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Spatial-Temporal Clustering of Hand, Foot, and Mouth disease at the sub-district level in Shenzhen City, China (2010-2014)

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Abstract

Background: Hand, foot, and mouth disease (HFMD) is known to be a highly infection childhood illness. In recent years, the number of reported cases of HFMD has significantly increased in mainland China, especially in Southern China. This study aims to explore the epidemiological features, spatiotemporal patterns of HMFD at the sub-district level in Shenzhen City.

Methods: Data of reported HFMD cases for each sub-district from 1 January 2010 to 31 December 2014 came from the Chinese Center for Disease Control and Prevention. Cluster analysis, spatial autocorrelation and retrospective scan methods were used to explore the spatiotemporal patterns of the disease, and were performed on the map of Shenzhen.

Results: Annualaverage incidence rate of HFMD was 302.72 per 100,000 in Shenzhen City. Most HFMD cases (80.07%) were aged within 0–3 years old of which male-to-female sex ratio was 1.62, and the incidence seasonal peaks were May and September frequently. The dominant pathogen was EV 71 (58.11%) and Cox A16 (37.00%). HFMD had positive spatial autocorrelation at sub-district level with Moran's I from 0.14 to 0.21 (P<0.001). Two spatial- temporal clusters were detected from 2010 to 2014 in the landscape of the whole Shenzhen City.

Conclusions: These findings suggested that the authorities in those regions should be more cooperative and pay further attention, as to conduct timely prevention and control measures for HFMD. A small scale of sub-district level will be helpful to prevent HFMD more accurately.

Keywords: HFMD; Spatial analysis; Cluster

Background

Hand, foot, mouth disease (HFMD), is a common infection disease in East and Southeast Asia, which is mainly infected by human enterovirus 71 (EV-A71) and Coxsackievirus 16 (CV-A16) [1-7]. In China, most HFMD were on scattered children under 5 years old [3,8,9]. Previous epidemiological studies of HFMD have indicated that diverse seasonal patterns of HFMD incidence were observed in southern and northern China [10-13]. Similarly, several spatial analyses have previously been conducted to describe spatial patterns, cluster locations and risk ratios of HFMD in some provinces in mainland China, such as Guangxi, Zhejiang, Beijing, Shandong, Hunan, and Chongqing [11-15]. However, these spatial analyses were based on a large scale, such as province, city, or country. These results based on country and province was not working for HFMD control in sub-district level. There were few studies analyzed on a sub-district level and the distribution of HFMD in Shenzhen at sub-district spatial scale level is still not clear. Therefore, an analysis of Shenzhen city on the sub-district level to explore the spatial characteristic and space-time clusters of the HFMD were conducted so as to prevent HFMD more accurately.

Methods

Data Collection

Shenzhen is located on the coast of southern China, south of Guangdong province, adjacent to Hong Kong. Shenzhen is located in the south of the tropic of cancer, between longitude 114°46' and 113°37' east, latitude 22°27 'and 22°52' north (Figure 1). It includes 57 sub-districts belonging to 10 regions during the study period, with a total land area of 1196.85 square kilometers. The data of HFMD cases from 1 January 2010 to 31 December 2014 in Shenzhen were collected from the National Notifiable Disease Surveillance System (NNDSS) of the Shenzhen Center for Disease Control and Prevention (Shenzhen CDC).

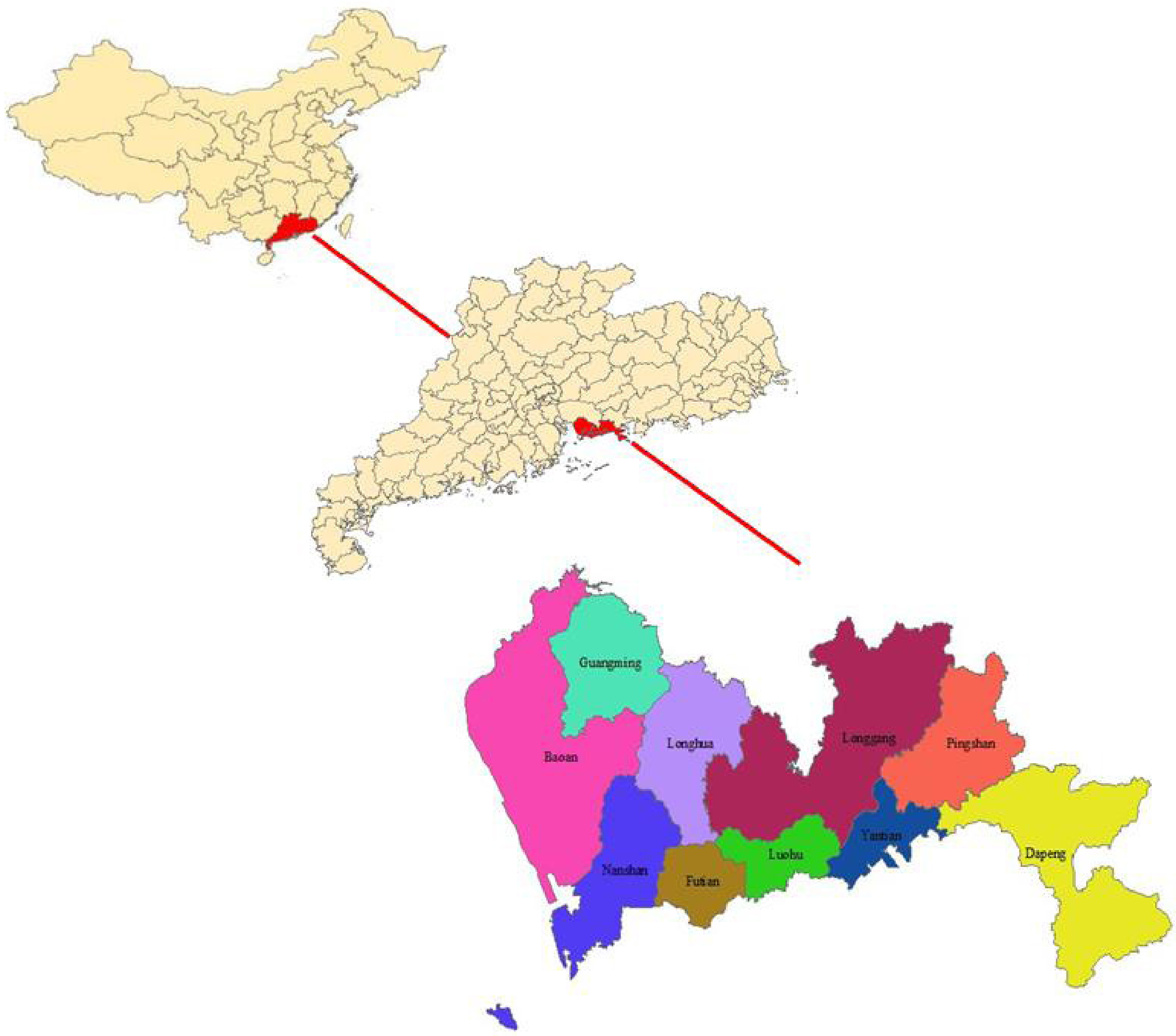

Figure 1: The study area, Shenzhen City

Data Analysis

Spatial Autocorrelation Analysis

The autocorrelation statistic (Global Moran's I) was used to explore the global spatial autocorrelation of HFMD cases. The significance of Moran's I was assessed using Monte Carlo randomization. A statistically significant ($P<0.05$) estimate of Moran's I indicates that neighboring counties have a similar incidence of HFMD and that the cases are likely to cluster at the sub-district level in Shenzhen City. ArcGIS 10.3 (ESRI, Inc. Redlands, CA, USA) was used to perform this analysis.

Retrospective Space-Time Scan Statistics Analysis

Kulldorff 's method of retrospective space-time scan statistic was used to detect the geographical clusters of HFMD cases at the sub-district level based on a Poisson model [16,17]. Based on a moving cylindrical window with dynamic changes of circular base and height corresponding to space and time respectively, the space-time scan statistic can be used to detect possible spatial-temporal clusters by producing an infinite number of overlapping cylinders with different radiuses. For each window, the expected number of cases can be inferred by using the discrete Poisson model or Bernoulli model with the observed number of cases and the number of the population within/outside the moved windows (the potential clusters) of candidate regions during candidate time. The relative risk (RR) can be calculated by the ratio of the observed number to the expected number within the windows and outside the windows. The log likelihood ratio (LLR) is calculated by a likelihood function. The most likely cluster is the one with the maximum LLR and the significance of it can be inferred through Monte Carlo tests with 1,000 permutations [16-20].

In this study, the retrospective space-time statistic was used to analyze the spatial-temporal clusters of the collected data. It was specified that the maximum spatial size of the clusters represent 50% of the total population at risk and the maximum temporal size of the clusters is 50% of the study period. The cluster with maximum LLR was regarded as the most likely cluster while others that also have significant P-values were named as secondary clusters. The space-time cluster analysis was performed using SaTScanTM9.4.4. [http://www.satscan.org/].

Results

A total of 160,379 HFMD cases were included in this study. The annual average incidence rate of HFMD in Shenzhen City was 302.72 per 100,000, ranging from 222.81 to 458.19 per 100,000 [21]. Table 1 summarized the social-demographic characteristics of HFMD cases. Zero to three years old children were the majority of the HFMD victims, which accounted for 80.07% over the study period. Of all HFMD cases, males accounted for 61.89%, and female was 38.11% of the total cases. The majority of HFMD cases were preschoolers (scattered children 75.91%). Among 1,535 genotyped cases between 2010 and 2014, Cox A16, EV 71 and other EV accounted for 37.00%, 58.11% and 4.89% respectively.

	2010	2011	2012	2013	2014	Total
Age						
0-3 year	18241	20160	24677	28055	37287	128420
>3 year	4869	4499	6003	4487	12101	31959
Sex						
Male	14442	15696	19183	19944	30002	99267
Female	8668	8963	11497	12598	19386	61112
Occupation						
Scattered children	17018	18856	22688	27268	35910	121740
Nursery children	5002	4825	6835	4059	11435	32156
others	1090	978	1157	1215	2043	6483
Pathogen						
Cox A16	57	24	4	119	364	568
EV 71	110	117	36	230	399	892
Other EV	1	18	11	11	34	75

Table 1: Social-demographic characteristics of HFMD cases and the pathogen types of some cases in Shenzhen City, 2010–2014

Seasonal and Geographic Distribution of HFMD Cases

Figure 2 shows the epidemic trend of monthly number of HFMD cases in Shenzhen. A majority of cases occurred during April to October. There were two peaks of HFMD in every year, except in 2013(only one). The first peak occurred in May frequently. The second peak occurred in September.

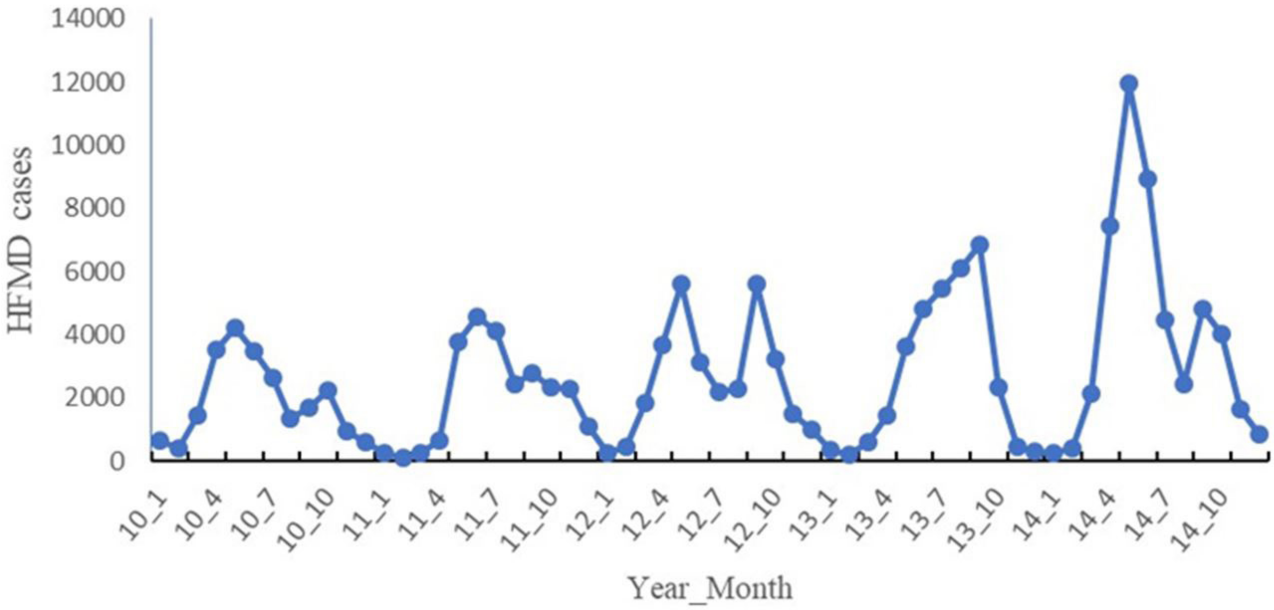

Figure 2: Monthly number of HFMD cases reported in Shenzhen City, 2010-2014

A total of 57 sub-districts were included in the analysis. Figure 3 shows the spatial distribution of HFMD incidence in sub-districts across Shenzhen City from 2010 to 2014. The incidence of HFMD varied among the sub-districts and higher incidence was shown in northeastern region compared to the western region of Shenzhen.

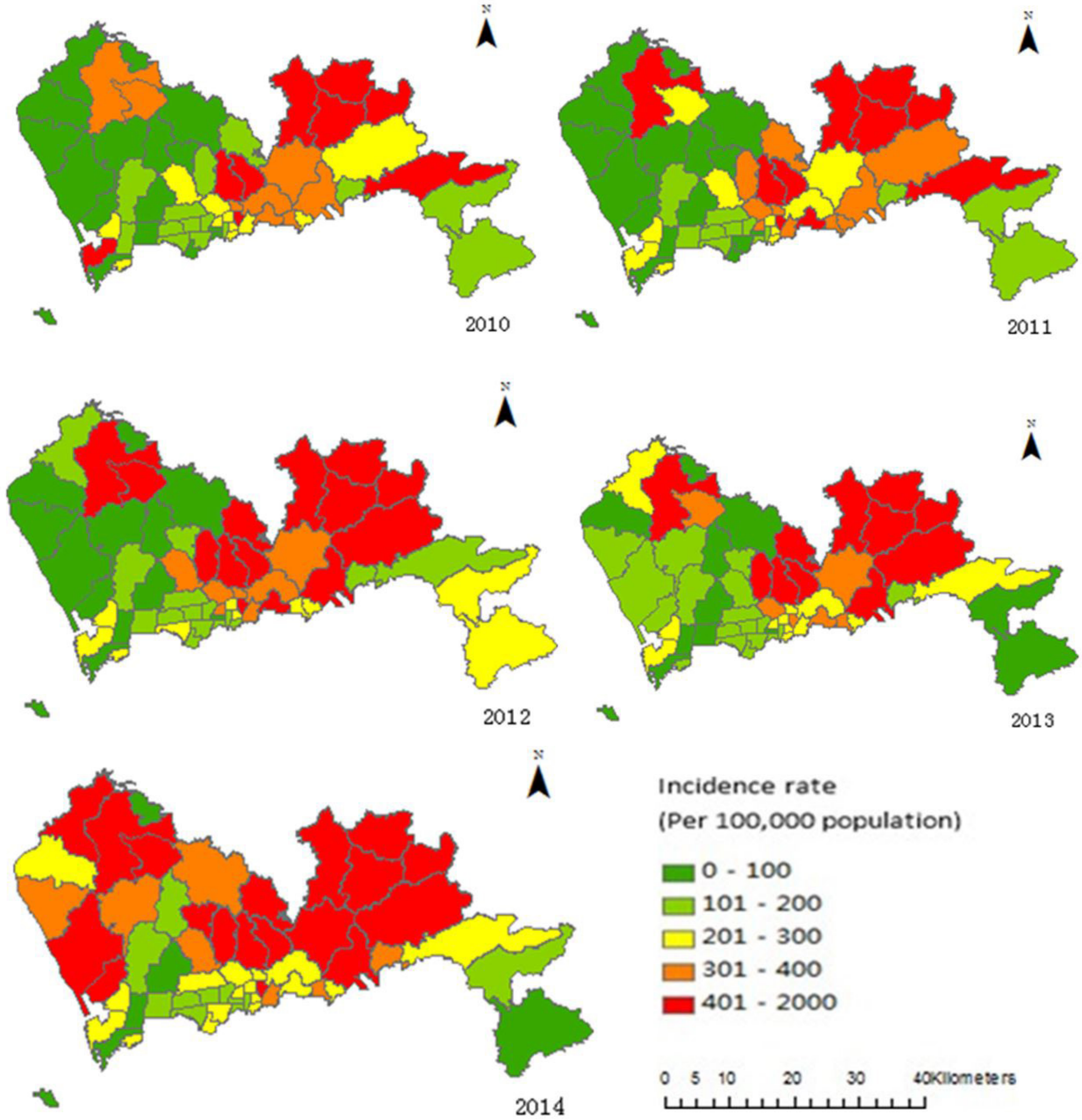

Figure 3: Annual incidence rates of HFMD per sub-district (1/100000) in Shenzhen City, 2010- 2014

Spatial Autocorrelation Analysis

A global spatial autocorrelation was found at the sub-district level in Shenzhen from 2010 to 2014 (Moran's I > 0.14, P < 0.001) (Table 2). This finding meant that the spatial distribution of HFMD was spatially aggregated in the whole city. High-high and low-low clusters indicate the clustering of HFMD in a particular location with similar values. For example, a high-high cluster means that a sub-district with high incidence is surrounded by sub-districts with high incidence. Low-high and high-low clusters indicate spatial outliers that could be clues to unusual cases. High-high clusters were mainly distributed in the northeastern of Shenzhen, near by the Huizhou City (Longgang, Kengzhi, Pingdi, Longcheng) (Figure 4). There were four high-high clusters (Longgang, Kengzhi, Pingdi, Longcheng) from 2010 to 2014. Based on the four clusters, there were more high-high clusters of Nanwan sub-district in 2011 and 2012, Pingshan in 2013, Pingshan and Pinghu in 2014 (Table 3). A low-low cluster was found in the interior area. There was only one low-low cluster (Taoyuan) in 2010 to 2012. In 2014, Taoyuan and Shahe sub- district were the two low-low clusters (Table 3 and Figure 4). The majority of sub-districts were shown to have negative spatial associations (high-low or low-high clusters) and were scattered across Shenzhen City (Figure 4).

Year	Moran's I	Z score	P-value
2010	0.14	3.74	<0.001
2011	0.17	4.34	<0.001
2012	0.17	4.27	<0.001
2013	0.18	4.62	<0.001
2014	0.21	5.23	<0.001

Table 2: Results of the spatial antocorrelation analysis onHFMD incidences at the sub-district level in Shenzhen City, 2010–2014

Year	High- High Cluster	Low-Low Cluster
2010	Longgang, Kengzhi, Pingdi, Longcheng	Taoyuan
2011	Longgang, Kengzhi, Pingdi, Longcheng, Nanwan	Taoyuan
2012	Longgang, Kengzhi, Pingdi, Longcheng, Nanwan	Taoyuan
2013	Longgang, Kengzhi, Pingdi, Longcheng, Pingshan	—
2014	Longgang, Kengzhi, Pingdi, Longcheng, Pingshan, Pinghu	Taoyuan, Shahe

Table 3: Spatial correlation cluster for HFMD incidence, 2010–2014

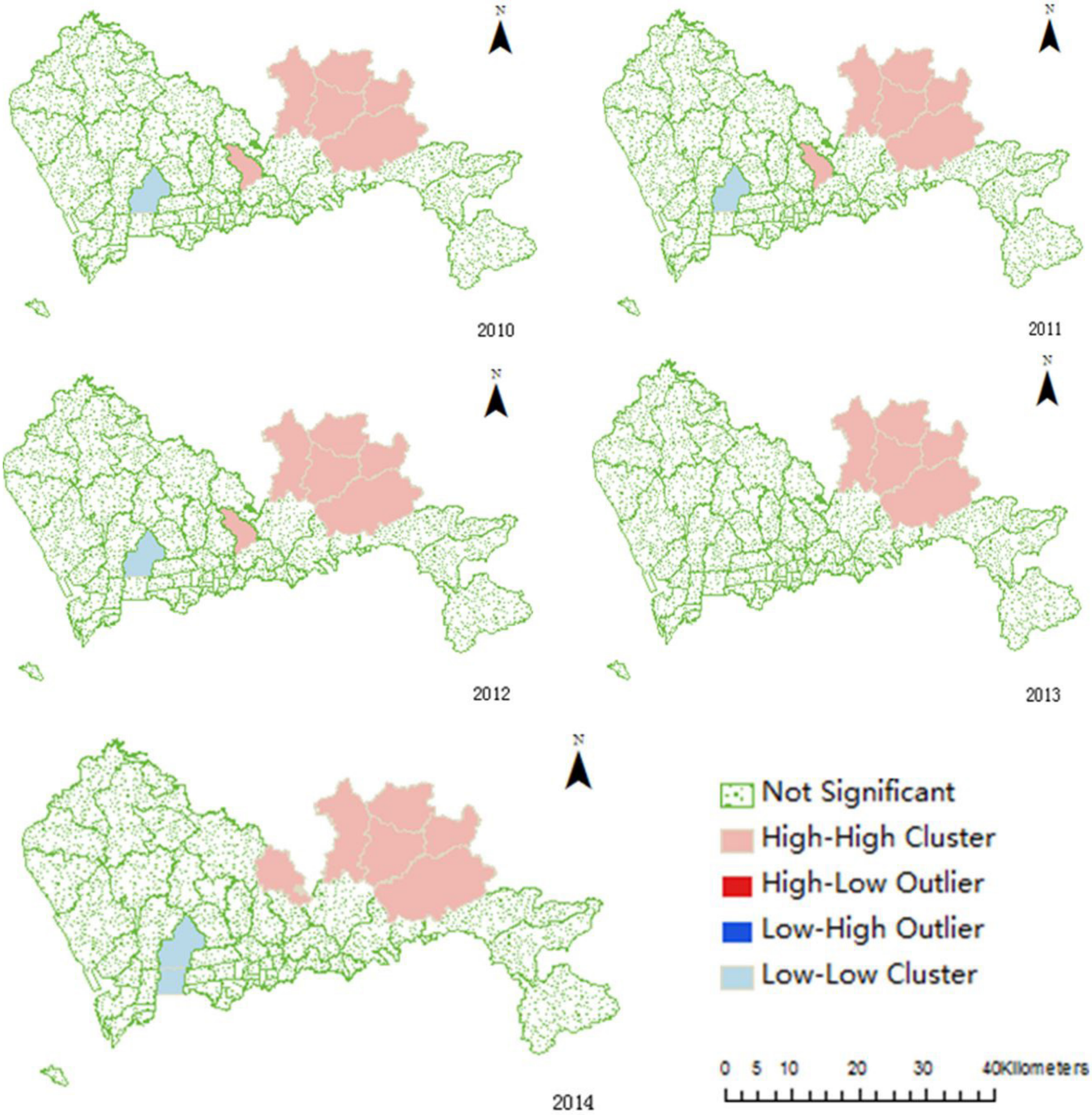

Figure 4: Spatial correlation cluster maps for HFMD incidence, 2010–2014

Spatiotemporal clusters were identified using the space-time scan statistics method. At least two cluster areas were found each year during the study period (Figure 5). The centroid of the most likely cluster in 2010 was located at the Meisha sub-district 22.60N, 114.32E, of which the radius was 5.9 km. The relative risk of the cluster was 5.90, and the cluster time was from 1 April to 31 July 2010. In 2011, the most likely cluster was observed in the Pingshan sub-district (22.69N, 114.35E). The relative risk of the cluster was 6.55, and the cluster time was from 1 May to 31 October 2011. The most likely clusters during 2012–2014 were located in Longcheng sub-district. The relative risks ranged from 4.90 to 7.36, and the cluster time lasted from September 2012 to October 2013 (Table 4). All secondary clusters of HFMD are shown in Figure 5. The most likely cluster is located in the northeastern of Shenzhen City, near by the Huizhou City. The secondary clusters were merged into a large area in the western side of Shenzhen.

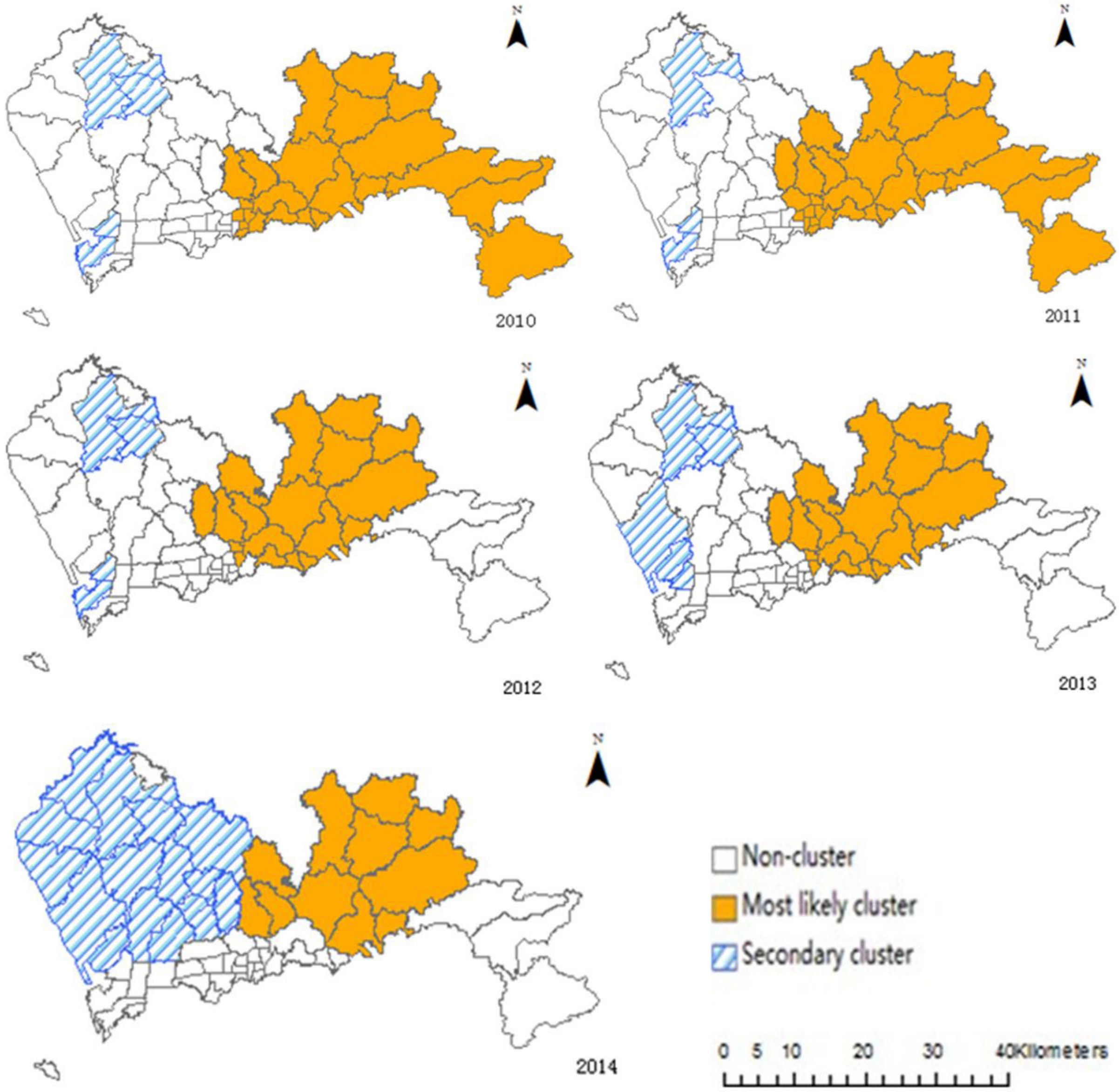

Figure 5: The detected spatial -time clusters of HFMD at the sub-district level in Shenzhen City, 2010–2014

Years	Cluster areas (n)	Cluster Time	Coordinates / radius(km)	Relative Risk	P-value
2010	23	Apr 1 - Jul 31	(22.604718 N, 114.319780 E) /21	5.9	<0.001
2011	28	May 1- Oct 31	(22.697101 N, 114.352779 E) /30.16	6.55	<0.001
2012	18	Apr 1 - Sep31	(22.708425 N, 114.229695 E) /17.51	4.9	<0.001
2013	18	May 1- Oct 31	(22.708425 N, 114.229695 E) /17.51	7.36	<0.001
2014	11	Apr 1 - Jun 30	(22.708425 N, 114.229695 E) /15.79	6.53	<0.001

Table 4: The scanning results of spatial-time cluster analysis of HFMD at the sub-district level in Shenzhen City, 2010–2014

Discussion

The incidence rate of HFMD in Shenzhen was increased from 2010 to 2014, which was higher than the average level in China [3] and neighboring provinces of Guangxi [10] and Hunan [14], and similar to the incidence rate of HFMD in Beijing [12] and Zhejiang [11]. In this study, we used the spatial analysis at the sub-district level in a city. The incidence of HFMD varied greatly between the sub-districts, and a rising trend was observed in recent years (Figure 1), indicating that more effort is needed to prevent and control the disease in those high incidence sub- districts. Consistent with previous studies in China provinces, children, especially boys under-five, were the most susceptible group [8-15]. The predominant pathogen was EV71, which is similar to other studies in Southeast Asia [4,22] and China [23], but different from Japan (Cox 16) [24]. However, the percentage of EV71 was different in different provinces [10-15]. Season peak was similar to Beijing [12] and southern provinces, such as Zhejiang, Chongqing, Hunan, Guangxi [10-11,14-15], but different from Shandong province (only one) [13].

The sub-districts with high incidence rate of HFMD were located in northeastern Shenzhen, near the Huizhou City, where there could be more population mobility, and with worse health situation. The most likely clusters were located at the Longcheng sub-district, which is near the city boundaries, and adjacent to Dongguan and Huizhou city. The results indicated that more resources and cooperation should be focus on these area. This was similar to the spatial autocorrelation patterns in the whole mainland China at province spatial scale levels [10-15]. Further spatial autocorrelation analysis should be completed to demonstrate the spatial epidemic nature at much smaller spatial scale levels, including community level. Focus should be given to the sub-districts with high incidence rates and interventions should be proposed so as to control the HFMD affectively. The limitation of this study are acknowledged as the following. First, the level of spacial measurement should be set at the community level. The more specific the spatial level, the more accurate clusters can be found. Furthermore, the social economic data based on the sub-district were collected, which could be indicating the possibility for more reasons for high HFMD incidence rates [25-27].

Conclusions

In summary, this study highlighted that the HFMD incidence from 2010 to 2014 in Shenzhen City, exhibited dynamic spatial-temporal distribution at the sub-district level. The sub-districts with high incidence rates were located in the northeastern section of Shenzhen, indicating that more focus is needed in those areas. The government and authority in those regions should cooperate and give more attention to these areas and provide public health measures to maximize prevention of this disease. It will be more useful to conduct accurate measures to prevent the HFMD at sub-district level.

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