ORIGINAL RESEARCH

Spatiotemporal Epidemiology of the Gonorrhea Epidemic in Relation to Neighborhood-level Structural Factors in an Eastern Province of China, 2016-2020

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ABSTRACT

Context • Gonorrhea, a highly communicable, sexually transmitted infection, remains a major public-health concern globally. In recent years, Zhejiang province, an eastern province, has had the highest incidence of gonorrhea in China.

Objective • The study intended to identify the geographic distribution patterns and spaciotemporal clustering characteristics of the disease's incidence in Zhejiang between 2016 and 2020, to understand the spatial epidemiology of gonorrhea and to pinpoint the locations with relatively high risks of gonorrhea, the hotspots, which could be the key areas for disease prevention and control.

Design • The research team performed a retrospective, spaciotemporal-clustering analysis of data about newly reported gonorrhea cases from January 2016 to December 2020 in Zhejiang province, using the China Information System for Disease Control and Prevention.

Setting • The study took place at the Zhejiang Provincial Institute of Dermatology in Huzhou, China.

Outcome Measures • The research team: (1) used the Geographic Information System software-ArcGIS 10.8 software to draw statistical maps; (2) conducted a spatial-pattern clustering analysis at the district or county level; (3) performed an autocorrelation analysis using Getis-Ord (Gi*) statistics to detect spatial patterns and the hotspots of gonorrhea incidence; and (4) used SaTScan9.7 to analyze the space-time clusters.

Results • Zhejiang province reported 85 904 gonorrhea cases from 2016 to 2020, with a male to female ratio of 3.81:1. The average annual incidence rate of gonorrhea was 30.50 per 100 000 individuals in the population, ranging from 22.73 cases to 39.65 cases, and the annual incidence showed a significant downward trend over the five years ($\chi^2 = 16.142$, $P < .001$). The northern and central areas had a higher incidence than the southern area did. Autocorrelation analysis showed that the gonorrhea incidence had a significantly clustered distribution (Moran's I from 0.197 to 0.295, Z score from 4.749 to 6.909, $P < .001$). The high-high cluster areas were mainly in the urban districts of Hangzhou and some counties and districts of Jiaxing. The Gi* statistics further indicated that the hotspots of gonorrhea were mainly in Hangzhou, Jiaxing, and Huzhou. The Kuldorff's scan identified two clusters, mainly composed of 36 counties or districts in northern Zhejiang, such as Hangzhou and Jiaxing, and central Zhejiang, such as Jinhua and Shaoxing.

Conclusions • The gonorrhea incidence rates in northern and central Zhejiang from 2016 to 2020 were higher than those in southern Zhejiang. An area of relatively higher risk for gonorrhea existed mainly in the urban districts of Hangzhou and some counties and districts of Jiaxing, Jinhua, and Shaoxing. In the future, the research team plans to focus on strengthening the prevention and control measures against gonorrhea in those areas. (*Altern Ther Health Med.* 2023;29(6):350-357).

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Gonorrhea is a highly communicable, sexually transmitted infection that the bacterium neisseria gonorrhoeae causes. If not appropriately managed, gonorrhea can result in severe complications, such as pelvic inflammatory disease, ectopic pregnancy, infertility, epididymitis, gonococcemia, and disseminated gonococcal infection[1] and can also facilitate the further transmission and increase the risk of infection with human immunodeficiency virus (HIV).[2-4]

According to the World Health Organization (WHO), about 88-million new cases of gonorrhea occur every year globally, with the disease ranking second in the incidence of sexually transmitted diseases.[5] The widespread prevalence of gonorrhea is an urgent public-health and social issue worldwide.

Gonorrhea in Men and Women

Yue et al found that more gonorrhea cases occurred in men than women at the national level in China.[6] There were reports that the gonorrhea incidence in women was higher in some developed countries, such as the USA, than that of men.[7]

Some studies have indicated that female gonococcal infections often demonstrate insignificant or atypical symptoms and that diagnosis must rely on a neisseria-gonorrhoeae culture or a polymerase chain reaction (PCR) test, with the failure to use those tests resulting in a lower rate of visits or detection of infected persons; diagnosis in males can also occur using a smear examination.[8-10] The PCR test commonly used in developed countries is insufficiently deployed in Chinese medical institutions, with only 35.59% of medical institutions at 105 STD monitoring points in China carrying out gonococcal cultures and only 9.35% carrying out PCR tests for gonorrhea diagnosis.[11]

Li et al's survey found that gynecological outpatient clinics diagnosed 80.31% of female gonorrhea in China, suggesting that those clinics are the main places to find and report gonorrhea for Chinese women.[12]

Some gynecologists are unwilling or unable to perform gonococcal cultures. Instead, they often diagnose and treat patients based on therapies for other gynecological inflammations, such as cervicitis and urethritis, resulting in missed diagnoses and missed reporting.[13]

Economic and Social Factors

The prevalence of STDs is closely related to social, economic, and cultural factors. Economically developed areas tend to have higher population mobility and more high-risk sexual behaviors, which can lead to an increase in the incidence of STDs.[14-16]

Migrants in China, called floating people, live and work in areas other than those in which they originally registered, for various reasons and without a valid certificate of residence. Most are in the sexually active age and often have a lower education level, lower income, poorer healthcare awareness, and weaker social restraints than other populations. They are at risk of suffering from reproductive-tract infections, sexually transmitted diseases, and AIDS.[17-19]

Spatiotemporal Analysis

With people's increasing mobility and the rapid development of the service industry in China, the spread of gonorrhea has become increasingly complicated. Spatiotemporal analysis of gonorrhea transmission may be conducive to identification of high-risk areas. It's necessary to analyze the epidemiological characteristics of gonorrhea and the factors influencing its spread at a deeper level.

Researchers have widely used the Geographic Information System (GIS) in spatial epidemiology and disease investigation.[20] With the assistance of spatial statistics, spatial epidemiology can describe and analyze the distribution of diseases, health conditions, and latent factors.[21,22] Researchers commonly perform statistical analyses using space-time scans to detect and evaluate the characteristics of disease clusters in terms of both space and time.[23-26]

Zhejiang Province

In recent years, Zhejiang province, an eastern province, has had the highest incidence of gonorrhea in China. Cai et al's study for 2004-2012 found relatively higher risk areas for gonorrhea incidence in the urban districts of Hangzhou and in some counties and districts in the cities Jiaxing, Jinhua, and Shaoxing in the northern and central Zhejiang provinces.[27]

Several studies generally showed a downward trend in incidence in Zhejiang province from 2016 to 2020, which was different from other provinces, such as Beijing, Hainan, Yunnan, and Jiangxi.[28-31] The decrease was possibly due to the reinforcement of standardized diagnosis and treatment services for sexually transmitted diseases (STDs) and timely intervention for high-risk behavior in recent years in China. These actions may have effectively controlled the source of infection through timely and standardized treatment of gonorrhea patients, with the transmission of STDs being blocked to a certain extent through timely intervention for high-risk behaviors and the promotional use of condoms.

Current Study

The current study intended to identify the geographic distribution patterns and spaciotemporal clustering characteristics of gonorrhea's incidence in Zhejiang between 2016 and 2020, to understand the spatial epidemiology of gonorrhea and to pinpoint the locations with relatively high risks of gonorrhea, the hotspots, which could be the key areas for disease prevention and control.

METHODS

Procedures

Area and population. The research team performed a retrospective spaciotemporal-clustering analysis of data about newly reported gonorrhea cases from January 2016 to December 2020 in Zhejiang province, using the China Information System for Disease Control and Prevention. The study took place at the Zhejiang Provincial Institute of Dermatology in Huzhou, China.

Zhejiang province is located south of the Yangtze River delta along the southeastern coast of China and is one of the smallest provinces in China, with a population of 58.50 million and a land area of 105 400 square kilometers, about

1% of China.[32] This coastal province is divided into 11 municipalities and subdivided into 93 counties or districts, and the study covered all counties and districts.

Data source. The research team obtained: (1) data about the gonorrhea cases from the China Information System for Disease Control and Prevention[33]; (2) the population data from the Zhejiang Provincial Bureau of Statistics[34]; and (3) the map of the county-and-district-level administrative divisions in Zhejiang Province from the National Basic Geographic Information System.[35]

Descriptive analysis. The research team conducted this analysis using the SPSS 19.0 software (IBM SPSS Inc., Chicago, USA). The team: (1) collected data for all gonorrhea cases, including their dates of onset, to determine the temporal patterns of the disease; (2) summarized all descriptive information for the gonorrhea cases annually according to the geographic counties and districts; (3) calculated the incidence rates for each county and district; (4) generated a choropleth map, a statistical thematic map, of temporally smoothed gonorrhea incidence using the software ArcGIS 10.8 (Esri, California, USA) to present both the interannual variation and intercounty disparity.

Spatial pattern analysis. The research team: (1) used Global Moran's I index tool[36] (Esri, California, USA) to distinguish the spatial autocorrelation patterns of gonorrhea in Zhejiang from 2016 to 2020, using the software ArcGIS 10.8; and (2) determined whether the data's distribution pattern was clustered, dispersed, or random, following He et al's techniques.[37]

The research team: (1) used a local Moran's I analysis to determine whether the spatial correlations were positive—high-high or low-low clusters—or negative—high-low or low-high clusters; (2) analyzed the spatial associations between each individual spatial district and its neighboring districts[38]; and (3) according to the geographically adjacent relationship of administrative divisions at the district or county level, generated the spatial weight matrix using the spatial concept of *contiguity edges corners* which were constructed to detect the spatial relationships among the districts.

Hotspot analysis. The research team: (1) assessed the local spatial autocorrelation using Getis-Ord Gi* statistic in ArcGIS 10.8 to explore additional information about the intensity and existence of core hotspot or cold-spot clusters of gonorrhea incidence in the study's area. Two previous studies have described the Gi* statistic.[39,40]

This analysis provides more intuitive results (Visualize hotspots or coldspots in the map), with a better visual exploration and has the advantage of distinctive high-value clusters (hotspots) or low-value clusters (cold spots). A statistically significant Z score for a district identifies the presence of hotspot and cold-spot clusters of gonorrhea incidence, relative to the hypothesis of spatial uncertainty.

A high Z-score means a more closely clustering of high values(hotspots), and low values(cold spots).[41,42] A positive Z-score (Gi*) indicates that the district and its neighboring districts had a relatively high gonorrhea occurrence, a hotspot, compared to other districts. In contrast, a negative *Z* score (Gi*) indicates a cold spot.

Spaciotemporal analysis. The research team conducted a retrospective space-time scan analysis based on a discrete Poisson probability model using SaTScan 9.7 (Martin Kulldorff together with Information Management Services Inc, USA) to detect clusters of gonorrhea incidence in the study's area. The analysis applied Poisson-based model to formulate a process of gonorrhea incidence regarding a known underlying population at risk. The model expresses the probability of a given number of events occurring in a fixed interval of time or space.

The research team set the spatial size of the scanning window at 50% of the total population at risk. The statistical significance of each cluster in the study's area was based on a comparison of the likelihood ratio (LLR) with the maximum number of the replications being set to 999. The team achieved this comparison using a Monte Carlo simulation, a mathematical technique that predicts possible outcomes of an uncertain event.

The team assumed the window with the maximum LLR to be the most likely cluster—the cluster least likely to be caused by chance—and identified other windows with a statistically significant LLR as secondary clusters.

Outcome measures. The research team: (1) used the Geographic Information System software-ArcGIS 10.8 software to draw statistical maps; (2) conducted a spatial-pattern clustering analysis at the district or county level; (3) performed an autocorrelation analysis using Gi* statistics to detect spatial patterns and the hotspots of gonorrhea incidence; and (4) used the SaTScan9.7 to analyze the space-time clusters.

Outcome Measures

Spatial pattern analysis. A value for the Global Moran's I Index that is near +1.0 indicates clustering; a value near -1.0 indicates dispersion; and zero means complete spatial randomness.[43] The high incidence area is surrounded by the surrounding high incidence area, low-low (the low incidence areas are surrounded by low incidence area), high-low (the high incidence areas are surrounded by low incidence areas), and low-high (the low incidence areas are surrounded by surrounding high incidence areas).

Hotspot analysis. The research team considered *Z* scores of >2.58 to identify a district as a significant hotspot, at a 99% confidence interval ($P < .01$). Likewise, the team considered a *Z* score between 1.65 and 2.58 to be significant at a 90% confidence interval ($P < .01$) and categorized those districts as being high risk. A *Z* score of <-2.58 indicated a clustering of low values, which indicated a cold-spot district.

Spaciotemporal analysis. The research team considered the relative risk (RR) of gonorrhea incidence inside and outside the scanning window to be statistically significant if $P < .05$.[44] The team identified the spatial units from the space-time scan analysis as 93 counties or districts in Zhejiang province, and the time units were from 2016 to 2020. The time frame of the scan analysis was set to be a month to control the time trends and to observe the cluster changes in the study's entire period.

RESULTS

Basic Characteristics and Temporal Patterns

Medical practitioners reported 85 904 cases of gonorrhea in Zhejiang province from 2016 to 2020 (Figure 1). Those cases included 68 043 males and 17 861 females, with a male to female ratio of 3.81:1.The average annual incidence of gonorrhea was 30.50 cases per 100 000 people, ranging from 22.73 to 39.65 cases per 100 000 people. Over the five years, the annual incidence was on a significant downward trend ($\chi^2 = 16.142$, $P < .001$).

Mapping the temporally smoothed gonorrhea incidence from 2016 to 2020 at the district and county level showed spatial heterogeneity (Figure 2). The gonorrhea incidence in northern and central Zhejiang were higher than that in the southern region. The number of counties and districts with an annual incidence higher than 50 cases out of 100 000 people increased from 13 in 2016 to 23 in 2017, mainly in Hangzhou, Jiaxing, Jinhua, and Shaoxing. But since 2018, the incidence has decreased year by year. In 2020, Tonglu county in Hangzhou was the only area with an incidence rate higher than 50 cases out of 100 000 people.

During the study's five-year period, seven counties and districts had an average annual incidence of more than 50 out of 100 000 people, including Yuhang district and Tonglu county in Hangzhou, Nanhu district and Tongxiang county in Jiaxing, Yiwu and Yongkang county in Jinhua, and Keqiao district in Shaoxing. All were in northern and central Zhejiang. The areas with a lower incidence were mainly in Wenzhou and Lishui, located in southern Zhejiang.

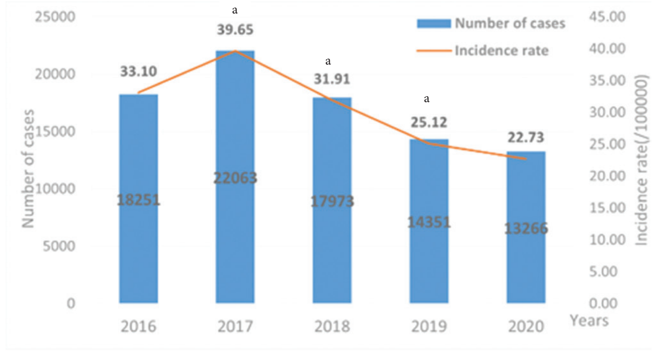
Spatial Patterns

Table 1 shows that significant positive spatial clustering of gonorrhea incidence existed in Zhejiang province in each year from 2016 to 2020 (Moran's I from 0.197 to 0.295, Z score from 4.749 to 6.909, $P < .001$).

The local Moran's I analysis revealed diverse cluster patterns of districts with a high gonorrhea incidence—high-high and low-low clusters—during the study's period (Figure 3). During 2016-2020, the high-high aggregation area consisted of 12 counties and districts, such as Xihu and Gongshu district in Hangzhou, Xiuzhou district and Haining county in Jiaxing, and Deqing county in Huzhou. The low-low aggregation area consisted of 11 counties and districts, such as Lucheng and Longwan district in Wenzhou, Qingtian county in Lishui, and Huangyan district in Taizhou.

The low-low aggregation areas changed over the years but were mainly located in some districts and counties of Wenzhou and Lishui, the southern region of Zhejiang. From 2016 to 2017, another high-high aggregation area existed in some counties and districts of Jinhua, the central region of Zhejiang.

Figure 1. Numbers of Reported Gonorrhea Cases and Incidence Rates in Zhejiang Province From 2016 to 2020



[a]$P < .001$, indicating that significant downward trend in gonorrhea cases had occurred between 2016 and 2020.

Figure 2. Geographical Distribution of Gonorrhea Incidence in Zhejiang Province, 2016-2020. The maps show the districts and counties in the province.

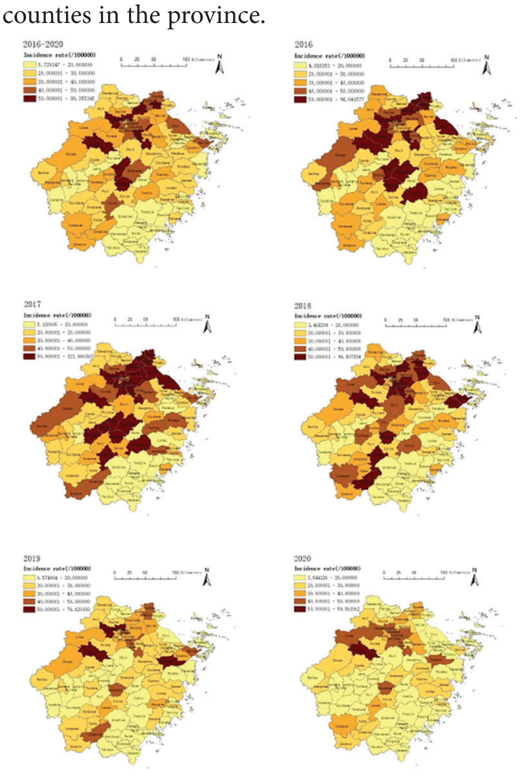


Table 1. Global Spatial Autocorrelation of Gonorrhea Incidence in Zhejiang Province, 2016-2020

Years	Moran's I	*Z* Score	*P* value
2016	0.250	5.921	<.001[a]
2017	0.254	6.060	<.001[a]
2018	0.211	5.045	<.001[a]
2019	0.197	4.749	<.001[a]
2020	0.295	6.909	<.001[a]

[a]$P < .001$, indicating that significant positive spatial clustering of gonorrhea incidence existed in Zhejiang province in each year from 2016 to 2020

Figure 3. Local Spatial Autocorrelation of Gonorrhea Incidence in Zhejiang Province, 2016-2020. The maps show the districts and counties in the province.

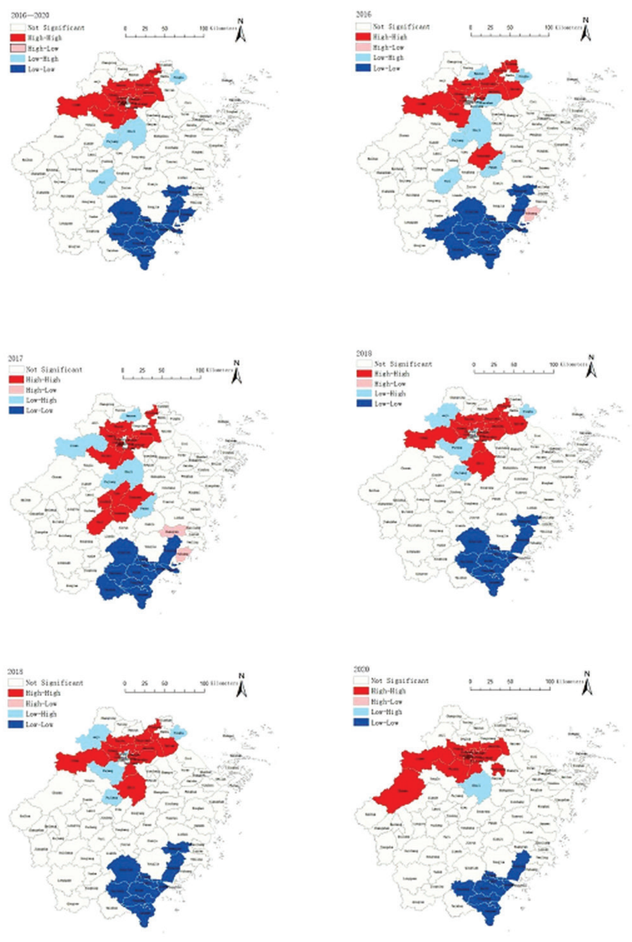


Figure 4. Local Hotspot Analysis of Gonorrhea Incidence in Zhejiang Province, 2016-2020. The maps show the districts and counties in the province.

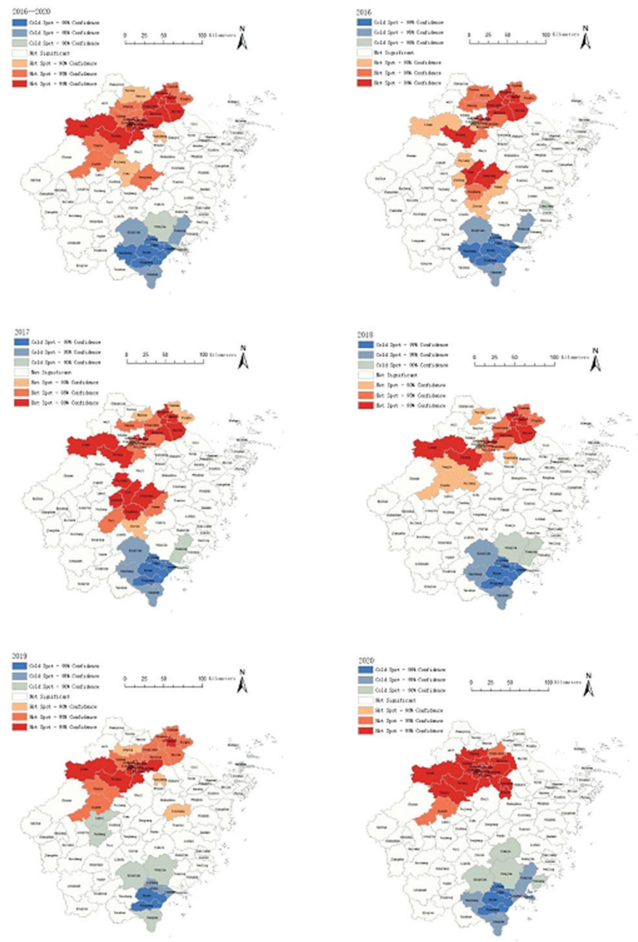


Table 2 shows that the Gi* statistics indicated that a significant number of high-value clusters of gonorrhea incidence existed in Zhejiang province in each year from 2016 to 2020 (General G Score from 0.079 to 0.084, Gi Z Score from 6.534 to 7.646, $P < .001$).

The locations and sizes of hotspot clusters varied over the study's years. However, they consistently existed in the urban districts of Hangzhou, such as Xiaoshan in the Fuyang district, and some counties and districts of Jiaxing and Huzhou, such as in the Xiuzhou district in Tongxiang, Haining and Deqing county.

During 2016-2017, the clustering in some counties and districts in Jinhua, such as in Yiwu and Dongyang county, comprised other hotspots, but the clustering disappeared after 2018 (Figure 4). In 2020, Keqiao and Yuecheng district in Shaoxing merged with hotspot clusters in Hangzhou. In contrast to the variance in hotspots, the cold-spot clusters were constantly concentrated in the counties and districts of Wenzhou.

Table 2. Global Hotspot Analysis of Gonorrhea Incidence in Zhejiang Province, 2016-2020

Years	General G Score	Gi Z Score	*P* value
2016	0.081	6.534	<.001[a]
2017	0.084	7.273	<.001[a]
2018	0.079	6.647	<.001[a]
2019	0.079	6.590	<.001[a]
2020	0.082	7.466	<.001[a]

[a]$P < .001$, indicating that a significant number of high-value clusters of gonorrhea incidence existed in Zhejiang province in each year from 2016 to 2020

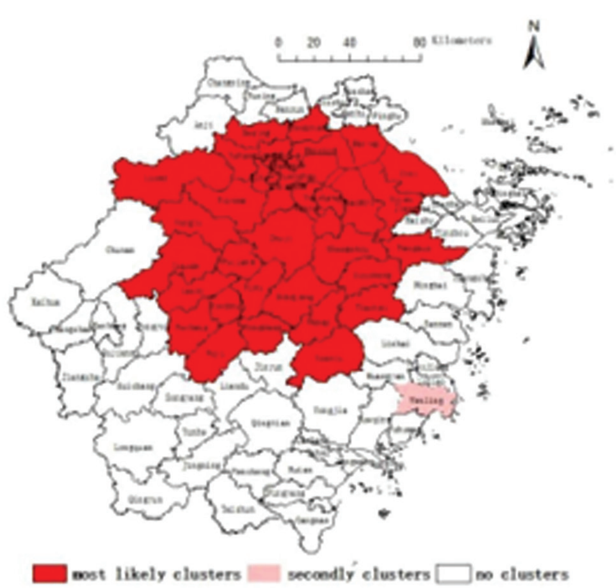
Abbreviations: Gi, Getis-Ord.

Table 3. Spaciotemporal Cluster Analysis of Gonorrhea Incidence in Zhejiang, 2016-2020.

Cluster Distribution	Cluster Districts	Cluster Timeframe	Relative Risk	Likelihood Ratio	*P* value
Most Likely Clusters	In Hangzhou: Lin'an, Gongshu, Fuyang, Yuhang, Xiaoshan, Binjiang, Shangcheng, Xiacheng, Jianggan, Xihu, Tonglu, Jiande In Ningbo: Fenghua, Cixi, Yuyao In Jiaxing: Haiyan, Haining, Tongxiang In Huzhou: Deqing In Shaoxing: Keqiao, Yuecheng, Shangyu, Xinchang, Zhuji, Shengzhou In Jinhua: Jindong, Wucheng, Pujiang, Pan'an, Wuyi, Dongyang, Yiwu, Yongkang, Lanxi In Taizhou: Tiantai, Xianju	March 2016 - August 2018	2.04	4675.94	<.001[a]
Secondary Clusters	In Taizhou: Wenling	June 2016 - November 2018	2.55	222.03	<.001[a]

[a]$P < .001$, indicating that a significant probability existed that the most likely clusters covered the 36 listed counties and districts, with a cluster time ranging from March 2016 to August 2018, and that the secondary clusters covered the listed county from June 2013 to November 2018.

Figure 5. Spaciotemporal Cluster Analysis of Gonorrhea in Zhejiang Province, 2016-2020. The red represents the most likely clusters; the pink represents the secondary clusters; and the white represents no clusters in the study's area.



Spaciotemporal Cluster Analysis

Table 3 and Figure 5 show that a significant probability existed that the most likely clusters covered 36 counties and districts, mainly in Hangzhou, Jiaxing, Jinhua, and Shaoxing, with a cluster time ranging from March 2016 to August 2018 (RR = 20.04, LLR = 4675.94, $P < .001$). A significant probability existed that the secondary clusters were in Wenling county of Taizhou, with a cluster time ranging from June 2016 to November 2018 (RR = 2.55, LLR = 222.03, $P < .001$). After 2018, no statistically significant spatiotemporal clusters have been detected.It may be that the temporal and spatial clustering characteristics were not significant because of the decreased incidence of gonorrhea.

DISCUSSION

The current study demonstrated that the northern and central areas in Zhejiang province had a higher gonorrhea incidence than the southern area. The study also identified that a relative higher risk area for gonorrhea incidence was mainly detected in urban districts of Hangzhou and some counties/districts of Jiaxing, Jinhua and Shaoxing, the northern and central of Zhejiang province, which is consistent with the findings of Cai et al's study.[27]

The current study also showed that more gonorrhea cases occurred in men than women in Zhejiang Province, which is similar to the characteristics of the national gonorrhea epidemic.[22] The research team has hypothesized that gonorrhea cases of women may be underreported. In the future, the current research team intends to improve the monitoring grid for gonorrhea, and strengthen the monitoring of gonorrhea in medical institutions. It's also necessary to strengthen the provision of information to women to promote their self-care awareness and enhance their awareness of the need for active medical treatment.

The current study's spatial autocorrelation analysis showed that the gonorrhea incidence in Zhejiang province was clustered. The study found statistically significant clusters of gonorrhea incidence, including hotspots clusters, in different counties and districts in each year of the study. The high-high agglomeration areas and hotspots were mainly concentrated in the urban districts of Hangzhou and some counties and districts that were located in the northern region of Zhejiang.

The low-low agglomeration areas and cold spots were mainly concentrated in the counties and districts of Wenzhou, located in the southern region of Zhejiang, which is consistent with Cai's earlier report.[27] Therefore, the results of the current study suggest that the urban districts of Hangzhou and some districts and counties of Jiaxing such as Xiuzhou, Haining, and Tongxiang should be the key areas for the prevention and control of gonorrhea in Zhejiang province.

In addition, medical practitioners shouldn't ignore Jinhua and Shaoxing, located in the central region of Zhejiang, because some counties and districts, such as Yiwu, Dongyang, and Yongkang in Jinhua and Keqiao and Yuecheng district in Shaoxing were high-high agglomeration areas and hotspots in some years of the study.

The spaciotemporal analysis found that the most likely clusters of gonorrhea in Zhejiang mainly occurred in Hangzhou, Jiaxing, Shaoxing, and Jinhua. These counties and districts have more developed industry, a denser population, and higher population mobility, which can increase the difficulty of prevention and control of STDs such as gonorrhea.

Therefore, the current research team believes that China should rationally adjust health resources in key areas of gonorrhea transmission and create health-education methods for the floating people, such as using WeChat, TikTok, or other social-media platforms that offer short-time consumption, fast dissemination, and wide acceptance, to improve the effect of health education and intervention in high-risk behaviors. This current study holds the promise of providing an epidemiological basis for precise prevention and control strategies.

The research team based the current study on the information about gonorrhea cases obtained from the China Information System for Disease Control and Prevention. Additional information such as patient's ethnic customs, floating-population distribution, educational levels, and high-risk behavior was insufficient. Therefore, it was difficult to evaluate the incidence with respect to other risk factors and speculate on the cause of the incidence aggregation. In the future, the research team needs to conduct further special investigations and acquire more detailed information to explore the deep-seated reasons for the regional aggregation.

CONCLUSIONS

The gonorrhea incidence rates in northern and central Zhejiang from 2016 to 2020 were higher than those in southern Zhejiang. An area of relatively higher risk for gonorrhea existed mainly in the urban districts of Hangzhou and some counties and districts of Jiaxing, Jinhua, and Shaoxing. In the future, the research team plans to focus on strengthening the prevention and control measures against gonorrhea in those areas.

AUTHORS' DISCLOSURE STATEMENT

The authors declare that they have no conflicts of interest related to the study. The Zhejiang Provincial Natural Science Foundation of China under Grant NO.LGF22H260008, LGF20H260004 supported the study.

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