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Investigation of tuberculosis clusters in Dehradun city of India

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ABSTRACT

Objective: To investigate the presence of statistically significant geographical clusters of tuberculosis (TB) using Geographical Information System and spatial scan statistics in Dehradun, India. **Methods:** The spatial scan statistic implemented with a software program, SaTScan v6.1, was used to test the presence of statistically significant spatial clusters of TB and to identify their approximate locations ($P< 0.05$ for primary clusters and $P<0.1$ for secondary clusters). Geographical Information System was used for geographical analysis. **Results:** Significant high rate spatial clusters were identified in seven wards of the Dehradun Municipal area. **Conclusions:** There is sufficient evidence about the existence of statistically significant TB clusters in seven wards of Dehradun, India. The purely spatial scan statistics methodology used in this study has a potential use in surveillance of TB for detecting the true clusters of the disease.

1. Introduction

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis* and spreads through air by a person suffering from TB. The World Health Organization (WHO) report on the Global Burden of Disease in 1990 ranked TB as the seventh most morbidity-causing disease in the world, and expected it to continue in the same position up to 2020. In 2001, the WHO estimated that 1.86 billion persons (32% of the world population) were infected with TB. Each year, 8.74 million people develop TB and nearly 2 million die. Unless properly treated, an infectious pulmonary TB (i.e., the TB of lungs) patient can infect 10-15 people in a year[1]. TB is the most common opportunistic disease that affects people infected with human immunodeficiency virus (HIV). As HIV debilitates the immune system, vulnerability of TB is increased by many fold. It is estimated that without HIV, the lifetime risk of TB-infected people developing TB is only 10%, compared to over 50% in the case of people co-infected with HIV and TB. HIV is also the most powerful risk factor for the progression of TB-infection to the disease. In a reciprocal manner, TB accelerates the progression of HIV into acquired immune deficiency syndrome (AIDS), thus shortening the survival of patients with HIV infection. Fortunately, TB is a curable disease even among the HIV-infected people. The prevalence of TB and HIV co-infection worldwide is 0.18% and about 8% TB cases have HIV infection.

In 2009, out of the estimated global annual incidence of 9.4 million TB cases, 1.98 million were estimated to have occurred in India, thus accounting for one fifth of the global burden of TB. TB is one of the leading causes of mortality in India, killing 2 persons every three minutes, nearly 1 000 every day. Each year nearly 2 million people in India develop TB, of which around 0.87 million are infectious cases. It is estimated that annually around 330 000 Indians die due to TB[1]. As per the WHO 2009 Global TB Control Report, TB mortality in the country has reduced by 43%, from an estimated 42/lakh population in 1990 to 24/lakh population in 2009, and the prevalence of TB in the country has reduced by 67%, from 568/lakh population in 1990 to 185/lakh population[2]. In India, every year TB results in 300 000 children leaving schools. Economic burden to the society is to the tune of approximately $ 3 billion[1]. The emergence of TB/HIV co-infection poses an additional challenge to the control of TB in India. According to the 2006 Report on Global AIDS Epidemic, India now has the highest number of people living with HIV. It has 5.7 million HIV infected persons by the end of 2005, against 5.5 million in South Africa[3]. With such a magnitude of disease and looming danger of HIV co-infection, TB is the biggest public health challenge for India.

To control this scourge, the National Tuberculosis Control

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Program (NTCP) was adopted in India in 1962. However, the desired results were not forthcoming. The diagnosis was over-dependence on X-ray. Treatment management were often non-standard and incomplete treatment was the norm rather than an exception. On recommendations of an expert committee in 1992, a revised strategy to control TB was adopted under the name of RNTCP. The RNTCP has now completed over 11 years of its implementation, with 3 years of full nationwide coverage. Since its inception, the program has initiated treatment to over 11 million patients, thus saving nearly 2 million additional lives[1].

The use of Geographical Information System (GIS) with spatial statistics, including spatial filtering and cluster analysis has been applied to many diseases to analyze and more clearly display the spatial patterns of disease[3-9]. Yu and Christakos studied the spatiotemporal modelling and mapping of the bubonic plague epidemic in India during 1896-1906 using stochastic concepts and geographical information science techniques[10]. Paolo Jr and Nosanchuk took an overview of the situation of TB in New York city during 1980-2002 and found that the New York city continued to face significant challenges from the persistent pathogens of TB[11]. Tiwari *et al* used GIS and spatial scan statistic to detect the geo-spatial hotspots of TB in Almora district of India and found significant high rate spatial and space-time clusters in three areas of the district[12]. Nunes used GIS and spatial scan statistic to study the TB incidence in Portugal[13].

2. Materials and methods

2.1. Study area

The city of Dehradun is situated in the south central part of the Dehradun District of Uttarakhand, India. For the control of TB in the region, the Dehradun district has been divided in to three Tuberculosis Units (TUs), situated at Dehradun, Rishikesh and Chakrauta. The microscopic test of sputum for detection of TB can be carried out at sixteen Microscopic Centres (MCs) of the district.

2.2. Data collection

For the present study, the secondary data of the TB patients treated in Dehradun Tuberculosis Unit of Dehradun District, situated at Doon Hospital, Dehradun were collected. The data was recorded directly from the Tuberculosis Register of this TU during January 1, 2007-May 31, 2008. This data contained the personal information like age, sex, religion, address, etc. and treatment details. On the basis of these details, patients were divided into 45 wards of Dehradun Municipal area created on the basis of 2001 census. The list of these wards, population and area details were taken from Dehradun Municipal Board. During January 1, 2008-May 31, 2008, there were in all 829 TB patients registered in Dehradun TU, out of which 478 patients (302 male and 176 female patients) belonged to Dehradun Municipal area. Similarly, during January 1, 2007-December 31, 2007, there were in all 1 850 TB patients registered in dehradun TU, out of which 1 044 patients (659 male and 385 female patients) belonged to Dehradun Municipal area.

2.3 Data analysis

The spatial scan statistic developed by Martin Kulldorff implemented in a software program, SaTScan v6.1[14], was used to test the presence of statistically significant spatial clusters of TB and to identify their approximate locations. Purely spatial analysis, which does not take time into account, was performed to detect the TB clusters in the study region. The spatial scan statistic imposes a circular window on the map and lets the center of the circle move over the area so that at different positions the window includes different sets of neighboring census areas. If the window contains the centroid of the census area, then that whole area is included in the window. For each circle centroid, the radius of the circular window is varied continuously from 0 up to a maximum radius so that the window never includes more than 50% of the total population at risk. The spatial scan statistic is based on the likelihood ratio test. As the likelihood ratio is maximized over all the circles, it identifies the circle that constitutes the most likely cluster. Its P-value is obtained through Monte Carlo hypothesis testing technique. To find the distribution of the test statistic, 999 random Monte Carlo replicates of the data set under the null hypothesis of no significant clusters are generated, calculating the test statistic for each replica.

Identification of spatial high/low clusters was done under Poisson probability model assumption. The maximum spatial cluster size was first set to include up to 50% of population for both excesses and deficits and then set at 10% and 5%, to test the excesses and deficits separately because testing at the 10% and 5% levels can identify smaller, more defined areas. For statistical inference, 999 Monte Carlo replications were performed. For purely spatial analysis, the null hypothesis of no significant clusters is to be rejected when the simulated P-value was less than or equal to 0.05 for the primary clusters and 0.1 for the secondary clusters since the later have conservative P-values. For geographical analysis the GIS was used. All the geographical and cartographic outputs were presented by the ArcGIS 9 application software.

3.Results

With the maximum spatial cluster size as $\leqslant$5% of the total population, the spatial cluster analysis identified the most likely significant cluster for high occurrence of TB in the Dharampur ward of Dehradun for 2008. The overall relative risk (RR) within the cluster was 2.81 with an observed number of 29 cases treated between January 1, 2008 and May 31, 2008, compared with 10.75 expected cases. Statistically significant secondary cluster for high occurrence of TB were also detected at Khudbura, Ajabpur, Adhoiwala and Patel Nagar wards (Table 1).

The spatial cluster analysis identified the most likely significant cluster for high occurrence of TB in the Adhoiwala ward of Dehradun for 2007. The overall RR within the cluster was 3.12 with an observed number of 117 cases treated between January 1, 2007 and December 31, 2007, compared with 40.62 expected cases. Statistically significant secondary cluster for high occurrence of TB were also detected at Dharampur, Gandhi Gram, Rajpur, Ajabpur and Khudbura wards of Dehradun(Table 1).

The overall RR within the cluster was 0 for the year 2008 and 0-40 for the year 2007 at Mansinghwala, and the low rate dusters were also at Aryanagar, Maharanibag and Salawala in 2007. While Maharanibag had the lowest overall RR in 2007. The details were shown in Table 2.

Figure 1& 3 showed the spatial representation of high rate clusters in 2007 and 2008, respectively, and Figure 2 showed the geographical view of high rate TB zones in 2008. Table 3 provideed the information regarding the high rate TB zone in 2008, which consisted of 19 wards of the city with total number of 274 TB cases reported between January to May 2008, and the low rate zone, consisting of 22 wards in 5 groups with 77, 86, 5, 28 and 15 TB cases, respectively.

Table 1
High rate clusters for 2007 & 2008.

Year	Location	No. of cases	Relative risk	Log Likelihood	*P*-Value
2007	Adhoiwala	117	3.12	50.35	0.001
	Dharampur	64	2.82	24.17	0.001
	Gandhi Gram	60	2.15	13.30	0.001
	Rajpur	57	2.16	12.84	0.001
	Ajabpur	77	1.85	11.44	0.003
	Khudbura	39	2.06	7.88	0.008
2008	Dharampur	29	2.81	10.88	0.001
	Khudbura	25	2.95	10.19	0.001
	Ajabpur	35	1.85	5.19	0.022
	Adhoiwala	33	1.85	4.85	0.039
	Patel Nagar	18	2.26	4.54	0.057

Table 2
Low rate clusters for 2007 & 2008.

Year	Location	No. of cases	Relative risk	Log likelihood	*P*-Value
2007	Maharanibag	1	0.03	25.25	0.001
	Arya Nagar	5	0.20	12.63	0.001
	Jhanda Mohalla	2	0.11	12.39	0.001
	Karanpur, Bakralwala	13	0.33	11.83	0.001
	Shivaji	2	0.11	11.67	0.001
	Mansinghwala, Rispana	15	0.40	8.56	0.003
	Idgah, Sridev Suman Nagar	23	0.47	8.13	0.005
	Bhandaribagh	9	0.38	6.04	0.022
	Race Course(N)	9	0.42	4.64	0.071
	Salawala	7	0.38	4.59	0.084
2008	Mansinghwala	0	0.00	8.49	0.004
	Arya nagar	1	0.08	8.31	0.005
	Maha ranibag	2	0.15	7.65	0.010
	Salawala	1	0.12	5.23	0.065

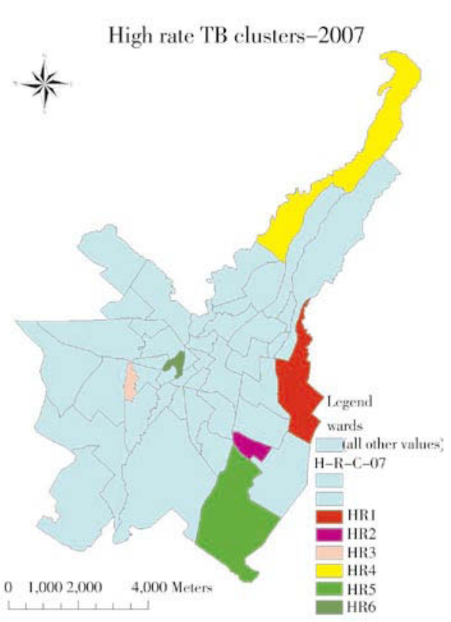

Figure 1. High rate TB clusters in 2007.

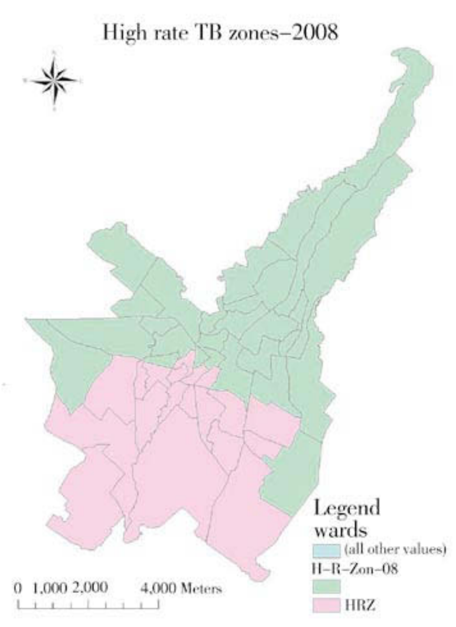

Figure 2. High rate TB zones in 2008.

Table 3
High and low rate zones for 2008.

	Location	No. of cases	Relative risk	Log likelihood	*P*-value
High zone	Bhandaribagh, Race Course(S), Patel Nagar, Chander Nagar, Lakhibagh, Ritha Mandi, Race Course(N), Ajabpur, Niranjanpur, Dharampur, Majra, Laxman Chauk, Gandhi Gram, Indresh Nagar, Dhamawala, Kanwali, Dalanwala (S), Jhanda Mohalla, Khudbura.	274	1.66	15.04	0.001
Low zone	Ballupur, Sri Dev Suman Nagar, Rajendra Nagar, Kaulagarh, Maharanibagh, Idgah, Shivaji Ward, Indra Colony	77	0.41	37.06	0.001
	Mahadevi KP , Bakralwala, Lunya Mohalla, Dhamawala, Karanpur, Dandi Pura, Chukhuwala, Jhanda Mohalla, Race Course(N)	86	0.44	33.44	0.001
	Arya Nagar	5	0.19	12.63	0.001
	Bhandaribagh, Race Course (S)	28	0.48	9.47	0.002
	Rispana,Mansinghwala	15	0.40	8.56	0.004

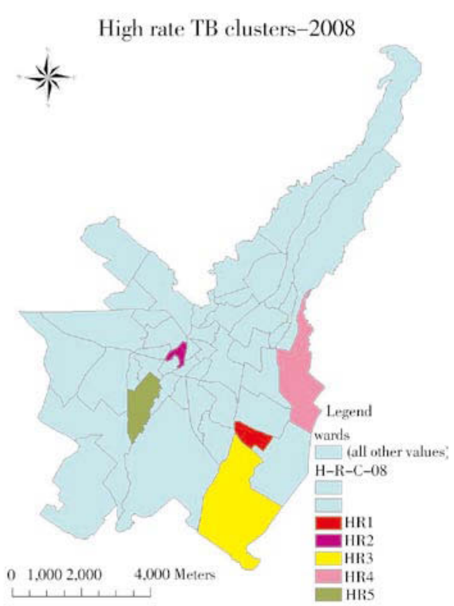

Figure 3. High rate TB clusters in 2008.

The results of the study suggested that there were statistically significant hotspots of *Mycobacterium tuberculosis* in 5 wards for 2008 and 6 wards of the city for 2007. One high rate zone of TB was also detected in Dehradun city, consisting of 19 wards for 2008.

4. Discussion

The basic problems in geographical surveillance for a spatially distributed disease are the identification of areas with exceptionally high prevalence, to test their statistical significance and to identify the reasons behind the elevated prevalence of the disease. A hotspot is an area of high response or an elevated cluster for an event. Cluster analysis identifies whether geographically grouped cases of disease can be explained by chance or are statistically significant. It detects true clusters of disease from cases grouped around population centres. Temporal, spatial and space-time scan statistics are commonly used for disease cluster detection and evaluation. Some of them are either able to detect clusters with no inference involved, or they do inference without the ability to detect the location of clusters. However, the spatial scan statistic developed by Martin Kulldorff can both detect and provide inference for spatial and space-time disease clusters. The spatial scan statistic implemented in SaTScan software[14] offers several advantages over the existing techniques for detection of disease clusters. The use of GIS with spatial statistics, including spatial filtering and cluster analysis has been applied to many diseases to analyze and more clearly display the spatial patterns of disease. Temporal, spatial and space-time scan statistics are now commonly used for disease cluster detection and evaluation, for many diseases including cancer, Creutzfeldt-Jakob disease,granulocytic ehrlichiosis, sclerosis, diabetes, giardiasis and TB[3-13]. The scan statistic was used for the first time by Tiwari *et al* to detect the clusters of *Mycobacterium tuberculosis*[12]. There had been very few studies to detect the statistically significant clusters of TB in Uttarakhand, India. The detection of these clusters may be highly useful in surveillance of the disease and finding the factors behind the spread of the disease and make suitable policies to control these factors.

The results of the study provide useful information on the prevailing epidemiological situation of TB in the Dehradun city of Uttarakhand, India. This will serve as a baseline for evaluating the impact of disease control measures and epidemiological trends in the coming years. This type of studies can help the district TB units to identify areas of high TB prevalence and chalk out strategies in a more focused way. This would initiate intensified case finding activities, further promotion of general health and hygiene, improving nutritional status of the community, compulsory Bacillus Calmette-Guerin (BCG) immunization of the children, and better coordination of government and private sector in the hotspots detected by the study. The scope of present study is limited to only the capital city of Uttarakhand, India. There is a scope involving the whole state of Uttarakhand and then the country as a whole. This would mean a critical appraisal of the RNTCP in the whole country. Further, it has been found that the hospitals of good repute get sizeable number of patients from other TUs. Therefore, District Tuberculosis Centres (DTC) must work to activate all hospitals by posting adequate staff and providing better facilities over there. One limitation of Directly Observed Therapy Short-course (DOTS) program is that it is more hospital centric, laying more emphasis on diagnosis and treatment and less on case finding at community level. Our study can identify areas of high prevalence, leading to intensification of case finding activities by district TB control units. This strategy can be highly useful in eradication of TB from the country. Future research will include investigating the effect of various socio-economic and environmental factors on the occurrence of TB in the hilly region of the state.

Conflict of interest statement

We declare that we have no conflict of interest.

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