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Bovine tuberculosis in San Luis Potosi, Mexico: spatial analysis and risk factors

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Abstract

A better understanding of the bovine tuberculosis (bTB) spatial distribution and the factors associated with increased risk is required to implement more effective control measures in Mexico. A cross-sectional study based on bTB testing on >1,600 herds in two regions of San Luis Potosi state, Altiplano and Huasteca, during 2018-2021 was conducted for the identification of spatial clustering and of bTB risk factors using the spatial scan statistic test and multivariable logistic regression models. The proportion of herds with at least one reactor was 17.9% in Altiplano and 38.6% in Huasteca, with one high risk cluster (HRC) present in each region. Larger herds (>20 animals) and those included in the HRC were exposed to a significantly increased risk of having at least one reactor in both regions. Given bTB caudal fold test limitations, herd disease freedom median posterior probability was calculated in an empirical Bayesian framework, classifying herds as “likely free” (> 94%) or “inconclusive”, the cluster and regression analysis was repeated, finding similar outcomes. Results demonstrated that certain herds are exposed to higher risk depending on their size and location in both regions, suggesting similar patterns of transmission; these findings can be used to further investigate how the disease spreads in San Luis Potosi.

Keywords

Cattle, Spatial distribution, Geographic Information System, Bayesian, *M. bovis*

Introduction

Bovine tuberculosis (bTB) is a chronic infectious disease widely distributed in the cattle population in Mexico (Mellado et al., 2021b), representing the second most important bacterial zoonosis after brucellosis (Gutiérrez Reyes et al., 2012). Although the disease is present at low levels in most of the country - in 86.2% of the territory the herd-level prevalence is <0.5% (SADER and SENASICA, 2021) -, the proportion of infected herds is nevertheless highly influenced by the production type, with an average prevalence in dairy herds of 16% compared to <0.5% in beef herds throughout the country (Gutiérrez Reyes et al., 2012; Rojas Martínez et al., 2021). In Mexico, the risk of bTB in the human population is exacerbated by the fact that up to 30% of the milk produced annually is not pasteurized, and there is tradition of raw milk based products consumption (Zendejas Martínez et al., 2007); furthermore, previous studies have reported the relationship between isolates of *Mycobacterium bovis*, the main causative agent of bTB, retrieved from cattle and humans in the country (Perera Ortiz et al., 2021; Sandoval-Azuara et al., 2017). In Mexico, the control and eradication of bTB is based on: a) the application of tuberculin tests to identify reactor animals that will be subsequently culled, b) post-mortem inspection in the slaughterhouse followed by sampling of animals presenting

compatible lesions for histopathological and bacteriological laboratory analysis; and c) the trace-back and quarantine of the herds of origin of reactors/animals with bTB lesions and their contacts (SENASICA-SAGARPA, 2015).

Regional differences such as livestock population heterogeneity, weather and terrain characteristics, as well as agricultural activities including trade fairs, have a significant impact on disease transmission (Gay et al., 2007). Nowadays, data on spatial location and status of herds for multiple diseases is routinely recorded in many countries, providing an opportunity to conduct spatial analyses to better understand the distribution of endemic diseases, assess the effectiveness of control measures and identify risk factors with an heterogeneous spatial distribution (Wolff et al., 2011; Zendejas Martínez et al., 2007). Therefore, the use of spatial statistics and Geographic Information Systems (GIS) could assist in the improvement of control programs for bTB. These tools have already been used to characterize the epidemiology of bTB in different regions of the American continent, e.g. for the identification of areas at a higher bTB risk in Argentina (Perez et al., 2002) and the State of Mexico (Zaragoza Bastida et al., 2017), and to predict bTB prevalence using ordinary kriging in Jalisco, Mexico (Zendejas Martínez et al., 2007). Similarly, in Brazil, the analysis of spatial and temporal distribution has also been recommended to support livestock health control (Baptista et al., 2021).

Identification of the main risk factors influencing disease incidence can help to better frame measures for effective prevention and control (Ciaravino et al., 2021; Mellado et al., 2021a). In Mexico the campaign against bTB was officially implemented in 1996, but limited epidemiological studies of bTB in the country have been conducted so far (Enríquez-Cruz et al., 2010). Two previously published studies aimed at the identification of bTB risk factors in the country, but they were focused on individual-level risk factors in dairy cattle from single farms (Mellado et al., 2021a, 2021b). However, in 2022, 92.6 % of more than 36 million cattle in Mexico was for beef production (SIAP, 2023). A case-control study conducted in Tamaulipas, a state in the northeast, using data from 1995-1998, found that older cattle and certain *B. taurus* breeds were linked to higher risk of bTB detection in the slaughterhouse (Enríquez-Cruz et al., 2010).

Given the zoonotic potential of bTB, a study looking into the molecular epidemiology of human TB in San Luis Potosí (SLP) concluded that surveillance of *M. bovis*-related cases in people should be optimized. The state of SLP ranks 14th (out of 32) in number of cattle in Mexico, 9th when only considering beef cattle heads (INEGI, 2007), and third if considering meat production of bovine origin (SIAP, 2021), thus highlighting the importance of beef cattle in the state. Information of SLP bTB situation available from academic studies (Enríquez-Cruz et al., 2010; Milián Suazo et al., 2012) and public data (SADER and SENASICA, 2021) is limited, and no attempts to characterize the spatial distribution of bTB in SLP have been conducted so far. Thus, our aim was to address this issue and to identify potential risk factors influencing the risk of bTB in cattle herds that may help to optimize bTB surveillance strategies and the control program in the state, taking also into consideration the limitations of diagnostic tests applied.

Materials and Methods

Study area

The study research area was the state of SLP, located in North-Central Mexico (Figure 1), between the geographical coordinates West -102.38° – -98.25° and North 24.56° – 21.09° . The state has a total cattle population of 1,021,808 animals according to the last available Agricultural National Survey (INEGI, 2019), distributed in 47,587 herds (INEGI, 2007).

Information on the bTB status of cattle herds was provided by the SLP State Committee for Livestock Promotion and Protection (Comite Estatal para el Fomento y Protección Pecuaria de SLP A.C. - CEFPP SLP), a non-governmental organization and auxiliary body of SADER (Secretariat of Agriculture and Rural Development, National Level). The CEFPP SLP, as part of bTB National Campaign, regionalizes the state according to the bTB prevalence (Figure 1). For this study, we used data from the two regions in the state where the bTB program is focused: A1 (also referred as Huasteca) and A3 (also referred as Altiplano), with a bovine population of 255,730 and 123,883 cattle distributed in 15,216 and 9,227 herds, respectively (representing around 50% of the whole cattle population in the state). Data were obtained from the last available Mexican census of agriculture and forestry (INEGI, 2007).

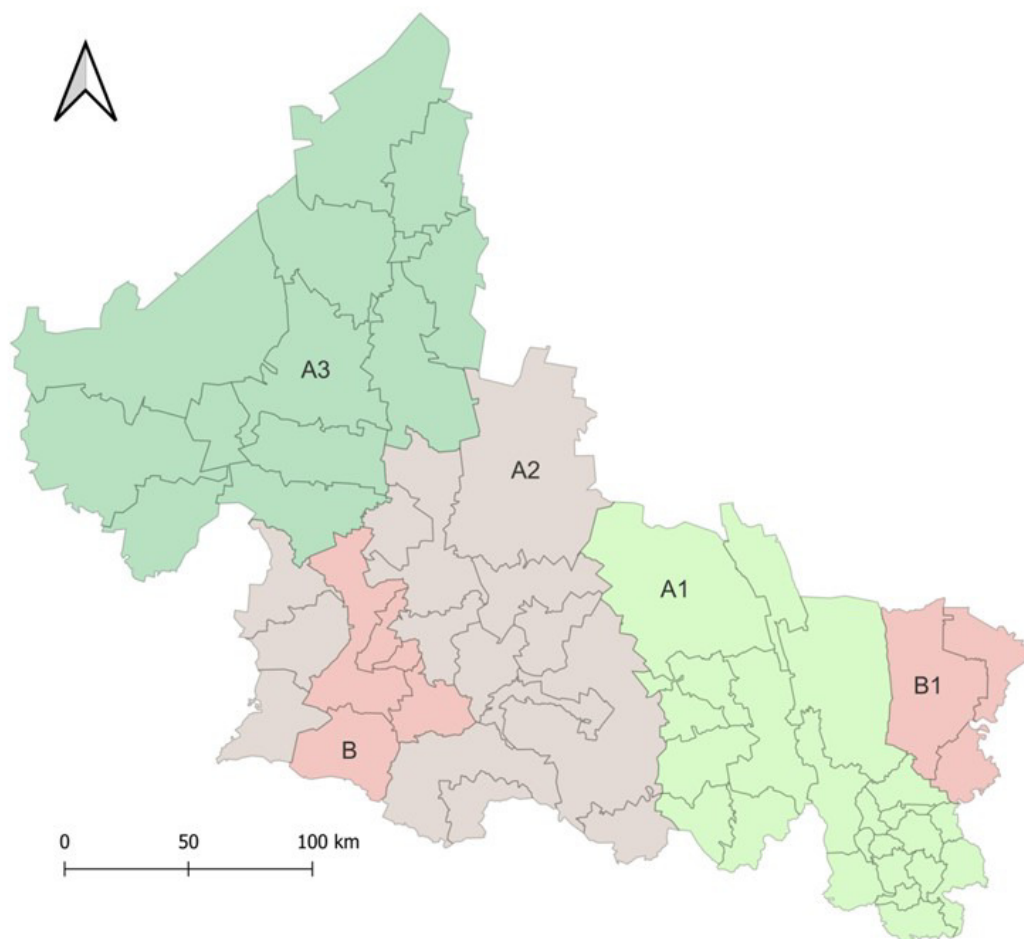


Figure 1. Bovine tuberculosis (bTB) regionalization in San Luis Potosí (SLP) state, Mexico, according to SLP State Committee for the Promotion and Protection of Livestock (CEFPP SLP).

Bovine Tuberculosis Control Program in Mexico

Disease control depends on the application of the Official Mexican Standard, which is based on a test and slaughter approach (Gobierno Mexico, 1995). Mexican states can be in one of three alternative phases (control, eradication and free) depending on their herd prevalence ($> 2\%$, $\leq 2\%$, and bTB free for 5 years, respectively). Regardless of the phase, the bTB status of all herds in a state must be determined every five years (“progressive verification of herds”, later referred as screening in the text). In herds with unknown bTB status or with a negative result in a previous herd test, bTB diagnosis is performed using the caudal fold test (CFT) through the inoculation of 0.1 ml of bovine purified protein derivative (bPPD) approximately 5 cm below the base of the tail in the caudal fold. Reactions are read 72 h after inoculation, and animals with an increase in skin thickness, redness, heat, pain, or necrosis compared to preinjection status are considered reactors. The CFT reactors are then subjected to the comparative cervical test (CCT) for confirmation and when CCT reactors are found the herd is considered positive, and reactors are sent to slaughter and sampled for histopathological and/or bacteriological confirmation of the infection.

Data collection

The data available for this study included information of “screening” testing based on CFT from 2018 to 2020 in Altiplano and from 2018 to 2021 in Huasteca. Information available included the location of the farms (coordinates and municipality), production type (beef or dairy/mixed), herd size, date of CFT testing, number of tested and reactor animals, and bTB status of the herd (reactor herd – if one or more reactor animals were found – or negative) based on CFT test results. Herd size was categorized into three levels (1 to 20, 21-50 and >50 animals) (Table I) based on the threshold for family farming in Mexico (INEGI and Colegio de Posgraduados, 1998) and previous studies (Almaw et al., 2021; Chenyambuga et al., 2010; Kara and Galic, 2022).

Spatial Analysis

Spatial clustering of bTB reactor herds was assessed using the Bernoulli model of the spatial scan statistic test through the SatScan software (v10.1) (Kulldorff, 2018). This test, previously utilized with similar purposes elsewhere (De La Cruz et al., 2014; Perez et al., 2002) was run in each study region (Huasteca/Altiplano) separately. Briefly, the spatial scan statistic consists of running a set of circular geographic windows centered over all possible clusters in the study region. Windows generated have a particular range of neighboring locations, and are evaluated by comparing the observed number of cases (here, herds with at least one CFT reactor) inside the window with the expected number if cases were randomly distributed in space, generated through 999 Monte-Carlo randomizations of case status to the farm locations. Maximum size of the scanning windows was set at 50% of the study area (Perez et al., 2002).

Additionally, the Getis-Ord G_i^* statistic (Ord and Getis, 1995) was calculated. This method is used in spatial data analysis to identify hotspots and coldspots within a geographic area. It considers each herd in the context of neighboring herds, suggesting the likelihood of spatial autocorrelation among adjacent herds. The calculation involves examining each feature's attribute value along with its neighboring features and their attribute values to compute a z-score for each feature, which indicates how significantly different the feature's value is from the mean. Resulting z-scores and p-values identify where features with high or low values compared with the mean population indicated clustering (Murad and Khashoggi, 2020). We used this method to examine the distribution of a continuous variable measuring the confidence in disease freedom based on test results (see below). This analysis was conducted in ArcGIS 10.1 SP1 (ESRI, Redlands, California, USA).

The spatial distribution of the herds and the regionalization in SLP based on bTB status was visualized using the Geographic Information System QGIS v3.26.3 (QGIS Development Team, 2022). In a proportion of the herds (17.3% and 73.8% in Huasteca and Altiplano respectively) coordinates were shared with another herd. The inaccurate registration of a shared geolocalization for multiple herds, particularly during the initial stages of the campaign in the Altiplano region, might be the cause. Because of this longitude and latitude coordinates of herds sharing locations in Altiplano were randomly shifted up to 0.05 decimal degrees in order to facilitate visualization of all herd locations.

Risk factor analysis

Firstly, a descriptive analysis of all variables was performed. The association between bTB status of the herd (reactor/negative) and available covariates (herd size group, production type, year and inclusion of the farm in a significant high-risk spatial cluster) was assessed using univariable logistic regression with a liberal p-value ($p < 0.2$). Potentially associated variables were then assessed for multicollinearity, utilizing the variance inflation factor (VIF) to maintain an average VIF below 5 across the variables included in a multivariable logistic regression model built following a backward stepwise process in which variables with p-values < 0.05 were retained. Statistical analyses were performed using R (R Studio Team, 2022).

Probability of disease freedom

To account for the limitations of sensitivity (Se) and specificity (Sp) of the CFT, the probability of disease freedom at the herd level was calculated considering the use of an imperfect test and the fact that not all the animals in the herds were always tested, in an empirical Bayesian framework, according to Beauvais et al. (2016). Briefly, we assumed that the Se and Sp of the CFT followed beta distributions with median 0.85 (Se) and 0.95 (Sp) based on the official Mexican bTB campaign epidemiological guide (SENASICA-SAGARPA, 2015) and 5th percentile (i.e., 95% probability of being above this value) 0.57 (Se) and 0.65 (Sp) based on Gomez-Buendia et al. (2023). We ran 100 simulations on herds from Huasteca and Altiplano separately, including herds with > 1 and < 552 animals (excluding 3 and 12 herds in Huasteca and Altiplano, respectively), to obtain the median posterior probability of a herd being free from the disease. This variable (probability of disease freedom) was then used to build a receiver operating characteristic (ROC) curve considering the detection of reactors in the herd as the outcome in order to identify the best threshold. The selected threshold was then used to classify herds as "likely free" (when the median probability of a herd was above the selected threshold) or "inconclusive" (median probability of disease freedom $<$ threshold). The ROC analysis was performed using the R package *pROC* (Robin et al., 2011).

The spatial cluster analysis (using the spatial scan statistic and adding now the Getis-Ord G_i^* statistic) and the risk factor analysis were conducted using this newly created binary variable as the outcome.

Results

After the exclusion of 19 duplicated records, a total of 1,617 herds, 751 (46.4%) located in Huasteca and 866 (53.6%) in Altiplano were included in the analysis. The median herd size was 25 animals (interquartile range IQR = 13-54) in Huasteca and 14 (IQR = 8-25) in Altiplano. The proportion of herds by size category varied depending on the region, with herds with >50 animals being the predominant category in both regions but representing 69.2% of all herds in Huasteca compared with 43.1% in Altiplano (Table I). Most herds were classified as beef in both regions (91.6% in Huasteca and 95.9% in Altiplano). Regarding the detection of bTB reactors, in Huasteca 290 out of the 755 herds (38.6%) had at least one reactor animal and a maximum of 20, whereas in Altiplano among 1 and 4 reactors were found in 155 (17.9%) herds.

Spatial analysis

The bTB regionalization in SLP state is presented in Figure 1. Herds were predominantly localized in the south-eastern and eastern parts of the regions Huasteca (A1) and Altiplano (A3), respectively (Figure 2). The Bernoulli model identified one high risk cluster in each region (Table II, Figure 2), comprising 57.4% and 27.7 % of the bTB reactor herds in Huasteca and Altiplano respectively. The Getis-Ord G_i^* statistic identified hot (e.g., including herds with a low confidence in disease freedom) and cold (herds with a high confidence in disease freedom) spots in both regions (Figure 3), with hot spots largely agreeing with the high risk clusters identified by means of the spatial scan statistic.

Variable	Huasteca						Altiplano					
	Total	Reactor (%)	OR ¹ (95%CI ²)	p-value	OR ¹ (95%CI ²)	p-value	Total	Reactor (%)	OR ¹ (95%CI ²)	p-value	OR ¹ (95%CI ²)	p-value
Type				0.26 ³							0.54 ³	
Beef	720	275 (38.2%)	1				793	140 (17.7%)	1			
Mixed	31	15 (48.4%)	1.52 (0.73-3.13)	0.26			73	15 (20.5%)	1.21 (0.64-2.14)	0.54		
Size				0.00 ³		0.00 ³					0.00 ³	0.00 ³
1-20	322	64 (19.9%)	1		1		579	67 (11.6%)	1		1	
21-50	221	82 (37.1%)	2.38 (1.62-3.51)	0.00	2.20 (1.49-3.27)	0.00	222	60 (27.0%)	2.83 (1.91-4.18)	0.00	2.80 (1.88-4.16)	0.00
>50	208	144 (69.2%)	9.07 (6.10-13.7)	0.00	7.77 (5.19-11.8)	0.00	65	28 (43.1%)	5.78 (3.31-10.0)	0.00	4.92 (2.78-8.65)	0.00
Year				0.01 ³							0.00 ³	
2018	104	35 (33.7%)	1				336	87 (25.9%)	1			
2019	196	72 (36.7%)	1.14 (0.70-1.90)	0.60			226	17 (7.5%)	0.23 (0.13-0.39)	0.00		
2020	190	61 (32.1%)	0.93 (0.56-1.56)	0.79			304	51 (16.8%)	0.58 (0.39-0.85)	0.01		
2021	261	122 (46.7%)	1.73 (1.08-2.80)	0.02					—	—		
Cluster				0.00 ³		0.00 ³					0.00 ³	0.00 ³
No	507	150 (29.6%)	1		1		574	74 (12.9%)	1		1	
Yes	244	140 (57.4%)	3.20 (2.34-4.41)	0.00	2.50 (1.78-3.54)	0.00	292	81 (27.7%)	2.59 (1.82-3.70)	0.00	2.35 (1.63-3.39)	0.00

OR¹ = Odds Ratio, CI² = 95% Confidence Interval, ³ = likelihood ratio test

Table I. Results from univariable and multivariable regression models using bTB farm status (farms with at least one reactor) as the outcome variable.

Cluster	Region	Latitude	Longitude	Radius	Herds	P_value	Observed	Expected	O/E	% Cases
1	Huasteca	21.4903	-99.0333	36.0 km	244	<0.001	140	94.22	1.49	57.4
2	Altiplano	22.8459	-101.6084	24.6 km	292	<0.001	81	52.26	1.55	27.7
3	Huasteca	21.4903	-99.0333	23.34 km	64	<0.001	43	22.07	1.95	67.2
4	Altiplano	22.9422	-101.9138	28.42 km	175	0.051	38	21.52	1.77	21.7

Table II. Results from Cluster analysis using reactor status and positive (bTB freedom probability below 94%) (case/control) as the outcome variable.

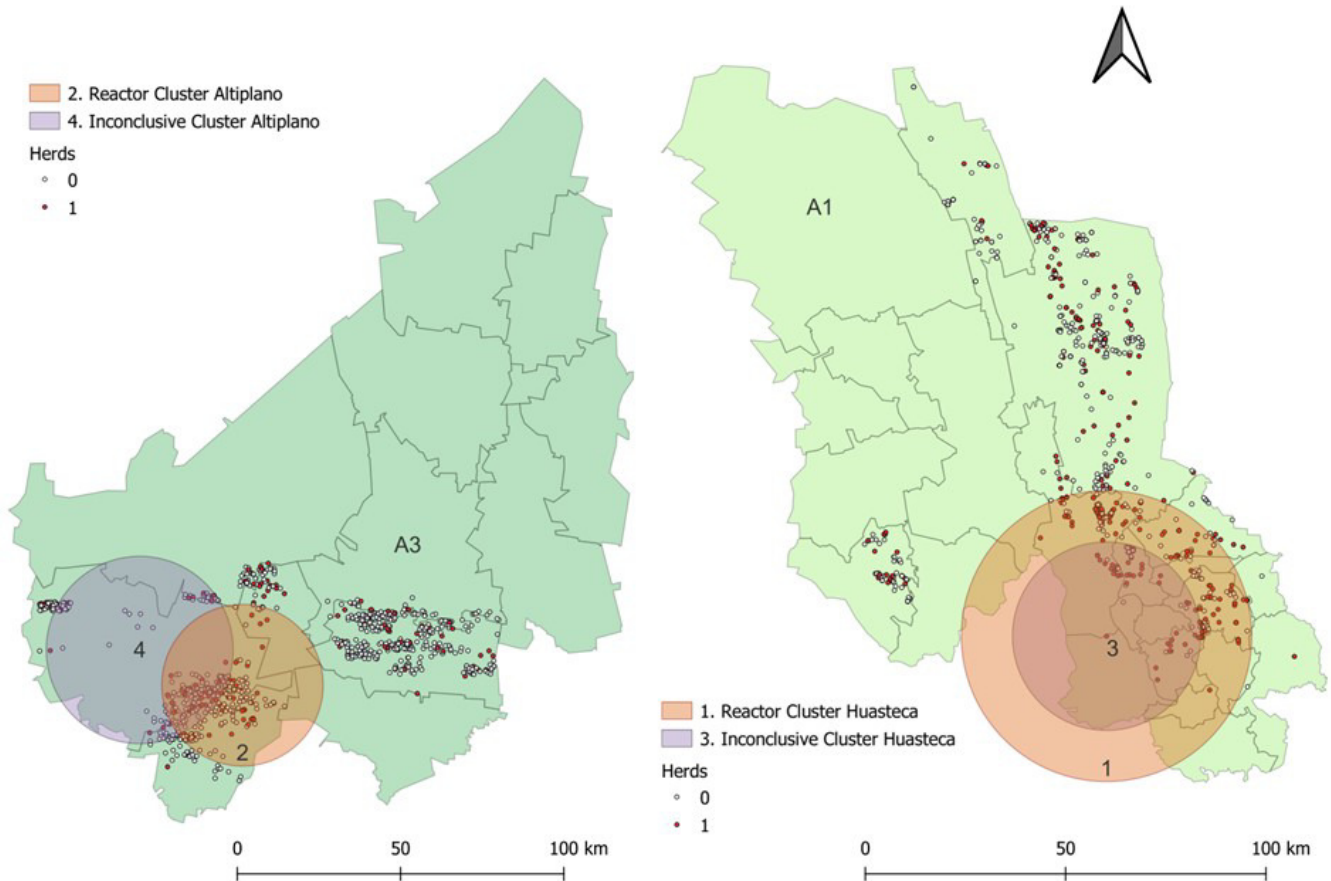


Figure 2. Spatial distribution of 1,617 cattle farms and high-risk clusters of bTB reactor farms in Altiplano (left) and Huasteca (right). Red and white dots denote presence/absence of at least one Caudal Fold Test reactor in the herd.

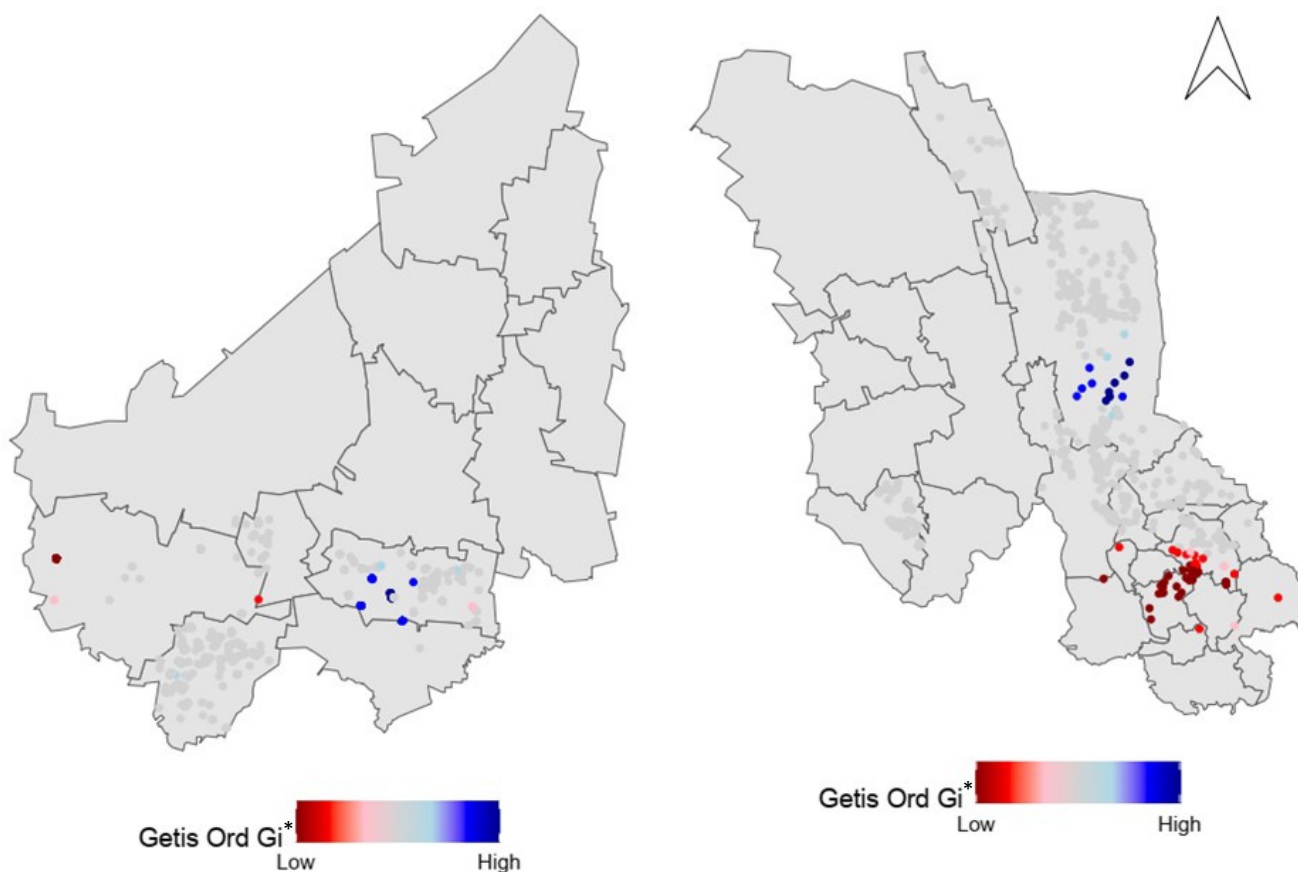


Figure 3. Location of cold and hot spots of disease freedom in Altiplano (left) and Huasteca (right) according to Getis-Ord G_i^* . Red and blue dots denote low confidence in disease freedom (hot spot) / high confidence in disease freedom (cold spot)

Risk factor analysis

The proportion of herds with at least one CFT reactor was higher in herds with more than 20 animals in both regions: 52.7% vs. 19.9% in herds with ≤ 20 animals in Huasteca and 30.7% vs 11.6% in Altiplano, while the proportion of reactor herds was not associated with the herd production type ($p > 0.25$, Table I). The proportion of bTB reactor herds detected each year ranged from 32.1% to 46.7% for Huasteca and 7.5% to 25.9% in Altiplano, with more abrupt changes in different years in the latter region (Table I).

The variables herd size, year and inclusion in high risk cluster were initially selected based on the results from the univariable analysis. The year of testing showed a strong correlation with the location of the herds within each region that were tested in particular years (data not shown). Consequently, it also had a significant influence on inclusion in the high risk cluster (HRC). As a result it was not further considered in the model. Herd size group and inclusion in HRC were the final predictors in the multivariable model for both regions, with herds of >20 animals having an increased risk of being classified as a reactor herd compared with farms of 1-20 animals, particularly for herds with >50 cattle (Table II). Being inside the HRC still increased the risk to a similar extent in both regions once the herd size effect was considered in the model (Table I).

Probability of disease freedom

When the imperfect nature of the CFT test was considered, the probability of disease freedom at the herd level ranged between 44.9-99.9% (mean = 91.5%, median=95.7%) for the Huasteca region, and between 61.4-99.9% (mean=97.3%, median=98.3%) for the Altiplano region (Figure S1). The ROC analysis conducted in the overall population identified 94.7% as the optimal threshold, which classified as “likely free” 96.8% of the herds without reactors and as “inconclusive” 81.2% of the reactor herds.

The cluster analysis considering 94% as the threshold also identified one cluster in each region: a smaller cluster of inconclusive herds located inside the reactor cluster in Huasteca, and a borderline significant cluster ($p=0.051$) in Altiplano partially overlapping with the reactor cluster (Figure 2). When the risk factor analysis was repeated using likely free and inconclusive herds as the outcome, the same variables (size and inclusion in HRC cluster) were included in the final model, even though the effect sizes were different for the variable herd size (Table S1).

Discussion

Bovine tuberculosis is endemic in Mexico, and has a large impact on public and animal health (Verdugo Escárcega et al., 2020). Due to its importance, around 37.6% of the annual budget dedicated to animal health in the country is invested on the national bTB control program (SADER and SENASICA, 2021). In this context, the application of novel approaches to better understand the epidemiology of the infection in cattle in the country can help to save resources through more efficient surveillance, and to optimize the measures contemplated in the program. However, there is a lack of knowledge on several aspects of the epidemiology of bTB in Mexico, including the spatial distribution of the disease and the degree of spatial clustering of infected herds along with the risk factors increasing the probability of infection. This information can be key to better understand transmission routes and to design measures to prevent disease dissemination (Perez et al., 2002). In the study we addressed this issue by focusing on two regions of SLP, a state with a significant cattle production and a large variation of geographical and weather conditions (Miranda-Aragón et al., 2013). This study can help to redesign policies by implementing risk-targeted surveillance, allowing a more efficient allocation of scarce resources.

A spatial pattern in the distribution of bTB reactor herds was observed in both regions, with a high-risk cluster encompassing 50% and 25% of herds with at least one CFT reactor in Huasteca and Altiplano, respectively. These clusters may be suggestive of between-herd neighboring spread (Milne et al., 2022), that could be the result of a grazing management that promotes close contact among cattle (shared areas), or may signal the spread of the disease mediated by the local movement of infected cattle within a relative small and circumscribed region (Perez et al., 2002). In addition, the high bTB risk areas identified here could be also associated to the presence of infected wildlife reservoirs, as described elsewhere (LaHue et al., 2016; Tembo et al., 2020). This spatially heterogeneous distribution of bTB in SLP is in concordance with a previous research in the State of Mexico, where three cluster of bTB positive herds were found using search windows of $\leq 50\%$ and $\leq 25\%$ (Zaragoza Bastida et al., 2017). Interestingly, our results mirror previous studies focused on human TB: a study addressing the genetic diversity of the *Mycobacterium tuberculosis* complex in SLP identified a high incidence area for human tuberculosis in Huasteca, which largely overlapped with the HRC identified in the region in this study (López-Rocha et al., 2013). Even though most cases were due to *M. tuberculosis* (only five *M. bovis* among 237 spoligotyped isolates), this high incidence area for human TB was characterized by a large proportion of patients living in rural communities (86.3%) and working as farm workers (42.2%) compared with other regions ($<55\%$ and $<31\%$ respectively). The presence of overlapping high risk areas for both bTB and human TB should be further investigated in order to assess the possible link between human and bovine cases, ideally by including highly discriminatory characterization techniques like spoligotyping or whole genome sequencing that may be able to demonstrate if there is between-species transmission, as reported previously in other Mexican states (Perea-Razo et al., 2018; Perera Ortiz et al., 2021; Rodwell et al., 2010; Torres-Gonzalez et al., 2013).

Recognizing the evident importance (detection of significant clusters) of farm location on herd-level risk, presence in the HRC was included in the model alongside other variables that may be linked to identifying CFT reactors. Based on the results from the final multivariable model, we found no difference according to production type, which could be due to the very low proportion of non-beef herds, an issue also impacting other studies (Munroe et al., 1999). Furthermore, the simple beef vs. other herd types classification used in this study may not have fully accounted for the variation in management between herd types. Previous studies identified dairy farming as a risk factor for bTB in New Zealand (Porphyre et al., 2008) and Mexico (Zendejas Martínez et al., 2007). This may be a result of increased opportunities for *M. bovis* transmission in dairy herds, because of closer contact compared with beef extensive conditions, resulting in herds with higher prevalence that would be easier to detect (Perez et al., 2002). In addition, dairy cattle may live longer than beef animals, thus providing additional opportunities of exposure to bTB (J M Broughan et al., 2016). Further studies with more balanced populations would be needed to assess the impact of production type and production practices on bTB risk in SLP.

The association between bTB and herd size is consistent with previous findings worldwide, as this trait is the most frequently identified risk factor for bTB incidents (J. M. Broughan et al., 2016). This could be influenced by an increased likelihood of the infection entering the herd due to certain management practices (i.e., entry of new animals, use of larger pastures that increase the contact with neighboring herds), but also to increased probabilities of finding reactors in larger herds due to limitations in the specificity of bTB diagnostic tests (Humblet et al., 2009).

As mentioned above, a frequently cited risk factor that may elucidate, to some extent, the spatial distribution patterns observed in bovine tuberculosis (bTB) reactor herds in this study, is the potential presence of wildlife reservoirs in specific regions, serving as potential foci of infection for adjacent herds (Ciaravino et al., 2021; Marsot et al., 2016). The study of the role of wildlife on bTB epidemiology in Mexico is however scarce (Miller and Sweeney, 2013), with only two reports (Barrios-Garcia et al., 2012; Medrano et al., 2012). A study conducted in three Northeastern states (Cohauila, Nuevo Leon and Tamaulipas) that share borders with SLP revealed the presence of TB infection in deer populations, based on the presence of antibodies to bPPD (Medrano et al., 2012). Researchers found gross changes and histopathological findings suggestive of TB from 44 samples of deer lymph nodes and tonsils in Tamaulipas, although no isolates could be retrieved because of fungal contamination of the culture media (Barrios-Garcia et al., 2012). Given the presence of white-tailed deer in SLP (Ávila et al., 2011), this should be further considered. Along with studies focused on wildlife, social network analysis using animal movement data to establish contact patterns between farms could also help to identify potential routes of infection in reactor herds (Pozo et al., 2019). The implementation in SLP of the Electronic Mobilization Registry (Reemo) in 2016 was intended to provide traceability; the system in SLP is administered by the SEDARH (Secretariat of Agricultural Development and Hydraulic Resources, State Level), allowing SLP to position itself as one of the best states managing the Reemo system (Redaccion El Universal, 2020), however, to date, no research has been conducted in SLP or in Mexico with Reemo data. Since movement of animals can be a cause of active spread of bTB in the Mexican cattle population (Gutiérrez Reyes et al., 2012), combining bTB incidence data with animal movement and spatial locations will allow a better characterization of the epidemiology of bTB but also of other diseases (Albery et al., 2021).

Several important limitations should be considered when interpreting our results: first, the coordinates of 17.3% and 73.8% of all herds in Huasteca and Altiplano respectively were shared with another herd, thus suggesting that location of herds were not fully accurate. Second, bTB positivity here was only based on CFT test results; given the limited Sp of CFT (Bezoz et al., 2014; Mellado et al., 2015), it is thus possible that some herds were wrongly identified as reactors, particularly when only few CFT positive animals were identified. Nevertheless, when the cluster and multivariable analysis was repeated considering only as reactor herds those in which at least two positive animals were found, overlapping HRC and the same variables were identified as risk factors, thus suggesting that they were truly associated with an increased risk of bTB in a herd. Furthermore, when the limitations in Se and Sp of the CFT test were considered and herds were classified as likely free or inconclusive, the same variables were identified in the risk factor analysis, and overlapping spatial clusters were also found both using the dichotomous classification (likely free vs. inconclusive) or the continuous variable (confidence in disease freedom) based on the spatial scan statistic and the Getis-Ord G_i^* statistic, respectively, suggesting that our analyses identified herds that were truly at a higher risk of bTB. In any case, the inclusion of additional data (presence of wildlife reservoirs, animal movements, co-occurrence of other diseases, particularly those that could lead to cross-reactions in diagnostic tests such as paratuberculosis) including also animal-level factors (breed, age) could help to refine the analysis conducted here. Notwithstanding, in the context of scarcity of bTB epidemiological investigations in Mexico due to the limited availability of surveys and complete databases (Enríquez-Cruz et al., 2010), our results offer a first insight into large scale factors associated with detection of CFT reactors in SLP.

This study on the spatial epidemiology of bTB in the cattle population in SLP and the identification of the associated risk factors has demonstrated the presence of herds at higher risk linked to certain locations (HRC) and larger sizes, opening the field to further studies that can help to understand factors driving disease transmission/persistence such as the possible role of animal movements and wildlife as sources of infection, and the performance of screening and confirmation diagnostic tests used in the frame of the program. Our results represent a first step in the path towards bTB control in SLP, and may serve as a starting point for new investigations with a broader scope.

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Ethical Standards

Ethics approval

No ethical approval was needed because this study did not involve a prospective evaluation. The manuscript does not contain clinical studies or patient data, nor private information about animal owners.

Statement of Animal Rights

This study did not involve laboratory animals nor interactions with production animals.

Conflict of Interest Statement

None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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