1854.74, P < 0.001. Secondary aggregation area was centered at Laoshan County covering 6 counties, and aggregation time was from second quarter of 2012 to the third quarter of 2013. See figure 4 and table 3.

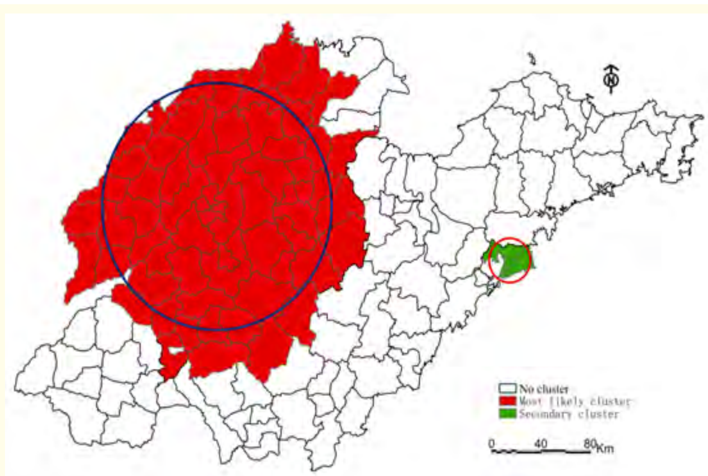

Figure 4: *Spatial and temporal scan of notification of smear positive TB in 2011 - 2015.*

Category	Degree of aggregation	Time (Quarter)	No. of country	Centre	Radius (km)	No. of cases	Expected no. of cases	RR value	LLR	P value
Active TB	Degree one	201402 - 201504	9	Donge	53.13	6328	4798	1.33	228.38	< 0.001
	Degree two	201401 - 201503	19	Hedong	103.89	12602	10859	1.17	142.12	< 0.001
		201103 - 201203	1	Huancui		853	477	1.79	120.22	< 0.001
		201301 - 201403	2	Laoshan	6.62	656	418	1.57	57.76	< 0.001
		201101 - 201203	1	Ningyang		874	595	1.47	57.4	< 0.001
		201102 - 201203	1	Decheng		616	442	1.39	30.53	< 0.001
		201202 - 201304	2	Huantai	12.75	837	629	1.33	16.93	< 0.001
		201401 - 201503	1	Taishan		552	452	1.22	10.3	0.0065
Smear positive	Degree one	201101 - 201204	65	Licheng	148.02	17713	11435	1.75	1854.74	< 0.001
	Degree two	201202 - 201303	6	Laoshan	23.97	1479	677	2.21	358.54	< 0.001

Table 3: *Spatiotemporal scan of TB in 2011 - 2015.*

Discussion

Although TB epidemic has been declining in China, the decease rate has been very slow. High burden of TB and MDR-TB pose the risks for spreading in the communities [9]. More effective TB control measures need to be explored. The development of GIS and spatial and temporal analysis technologies make it possible to carry out spatial epidemiological analysis, and to Spatial autocorrelation analysis and spatial aggregation analysis has become important approaches for investigating the infectious diseases, and are being used to study the features of hand-foot-mouth disease and malaria [10-12]. Previous studies demonstrate that incidence of TB has spatial heterogeneity, and which is affected by multiple factors such as economical situation, environment, climate, geographical locations, and health services [11,13]. Using spatial statistics to explore the distribution and aggregation of TB could help understand its distribution model and incidental hot spots [14]. TB control in those hot spots is one of the cornerstones for lowering the overall TB epidemic, so taking targeted measures aiming at these hot spots is expected to produce impactful results [15].

The global auto-correlation analysis in this study showed there were high spatial aggregations in the TB notification in 2011 - 2015. Local auto-correlation analysis indicated that: active TB hot spots were at Liaocheng prefecture (northwest Shandong), Linyi prefecture (south central Shandong), and Qingdao prefecture (southeast Shandong), with minor variations in different years around the mainstay hot spots. The spatial-temporal analysis revealed that active TB notification mainly aggregated at Liaocheng prefecture around 2014 - 2015, and secondary aggregation areas were Linyi prefecture, Qingdao prefecture, and some counties in Zibo prefecture. The coincidence of local auto correlation hot spots and spatial-temporal scan aggregation areas is not rarely seen in similar studies [16,17]. When under-reporting is not a serious issue, notification of cases may be used as an indicator to measure the burden of TB. The aggregation analysis of notification of active TB proved that northwest, south central and southeast parts of Shandong had higher TB burden than other areas in the province.

The notification of smear positive cases in 2011 - 2015 appeared spatial aggregation. Local auto correlation analysis indicated incidence hot spots were Liaocheng prefecture (northwest Shandong), Dezhou prefecture (north central Shanodng), Qingdao prefecture (southeast Shandong), and some areas of Linyi prefecture (south central Shandong), with minor variations in different years. Spatial-temporal scan found that the most possible aggregation areas were Liaocheng prefecture, Jinan prefecture, Taian prefecture, Dezhou prefecture in 2011 - 2012, and secondary aggregation was found to be Qingdao prefecture, which were similar to the yields of local auto correlation analysis. Smear positive cases pose higher transmission risks, and their notification reflects overall TB transmission risks [18]. So we could conclude that northwest, north central, and southeast parts of Shandong had higher risks for the transmission of TB.

Spatial epidemic analysis revealed polarized high notification. Possible reasons for high aggregation in northwestern, central-northern, and central-southern parts of Shandong could be under-developed economics, low medical service quality and health infrastructure [18]. However, Qingdao prefecture, a relative wealthy prefecture, had also high aggregation and the reason for that might be high volume of migrant workers in the area who may brought the disease into the prefecture [19]. And disease is easier to transmit in the area with high density of people, which increased the difficulties for controlling the disease [20]. Based on the findings on spatial analysis of active TB and smear positive TB, we could readily conclude that northwest and southeast parts of Shandong had higher TB burden as well as higher transmissions risks. Whereas south central parts of Shandong has high TB burden without high transmission risks. The study showed that northwest, north central, southeast and south central parts should be our priority areas for strengthened TB control efforts.

The study visualized the spatial distribution via GIS of active TB and smear positive TB in 2011-2015 in Shandong, established priority areas in Shandong, and provides evidences for formulating TB control policies and strategies. The study has a few limitations though. First, the extent to which that the indicator notification rate reflect real epidemic of TB is subject to patients' care seeking behavior, effectiveness of active case finding, regulation on case notification and etc. In addition, genotype, migrant population, poverty, communication and air pollution all may play a role in the distribution of TB, which might be the study topics for subsequent studies [20].

Conclusions

GIS is a powerful tool in detecting spatial-temporal features of infectious diseases. Notification of active TB and smear positive TB in 2011 - 2015 in Shandong had a spatial aggregation. Northwest and southeast parts of Shandong had higher TB burden as well as higher risks for TB transmission, while south central part of Shandong had higher TB burden only.

Declarations

Ethnical approval and consent to participate

Institutional Review Board (IRB) of Shandong Chest Hospital (NIH register numberIRB00006010) granted ethical approvals for the study and consented research procedures, with the following statements:

"The research data were mainly aggregated numbers about patient's notifiction in Shandong province, which were gathered from China's National Tuberculosis Information Management System, and no patients' personal information included in the study. Acquirement of patients' consent to participate was regarded as not pplicable".

Competing Interests

The authors declare that they have no competing interests.

Funding

The study did not require any funding.

Authors' Contribution

YL conducted data collection and analysis, and produce the first draft. HG and JC also assisted in data collection. XZ produced the concept of the paper, reviewed and improved the draft. XZ takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the manuscript.

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