Spatial analysis of bovine tuberculosis in the State of Mexico, Mexico

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Keywords

Bovine tuberculosis, Cluster, Geographic Information Systems, Mahalanobis Distance, México, Space-time analysis.

Summary

Bovine tuberculosis (bTB) is a chronic infectious disease that affects both domestic animals and wildlife. Veterinary epidemiology studies evaluate bTB using geographic information systems (GIS), which can characterise the spatial and temporal distribution of diseases and identify the geographic areas and animal populations at risk of contracting a disease. The present study used space-time permutation scan statistic to identify the spatial and temporal distribution of bTB from 2005 to 2010 in the State of Mexico with the goal of creating a similarity model using Mahalanobis Distance to identify areas suitable for bTB occurrence. Three significant clusters were identified using space-time permutation scan statistic and the similarity model identified several areas with suitable environmental and demographic characteristics. The results demonstrate that the occurrence of bTB in the State of Mexico is not randomly distributed.

Analisi spaziale della tubercolosi bovina in Messico

Parole chiave

Analisi spazio-tempo, Distanza di Mahalanobis, Sistemi informativi geografici (GIS), Stato del Messico, Tubercolosi bovina.

Riassunto

La tubercolosi bovina (TB) è una malattia infettiva cronica che colpisce animali domestici e selvatici. Gli studi epidemiologici impiegano i sistemi informativi geografici (GIS) per caratterizzare la sua distribuzione spaziale e temporale e individuare le aree geografiche e le popolazioni animali a rischio. Nel presente studio per identificare la TB, nel periodo 2005-2010, nello Stato del Messico, è stata impiegata la tecnica Spatial Scan Statistic di Kulldorff con l'obiettivo di creare un modello di somiglianza tramite la distanza di Mahalanobis e individuare aree idonee alla comparsa della TB. Impiegando la tecnica di Kulldorff sono stati individuati tre *clusters* significativi. Il modello di somiglianza ha permesso di identificare diverse aree con caratteristiche ambientali e demografiche adeguate. I risultati dimostrano che la presenza di TB nello Stato del Messico non è distribuita in modo casuale.

Introduction

Bovine tuberculosis (bTB) is a chronic infectious disease whose etiological agent is *Mycobacterium bovis* (*M. bovis*) (Karlson and Lessel 1970), and

which affects both domestic and wild animals (O'Brien *et al.* 2002, Phillips *et al.* 2003, Miller *et al.* 2007). Oral transmission of *M. bovis* occurs through consumption of contaminated grasses in extensive exploitation systems. Aerial transmission is more

prevalent in intensive exploitation implants, and young animals in this implants can also be infected by *M. bovis* contaminated milk (Phillips *et al.* 2003).

Bovine tuberculosis is important in Mexico and other Latin American countries because of the zoonotic potential of *M. bovis* infection through the consumption of raw milk and milk derivatives produced with unpasteurised milk, this problem is prevalent in developing countries (Abalos and Retamal 2004, de Kantor *et al.* 2008, Milián *et al.* 2010), where milk production is only partially pasteurised. In particular, in Mexico, only 30% of the milk production is pasteurised (SAGARPA 1996).

Bovine tuberculosis causes both direct and indirect economic losses in livestock: infected animals present reduced milk and meat production and either they will be euthanized or they will suffer premature death (Milián *et al.* 2002, Perez *et al.* 2002). Tuberculosis has particular economic impact for the international marketing of cattle and beef products because export products must be certified as bTB-free (Livingstone *et al.* 2006, OIE 2012).

In 1995, Mexico established a national campaign for the eradication of bovine tuberculosis that is still in place. This campaign uses the tuberculin test to diagnose tuberculosis in cattle farms. The policy for bTB control indicates that every animal testing positive should be sent to slaughter (SAGARPA 1996).

In slaughterhouses, samples from bovine tuberculosis typical lesions are collected for microbiological culture, and if *M. bovis* is isolated, the entire herd is quarantined. However, it is not always possible to trace the source of infection because of the lack of information on the origin of the involved animals (SAGARPA 1996, Milián *et al.* 2002, Collins 2006).

Currently, 31.25% of the States of the Mexican Republic (10 out of 32) have a prevalence lower than 0.5%, but in most of the Mexican territory, the prevalence is unknown or greater than 0.5%. However, the south of the State Mexico has a recognized geographical area with a prevalence lower than 0.5% (SAGARPA 2012).

Bovine tuberculosis can be clustered into certain geographical areas because of the presence of risk factors, such as sharing pastures, movement of infected animals within the geographic area and informal trade patterns (Perez *et al.* 2002, Phillips *et al.* 2003, Darren *et al.* 2008).

An important tool in veterinary epidemiology is the use of Geographic Information Systems (GIS), which permit the identification of geographic areas and animal populations that are at risk of contracting a disease and enable the identification of areas where preventive measures are needed. Geographic Information Systems have been used to monitor

diseases in time and space, thus generating a better understanding of the occurrence of diseases like bTB (Ward and Carpenter 2000a, Ward and Carpenter 2000b, Carpenter 2001) In 2005, Olea-Popelka and colleagues (Olea-Popelka *et al.* 2005) conducted an analysis of the spatial relationship between *M. bovis* strains in cattle and badgers in 4 areas in Ireland using the spatial scan statistic, thereby increasing the understanding of the epidemiology of tuberculosis in these geographical areas.

In 2007, Miller and colleagues (Miller et al. 2007) applied GIS technology and spatial scan statistic to study the resurgence of bovine tuberculosis among white-tailed deer in Michigan, USA. In Argentina in 2002, Perez and colleagues (Perez et al. 2002) used GIS and spatial scan statistic to identify district groupings of bTB and described their geographical distribution. In 2007, Zendejas and colleagues (Zendejas et al. 2007) applied GIS technology to monitor the geographic distribution of bTB in Guadalajara Jalisco, Mexico, by spatial interpolation.

Other spatial-statistical techniques permit the identification of areas with conditions similar to those found in areas where a disease already occurred. For example, the Mahalanobis Distance model is used to identify geographical areas similar to those where a specific event/disease occurred according to a predefined set of the variables (Ozdenerol 2008).

In this study, space-time permutation scan statistic and GIS were used to identify the spatial and temporal distribution of bovine tuberculosis from 2005 to 2010 in the State of Mexico. We also created a model using the Mahalanobis Distance model to identify suitable areas for the occurrence of bTB in which, yet, there are no reports of the disease occurrence.

Materials and methods

Study area and data collection

The research area of this study was the State of Mexico, located in the centre of Mexico between the geographical coordinates Longitude West -98.59 – -100.61 and Latitude North 18.35 – 20.28 (INEGI 2012a) (Figure 1).

Information on bTB-positive herds was obtained from the national eradication campaign that lasted from 2005 to 2010. The information was provided by the Comité de Fomento y Protección Pecuaria del Estado de México (CFPPEM), who reported a total of 122 positive herds, 50 herds in which *M. bovis* was isolated and 72 herds that tested positive for bTB but were diagnosed with a comparative cervical tuberculin.

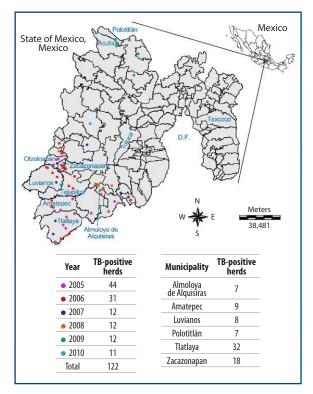


Figure 1. Geographic distribution of bovine tuberculosis positive herds from 2005 to 2010 in the State of Mexico.

Each locality with a case of bovine tuberculosis was used as a geographic unit. The geographical information were provided by the Instituto de Geografía Estadística y Catastral del Estado de México (IGECEM 2009). For the different analyses performed, both a Geographic Coordinate System WGS84 and a Universal Transverse Mercator Coordinate System (UTM) zone 14 North, were adopted.

Statistical analysis

Spatial and temporal analysis

Bovine tuberculosis clusters were identified using space-time permutation scan statistic, due to lack of information of the population at risk and controls. This statistic is based on a Generalized Likelihood Ratio (GLR). It uses a large number of transposed cylinders whose circular base defines the geographic area and the height represents the temporal parameter. The GLR is then calculated for each cylinder and the cylinder with the highest GLR is considered to constitute the most probable cluster. A Monte Carlo simulation is then used to calculate the p value (Kulldorff *et al.* 2005).

The parameters entered into the model were the geographical location of the bovine tuberculosis positive herds and the year of diagnosis. A discrete probability model was employed using search

windows of 50% and 25%, respectively. The analysis was conducted using the SaTScan software (V8.0) computer package to test the statistical significance and to determine the approximate location of each cluster.

Mahalanobis Distance model

The Mahalanobis Distance statistic (Mahalanobis 1936) was used to identify areas that have similar conditions to sites resulted positive for bovine tuberculosis. This model was defined using 80% (40 herds) of the herds in which *M. bovis* had been isolated, the following formula was used:

$$MD = (X - m)^T C^{-1} (X - m)$$

Where.

MD = the Mahalanobis Distance;

X = the vector of environmental and demographic data for each pixel, m is the vector of the mean values of the independent variables in the bovine tuberculosis cases;

C⁻¹ = the inverse covariance matrix of the independent variables;

T indicates whether a vector should be transposed.

The geographic coordinates of the 40 herds in which *M. bovis* had been isolated by CFPPEM were imported into the Idrisi Taiga 16.0 software in vector format; the vector was later converted into raster format. For this process, the spatial resolution of 93 meters was taken to reproduce the resolution of the digital elevation model of Science for Global Change. The raster was projected in the coordinate system UTM 14 North.

The selection of environmental and demographic variables was based on the results obtained by Wiliam and colleagues (Wiliam et al. 2002), who demonstrated that soil type, land use, topographic elevation, climatic factors such as temperature, anthropogenic effects like distance to roads and urban estates, and demographic aspects, such as population density, provide good indicators that can be used in the elaboration of bTB risk maps. Moreover, it has been also reported that soil use and type are closely related to the maintenance of bTB, since M. bovis has greater survival in soils with high concentrations of iron and low pH 6.5 to 6.8 (Young et al. 2005).

Soil use and soil type data were obtained in vector format from the Instituto Nacional de Estadística y Geografía (INEGI 2012b) and converted to raster format using Idrisi Taiga 16.0. The annual average temperature was obtained from 72 weather stations of the National Weather Service (CNA 2012) and the information was spatialized by interpolation with inverted distance weight in Idrisi Taiga 16.0. The

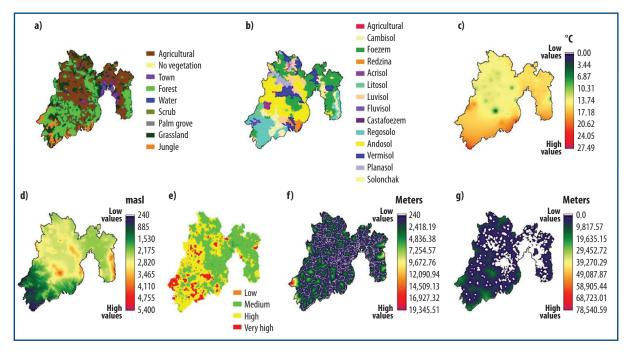


Figure 2. Demographic and environmental variables for the State of Mexico used in the Mahalanobis Distance model. **a)** Soil use; **b)** Soil type; **c)** Average annual temperature; **d)** Digital elevation model; **e)** 2005 marginality index; **f)** Distance from roads; **g)** Distance from urban polygons.

digital elevation model (DEM) was obtained from Science for Changing World (USGS 2012) with a spatial resolution of 93 meters (Figure 2).

The following demographic variables were considered: a) the marginality index 2005 (CONAPO 2005), which is a summary measure that categorizes the localities of the country depending on the lack of access to education, residence in inadequate housing, and lack of assets of the people. The marginality index is expressed in values, low = 1, medium = 2, high = 3 and very high = 4; this information was associated to each location and then interpolated with inverted distance weight; b) the distance among the roads of the State of Mexico, which was obtained from the road vector in Idrisi Taiga 16.0 (INEGI 2012b); and c) the distance from urban polygons, which was obtained from the soil use vector in Idrisi Taiga 16.0 (INEGI 2012b) (Figure 2).

All the environmental and demographic variables were used in raster format with a spatial resolution of 93 meters, projected in the coordinate system UTM 14 North.

The MD statistic follows an approximate Chi-square distribution with n - 1 degree of freedom, when n explanatory variables are multivariate normally distributed. Following the work of Clark (Clark 1993) and Farber and Kudmon (Farber and Kudmon 2003) which characterized suitable species habitats, p-values were determined based on the Chi-square distribution for each pixel, in this way defining statistically different pixels.

Maps and p-values calculation for each pixel in State

of Mexico were elaborated with the Idrisi Taiga 16.0. Pixels with high probability to identify areas that have similar condition to bovine tuberculosis positive sites were identified as pixels whose *p*-values were greater than 0.9 (high probability), whereas pixels whose *p*-values were between 0.5 and 0.89 were considered to be of moderate probability (medium probability). The MD model was evaluated through a simple descriptive analysis due to the lack of a representative test sample (only 10 herds) of herds with *M. bovis* isolates. The *p*-values for each herd were used to determine the model's accuracy.

Results

Information from 122 bovine tuberculosis positive herds, mainly located in the south of the State of Mexico from 2005 to 2010 was obtained. The municipalities with more than 7 bTB positive herds were: Tlatlaya with 32 herds positive for bTB; Zacazonapan with 18 positive herds; Amatepec with 9 positive herds; Luvianos with 8 positive herds; and Almoloya de Alquisiras with 7 positive herds. In the northern part of the state, 7 cases were registered in the municipality of Polotitlán (Figure 1).

Spatial and temporal analysis

Space-time permutation scan statistic, using a search window of < 50%, identified 1 cluster of bovine tuberculosis positive herds (p < 0.009). The centre of this cluster was located at Longitude West -100.25,

Table 1. Clusters of bovine tuberculosis positive herds detected by permutation spatial searches with windows of $\leq 50\%$ and $\leq 25\%$ in the State of Mexico.

Cluster	Search window	Centre coordinates	Radius (km)	Year	bBT positive herds*	GLR**	р
1	≤ 50%	-100.25, 18.90	31.9	2008-2010	58	6.3	0.009
2	≤ 25%	-100.28, 19.12	7.8	2008-2010	19	5.6	0.026
3	≤ 25%	-100.23, 18.54	19.2	2009-2010	28	5.4	0.031

^{*}Herds reported as positive for bovine tuberculosis by the Comite de Fomento y Potrección Pecuaria del Estado de México (CFPPEM). "GLR Generalized Likelihood Ratio.

Latitude North 18.9, and it had a radius of 31.91 km, in which 58 bTB-positive herds were identified from 2008 to 2010 (Table I). The location of the centre of this cluster corresponds to the municipality of Luvianos, and the cluster's radius covered all of the municipalities of Otzoloapan, Zacazonapan, and Tejupilco and portions of the municipalities of San Simon de Guerrero, Santo Tomas de los Platanos, Valle de Bravo, Temascaltepec Texcaltitlán, Sultepec, Amatepec and Tlatlaya (Figure 3).

By using a search window of < 25%, space-time permutation scan statistic identified 2 clusters of bovine tuberculosis positive herds (p < 0.05). The first cluster, with a p < 0.026, had its centre at Longitude West -100.28 and Latitude North 19.12, and it had a radius of 7.8 km, in which 19 bTB-positive herds were identified from 2008 to 2010. The location of the centre of this cluster corresponds to the municipality of Otzoloapan, and this cluster extends into the municipalities of Zacazonapan, Temascaltepec,

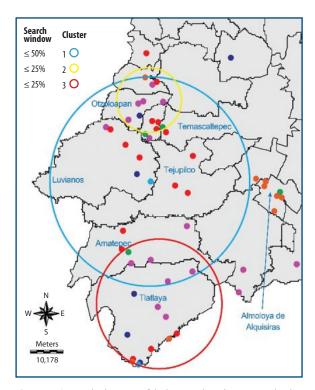


Figure 3. Geographic locations of the bovine tuberculosis positive herd clusters identified using a space-time permutation scan searches with windows of \leq 50% and \leq 25% in the State of Mexico.

Santo Tomas de lo Platanos, and Valle del Bravo. The second cluster, with p < 0.031, was located at Longitude west -100.23 and Latitude North 18.54, and it had a radius of 19.2 km, in which 28 bovine tuberculosis positive herds were identified from 2009 to 2010. The centre of the cluster corresponds to the municipality of Tlatlaya, and the cluster extends into a part of Amatepec (Table I, Figure 3).

Mahalanobis Distance model

The model identified the following areas as those with the highest probability of having similarity with bovine tuberculosis areas (*p*-values ≥ 0.9): the municipalities of Tlatlaya, Amatepec, Luvianos, Tejupilco, Otzoloapan, Zacazonapan, and Santo Tomas de los Platanos. The model identified the following areas as moderate similar (*p*-values 0.5 - 0.89): the municipalities of Temascaltepec, Ixtapan de Oro, and Valle de Bravo. North, Center, and east of the State of Mexico showed the lowest likelihood of having similar areas with bTB. (*p*-values < 0.5) (Figure 4).

This model showed that only 5 herds were located in areas with conditions similar to those positive for bovine tuberculosis with a moderate probability (p-value of 0.5 to 0.89), while other 5 herds had a low probability (p-values < 0.5).

Discussion

Bovine tuberculosis is a worldwide spread disease, and Mexico is no exception, with cases observed across the entire republic. In the State of Mexico, the most reliable information regarding positive cases of bTB are found in the South of the State, because the bTB eradication campaign is still ongoing in this area. The region is currently declared a zone with prevalence less than 0.5%.

Space-time permutation scan statistic analysis showed that bTB is not randomly distributed in the State of Mexico but rather clustered, and 3 clusters were identified. The first cluster was identified using a search window of < 50%, and 58 of the 122 bTB-positive cases were grouped together in a radius of 31.9 km in this cluster. The cluster extended to the municipalities of Amatepec, Luvianos, Sultepec, Tlatlaya, and Tejupilco, which contain the majority of cattle in the south part of the State, according to the

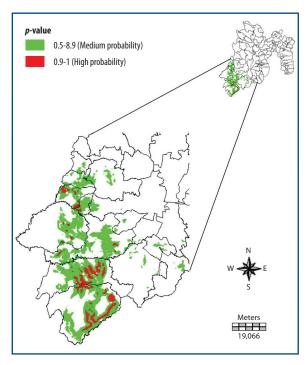


Figure 4. Suitability map for bovine tuberculosis in the State of Mexico identified using the Mahalanobis Distance statistic.

2007 census (INEGI 2007). This result is in agreement with the characteristics of the cluster identified in Argentina by Perez and colleagues (Perez *et al.* 2003), which is located in the states with the highest number of cattle.

The 2 remaining clusters were identified using a search window of \leq 25%. The first of these clusters contained 19 bTB-positive herds within a 7.8 km radius, whereas the other contained 28 herds within a radius of 19.2 km. These clusters were located in the municipalities of Zacazonapan and Tlatlaya, respectively, which contained the highest numbers of positive herds.

The clusters identified using a window of \leq 25% show a clear agglomeration of herds. This pattern was not observed in the cluster identified with a window of 50%, because it covers most municipalities in which the eradication of bovine tuberculosis was still in progress.

The Mahalanobis Distance Model using environmental and demographic variables allowed us to locate other areas in the south State of Mexico with moderate probability of similarity to the areas included in this study, where bovine tuberculosis and the causative agent of the disease have been isolated.

However, the model was not able to identify geographic areas in the rest of the State of Mexico, with high probability of similarity with bovine tuberculosis areas, because environmental and demographic conditions associated with the

occurrence of bTB are typical of the South state of Mexico. This situation was observed in the evaluation model, where only 5 herds showed moderate probability (*p*-value of 0.5 to 0.89).

Forests, jungles, and grasslands, the regosol type of soil, the highest temperatures and the lowest elevation corresponding to Tlatlaya (400 meters above sea level), predominate in the south State of Mexico (Figure 2). Forests, jungle, and grasslands are considered as risk factors. They have been associated with bTB transmission across species of wildlife such as white-tailed deer (*Odocoileus virginianus*) in Michigan USA (Miller *et al.* 2007). The South State of Mexico has a high or very high marginality, due to the few roads, and urban polygons are few and far between (Figure 2).

However, MD identified several areas with a very high probability (high probability *p*-value 0.9 - 1.0) of similarity with bovine tuberculosis areas in the south of State of Mexico, including the municipalities of Ixtapan del Oro and Valle del Bravo (medium probability *p*-value 0.5 - 0.89), for which bTB information was unavailable.

An important finding of our study was that the results of the spatial scan statistic and the MD are in agreement. The 3 identified clusters cover areas with medium and high similarity to areas with bTB. The MD model can be used to make comparisons in studying the spatial distribution of potential risk factor for bTB, but the use of more than 1 method is recommended for this type of study (Ward and Carpenter 2000 a, b).

The results of this research will be useful for epidemiological surveillance and to identify the main risk factors associated with bTB in the State of Mexico.

Furthermore, GIS proved to be a useful tool in this study of the geographical distribution of bTB in the State of Mexico. The space-time permutation scan statistic analysis showed that the disease is not randomly distributed but rather concentrated in certain municipalities in the south part of the State of Mexico. The MD model was used as to identify other areas in the State very similar to those experiencing bovine tuberculosis, and the results of the similarity analysis matched those of the statistic spatial scan.

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