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Prevalence and risk factors for bovine tuberculosis in the state of São Paulo, Brazil

Prevalência e fatores de risco paratuberculose bovina no estado de São Paulo, Brasil

Ricardo Augusto Dias[1*]; Francisco Miroslav Ulloa-Stanojlovic[2]; Ana Paula Cunha Belchior[3]; Rodrigo de Souza Ferreira[3]; Rita Coelho Gonçalves[3]; Ricardo Souza Costa Barão de Aguiar[3]; Paola da Rocha Sousa[3]; Arianne Mastrangeli Amici Santos[3]; Marcos Amaku[1]; Fernando Ferreira[1]; Evelise Oliveira Telles[1]; José Henrique Hildebrand Grisi-Filho[1]; Vitor Salvador Picão Gonçalves[4]; Marcos Bryan Heinemann[1]; José Soares Ferreira Neto[1]

Abstract

A cross sectional study was carried out between May and November 2011 to investigate the epidemiological situation of bovine tuberculosis (bTB) in the state of São Paulo, Brazil. The state was divided into seven regions. Three hundred farms from each region, with reproductive activity, were randomly chosen and included as primary sample units. A fixed number of bovine females, older than 2 years of age, were randomly selected and tested, using the comparative cervical tuberculin test. An epidemiological questionnaire based survey was conducted in the selected farms. Our results show that in the state of São Paulo, the apparent prevalence of positive farms was 9% (95% confidence interval, 95% CI = 7.8 – 10.5%). The prevalence in the individual regions varied between 3.5% (95% CI = 1.7 – 6.8%) and 13.9% (95% CI = 10.2 – 18.8%). The apparent prevalence of positive animals in the state was 1.3% (95% CI = 0.9 – 1.7%) and varied from 0.3% (95% CI = 0.2 – 0.6%) to 2.5% (95% CI = 1.4 – 4.5%) in the regions. The risk factors associated with tuberculosis in the state were (i) number of adult females in a herd is ≥ 24 (Odds ratio, OR = 1.91, 95% CI = 1.32 – 2.75), (ii) type of farm enterprise (dairy: OR = 2.70, 95% CI = 1.40 – 5.21; mixed: OR = 2.03, 95% CI = 1.08 – 3.82), (iii) milking process (milking parlor: OR = 4.12, 95% CI = 1.46 – 11.64; portable milking machine: OR = 2.94, 95% CI = 1.42 – 6.09), and (iv) pasture sharing (OR = 1.58, 95% CI = 1.07 – 2.33). The state of São Paulo should implement a structured surveillance system to detect and mitigate the disease. Further, an efficient animal health education program, which encourages the farmers to test replacement animals for bTB prior to introduction in their herds and to avoid pasture sharing with farms of unknown sanitary conditions should also be implemented.

Key words: Bovine tuberculosis. Prevalence. Risk factors. São Paulo. Brazil.

[1] Profs., Faculdade de Medicina Veterinária e Zootecnia, Universidade de São Paulo, USP, São Paulo, SP, Brasil. E-mail: dias@vps.fmvz.usp.br; amaku@vps.fmvz.usp.br; fernando@vps.fmvz.usp.br; bufalo@usp.br; grisi@vps.fmvz.usp.br; marcosbryan@usp.br; jsoares@vps.fmvz.usp.br

[2] Discente, Faculdade de Medicina Veterinária e Zootecnia, Universidade de São Paulo, USP, São Paulo, SP, Brasil. E-mail: miroslav@usp.br

[3] Discentes, Coordenadoria de Defesa Agropecuária do Estado de São Paulo, CDA, Campinas, SP, Brasil. E-mail: ana.belchior@cda.sp.gov.br; rodrigo.souza@cda.sp.gov.br; rita@cda.sp.gov.br; ricardo.barao@cda.sp.gov.br; paola@cda.sp.gov.br; arianne.mastrangi@cda.sp.gov.br

[4] Prof., Faculdade de Agronomia e Medicina Veterinária, Universidade de Brasília, UnB, Brasília, DF, Brasil. E-mail: vitorspg@usb.br

[*] Author for correspondence

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Resumo

Um estudo transversal foi realizado entre maio e novembro de 2011 para determinar a situação epidemiológica da tuberculose bovina (bTB) no estado de São Paulo, Brasil. O estado foi dividido em sete regiões. Trezentas propriedades com atividade reprodutiva de bovinos de cada região foram aleatoriamente selecionadas e consideradas unidades primárias de amostragem. Um número fixo de fêmeas bovinas com idade superior a dois anos foram aleatoriamente selecionadas e testadas usando o teste cervical comparativo. Um inquérito epidemiológico, utilizando um questionário específico, foi realizado em cada propriedade selecionada. Os nossos resultados indicam que no estado de São Paulo, a prevalência aparente de propriedades positiva foi de 9% (intervalo de confiança de 95%, IC95% = 7,8 – 10,5%). A prevalência nas diferentes regiões variou entre 3,5% (IC95% = 1,7 – 6,8%) e 13,9% (IC95% = 10,2 – 18,8%). A prevalência aparente de animais positivos no estado foi 1,3% (IC95% = 0,9 – 1,7%) e variou de 0,3% (IC95% = 0,2 – 0,6%) até 2,5% (IC95% = 1,4 – 4,5%) nas regiões. Os fatores de risco associados à tuberculose no estado foram (i) número de fêmeas adultas nos rebanhos ≥ 24 (Odds ratio, OR = 1,91, IC95% = 1,32 – 2,75), (ii) tipo de exploração (leite: OR = 2,70, IC95% = 1,4 – 5,21), misto: OR = 2,03, IC95% = 1,08 – 3,82), (iii) tipo de lactação (sala de ordenha: OR = 4,12, IC95% = 1,46 – 11,64; ordenha mecânica: OR = 2,94, IC95% = 1,42 – 6,09) e (iv) compartilhamento de pastagens (OR = 1,58, IC95% = 1,07 – 2,33). O estado de São Paulo deve implementar um sistema de vigilância estruturado capaz de detectar e mitigar a doença. Além disso, um programa de educação em saúde animal eficiente, capaz de encorajar os proprietários a testar animais de reposição para bTB previamente à introdução no rebanho e evitar o compartilhamento de pastagens com propriedades cuja condição sanitária é desconhecida, deve ser implementado.

Palavras-chave: Tuberculose bovina. Prevalência. Fatores de risco. São Paulo. Brasil.

Introduction

Bovine tuberculosis (bTB) is a chronic zoonotic disease caused by *Mycobacterium bovis* that in addition to cattle, affects small ruminants, humans, and other domestic and wild animals. The bacteria induce a chronic granulomatous caseous-necrotising inflammatory process in many organs depending on the route of entry. Though the main route of entry is inhalation (causing primary lesions in the lungs and accessory lymph nodes), it also can be ingested (causing primary lesions in the mesenteric lymph nodes) (DOMINGO et al., 2014). Apart from the risk to public health, the disease causes economic losses to the cattle industry (ZINSSTAG et al., 2006), especially in Africa, Central and South America, and Asia (OIE, 2015). Usually, the disease is endemic and is widespread over large territories connected by commercial relations, especially animal trade (GILBERT et al., 2005).

In 2001, the Brazilian Ministry of Agriculture, Livestock, and Food Supply (MAPA) launched the National Program for the Control and Eradication of Animal Brucellosis and Tuberculosis (PNCEBT), aimed at the reduction of the negative impact of bovine brucellosis and tuberculosis on human health and the promotion of competitiveness in the national livestock industry (LAGE et al., 2006).

The control measures implemented by the PNCEBT include control over the movement of reproducing animals and certification of tuberculosis-free farms (LAGE et al., 2006). The farmers pay for these activities such as diagnostic tests and veterinary services. The official veterinary service is only responsible for auditing the entire system.

In Brazil, recent studies carried out in 13 States, which hold 70% of the Brazilian cattle population, showed that the prevalence of tuberculosis infected herds varied between 0.36%, in the Federal District, and 7.6%, in the state of Espírito Santo (BAHIENSE et al., 2016; BARBIERI et al., 2016; GALVIS et al., 2016; GUEDES et al., 2016; LIMA et al., 2016; NÉSPOLI et al., 2016; QUEIROZ et al., 2016; RIBEIRO et al., 2016; ROCHA et al., 2016; SILVA et al., 2016; VELOSO et al., 2016; VENDRAME et al., 2016).

Even though no local surveys have been conducted, Grisi-Filho et al. (2011) reported that the prevalence of bTB is concentrated in high milk producing herds, in the state of São Paulo. Moreover, their results suggest that the infected farms were more likely to introduce and sell replacement animals without a prior tuberculin test.

The present study aims to estimate the prevalence of bTB and the associated risk factors in the state of São Paulo, in order to facilitate an effective management of the animal health policy.

Material and Methods

Sample design

The present study was designed by the Brazilian Ministry of Agriculture, Livestock and Food Supply (MAPA), the Collaborator Centre in Animal Health of the School of Veterinary Medicine of the University of São Paulo (FMVZ-USP), and the Animal Health Service of the state of São Paulo (Coordenadoria de Defesa Agropecuária – CDA). The fieldwork was performed between May and September 2011 by CDA staff members, who were trained in the standardized procedures.

In order to characterize regional differences in the epidemiological parameters associated with bTB, the state of São Paulo was divided into seven regions, based on the livestock production systems, livestock management practices, herd size, and trade systems (DIAS et al., 2009). The operational and logistic capacity of the CDA to perform the fieldwork, based on its 40 regional offices, was also taken into consideration while making the division. A map of the livestock regions was prepared using the ArcGIS 10.0 software.

In each region, a cross sectional study was performed to estimate the herd level and animal level prevalence of bTB using a two-stage sampling method. In the first stage, a pre-determined number of farms with reproduction activity were randomly selected (primary sampling units). In the second stage, a pre-determined number of bovine females, older than two years of age, were randomly selected (secondary sampling units).

In farms with more than one individual herd, the largest, economically important herd was chosen. The chosen animals were submitted to the same livestock management procedures, i.e. were exposed to the same risk factors. The choice of the primary sampling units was based on the official farm registry database. If a selected farm could not be visited by CDA staff, a new one was randomly selected to replace it. The number of selected farms per livestock region was estimated using the simple random sample formula, proposed by Thrusfield (2007) and Noordhuizen et al. (1997):

$$N = Z_{\alpha}^{2} * P * (1 - P) / d^{2}$$

where, N denotes the sample size, Z_{α} is the normal distribution value at a confidence level of 95%, P is the expected prevalence (20%), and d is the absolute error (5%).

The choice of the secondary sampling units was aimed at the appropriate classification of a farm as positive or negative. The herd sensibility and specificity concept (DOHOO et al., 2003) was used to achieve this objective. The values for sensitivity and specificity for the test protocol were 80% and 99.5% respectively (FLETCHER et al., 1988), and the value for expected prevalence was 20%. The calculations were performed using the Herdacc version 3 software and the selected sample size was the one that allowed a herd sensibility and specificity greater than 90%. Thus, 20 animals were sampled from farms with at least 99 females older than two years of age, and 40 animals were selected from farms with more than 99 females older than two years of age. In case the selected herd was smaller than the required sample size, all animals were sampled. The selection of females was casual systematic.

Herds, where up to 20 animals have been tested, were classified as infected herds when at least one animal tested positive for bTB. However, in case of herds where 40 animals have been tested, two positive samples were necessary to classify them as infected herds.

Test protocol

The comparative cervical tuberculin test was used to identify bTB positive animals in compliance with the recommendations of the Brazilian Brucellosis and Tuberculosis Control and Eradication National Program (LAGE et al., 2006). Tested animals were separated from the herd for 72 h before the results of the tests were determined. Animals with inconclusive results were retested, 60 days after the first test. If the second test result was inconclusive or positive, the animal was considered to be infected based on the criterion laid down by the national program (LAGE et al., 2006).

Prevalence estimation

The sample design allowed us to estimate herd and animal level prevalence in the state of São Paulo and in the individual livestock regions as well. The apparent prevalence and the respective 95% confidence intervals (95% CI) were estimated following the method established by DEAN et al. (1996). All calculations were statistically weighted (DOHOO et al., 2003). The statistical weight of each farm (W_f) in the calculation of the prevalence of infected herds across the whole state was:

$$W_f = \textit{number of farms in the region / number of sampled farms in the region}$$

The statistical weight of each infected bovine female, older than two years of age (W_a), in the calculation of animal level prevalence in the whole state was:

$$W_a = \textit{females} \geq \textit{2 years in the farm / sampled females} \geq \textit{2 years in the farm * females} \geq \textit{years in the region / females} \geq \textit{2 years in the sampled farms of the region}$$

In the above expression, the first term refers to the statistical weight of each sampled animal in the farm and the second term refers to the statistical weight of each farm in the livestock region.

The prevalence estimates and respective 95% CI of were calculated using EpiInfo 6.0 and SPSS version 9.0 software.

Analysis of risk factors

A questionnaire-based survey was conducted at each farm in order to generate data on the livestock management practices followed at the farm. All information generated was inserted into a database.

In this cross sectional study, risk factors such as production system (meat, milk, mixed), raising system (extensive, degree of confinement), cattle breeds, number of cows, total herd size, presence of other domesticated species, presence of wild species, animal trade, tuberculosis testing schedule, slaughter in the farm, pasture sharing, feeding calves with whey, indirect contact between farms, flooded pastures, and veterinary assistance were assessed. The assay parameters were chosen based on published literature (SKUCE et al., 2012; MARANGON et al., 1998).

These variables were organized based on a scale of increasing risk. The variables were re-categorized when necessary. The category with the lowest risk was always considered as baseline during comparison with the other categories. Quantitative variables were categorized using the third quartile as the threshold.

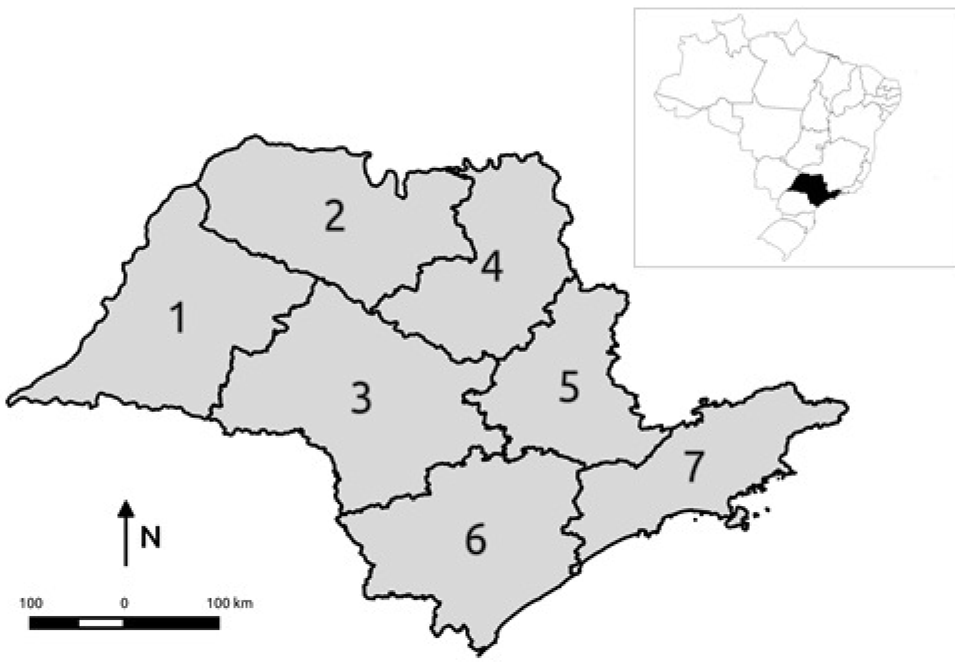
An exploratory univariate analysis was performed using the chi-square (χ^2) or Fischer exact test with all variables, including the data from the entire state. Risk factors with a significance level of less than 0.20 were selected for further multivariate analysis using logistic regression, based on the method of Hosmer and Lemeshow (1989). All calculations were performed using the SPSS 9.0 and EpiInfo 7.0 computer software.

In order to determine the correlation between the variables, a Spearman correlation test was performed. If two variables were correlated, the variable that was less associated with the dependent variable was excluded from the multivariate analysis.

Results

The state of São Paulo was divided into seven livestock regions (Figure 1), based on the classification proposed by Dias et al. (2009).

Figure 1. Map of the state of São Paulo showing the division of livestock regions.



The apparent herd level prevalence of tuberculosis in the state of São Paulo was estimated to be 9.0% (95% CI = 7.8 – 10.5), varying from 3.5% (95% CI = 1.7 – 6.8) in region 6 to 13.9% (95% CI = 10.2 – 18.8%) in region 5. The prevalence of tuberculosis infected farms in livestock region 6 is significantly lower than regions 2, 4, 5, and 7 (Table 1).

Moreover, there were no significant differences in the apparent herd level prevalence between farm enterprises (beef, mixed, and dairy) at each farm, and between the regions for each enterprise (Table 2).

The apparent prevalence of bTB infected females, older than 2 years of age, in the state of São Paulo was estimated to be 1.3% (95% CI = 0.9 – 1.7), varying from 0.3% (95% CI = 0.2 – 0.6) in region 1 to 2.5% (95% CI = 1.5 – 4.3) in region 5. The prevalence of bTB infected animals in livestock regions 1 and 6 is significantly lower than that in livestock regions 2, 4, 5, and 7 (Table 3).

The results from the univariate analysis are presented in Table 4. The results from the multivariate model are shown in Table 5.

Table 1. Apparent prevalence of bovine tuberculosis infected farms in the state of São Paulo.

Region	Farms with reproductive activities	Number of sampled farms	Number of infected farms	Prevalence (%)	CI 95% (%)
1	28,943	247	17	6.9	4.3 – 10.8
2	25,343	269	30	11.2	7.9 – 15.5
3	23,599	260	18	6.9	4.4 – 10.7
4	9,732	237	28	11.8	8.3 – 16.6
5	15,881	251	35	13.9	10.2 – 18.8
6	17,976	230	8	3.5	1.7 – 6.8
7	13,037	249	33	13.3	9.6 – 18.1
Total	134,511	1,743	169	9.0	7.8 – 10.5

Table 2. Apparent prevalence of bovine tuberculosis infected herds based on the farm enterprises in the state of São Paulo.

Region	Beef cattle			Dairy cattle			Mixed cattle		
	n	%	95% CI	n	%	95% CI	n	%	95% CI
1	4/115	3.5	1.3 – 8.9	11/95	11.6	6.5 –19.7	2/37	5.4	1.4 – 19.3
2	4/93	4.3	1.6 – 10.9	17/113	15.0	9.6 – 22.9	9/63	14.3	7.6 – 25.3
3	3/111	2.7	0.9 – 8.1	9/92	9.8	5.2 – 17.8	6/57	10.5	4.8 – 21.6
4	5/112	4.5	1.9 – 10.3	17/67	25.4	16.4 – 37.1	6/58	10.3	4.7 – 21.2
5	8/73	11.0	5.6 – 20.9	19/84	22.6	14.9 – 32.8	8/94	8.5	4.3 – 16.1
6	0/75	0.0		0/41	0.0		8/114	7.0	3.5 – 13.4
7	6/43	14.0	6.4 – 27.8	20/144	13.9	9.1 – 20.6	7/62	11.3	5.5 – 21.9

Table 3. Apparent prevalence of bovine tuberculosis infected cows in the state of São Paulo.

Region	Females ≥ 2 years of age	Sampled females ≥ 2 years of age	Infected animals	Prevalence (%)	95% CI (%)
1	1,193,467	3,678	21	0.3	0.2 – 0.6
2	823,073	3,201	57	2.2	1.1 – 4.2
3	984,312	3,305	35	1.0	0.5 – 2.1
4	264,744	2,484	68	2.5	1.4 – 4.5
5	364,848	2,568	73	2.5	1.5 – 4.3
6	392,063	2,319	11	0.4	0.2 – 0.8
7	308,948	2,723	55	1.9	1.2 – 3.0
Total	4,331,455	20,278	320	1.3	0.9 – 1.7

Table 4. Univariate analysis of the risk factors (p ≤0.20) for bovine tuberculosis in the state of São Paulo.

Variable	Proportion of infected herds	%	*p*
Number of females > 2 years of age			
1 – 23*	100/1,293	7.7	< 0.001
≥ 24	69/450	15.3	
Acquisition of breeding animals			
No	98/1,262	7.8	< 0.001
Yes	71/481	14.8	
Raising system			
Extensive	126/1,496	8.4	< 0.001
Any degree of confinement	43/247	17.4	
Farm enterprise			
Beef	30/622	4.8	< 0.001
Mixed	46/485	9.5	
Dairy	93/636	14.6	
Breed			
Beef	13/415	3.1	< 0.001
Mixed-breed	133/1,221	10.9	
European dairy	21/95	22.1	
Number of milking females			
1 – 9*	65/776	8.4	< 0.001
≥ 10	67/289	23.2	
Number of milkings per day			
0	38/694	5.5	< 0.001
1	93/915	10.2	
2 – 3	38/134	28.4	
Milking process			
None	38/694	5.5	< 0.001
Manual	91/922	9.9	
Mobile milking machine	31/103	30.1	
Milking parlor	9/24	37.5	
Total herd size			
1 – 56*	113/1,304	8.7	0.012
≥ 57	56/439	12.8	
Sharing of watering place			
No	152/1,449	10.5	0.013
Yes	17/294	5.8	
Sharing of pastures			
No	127/1,430	8.9	0.014
Yes	42/313	13.4	
Presence of wild animals			
No	53/687	7.7	0.024
Yes	116/1,056	11.0	
Equipment, production input, or personnel sharing			
No	132/1,457	9.1	0.043
Yes	37/286	12.9	
Artificial insemination			
No	152/1,627	9.3	0.062
Yes	17/116	14.7	

*Third quartile. **Fischer exact test.

Table 5. Final multivariate model of the risk factors for bovine tuberculosis in the state of São Paulo.

Variable	Odds ratio	95% Confidence interval	*p*
Number of females (≥ 2 years of age) ≥ 24	1.91	1.32 – 2.75	0.001
Farm enterprise			
Beef (reference category)			
Mixed	2.03	1.08 – 3.82	0.028
Dairy	2.70	1.40 – 5.21	0.003
Milking process			
None (reference category)			
Manual	1.09	0.62 – 1.94	0.760
Mobile milking machine	2.94	1.42 – 6.09	0.004
Milking parlor	4.12	1.46 – 11.64	0.008
Pasture sharing	1.58	1.07 – 2.33	0.021

r^2 = 10.7%

Discussion

We observed that the herd level prevalence of bTB in the state of São Paulo was 9.0% (95% CI = 78 – 10.5%), which is statistically equal to the prevalence in the state of Espírito Santo and is higher than the prevalence observed in the states of Minas Gerais, Paraná, Bahia, Rio Grande do Sul, Mato Grosso, Mato Grosso do Sul, Rondônia, Goiás, Pernambuco, and Santa Catarina e Distrito Federal (BAHIENSE et al., 2016; BARBIERI et al., 2016; GALVIS et al., 2016; GUEDES et al., 2016; LIMA et al., 2016; NÉSPOLI et al., 2016; QUEIROZ et al., 2016; RIBEIRO et al., 2016; ROCHA et al., 2016; SILVA et al., 2016; VELOSO et al., 2016; VENDRAME et al., 2016).

Although the prevalence of bTB infected herds in regions 2, 4, 5, and 7 were higher than the prevalence in region 6, a clear pattern indicating the concentration of the disease in the northern regions of the state (regions 2, 4, 5, and 7) was observed. These regions are traditional dairy producing areas in the country (BRASIL, 2006) (Tables 1 and 3). The association between dairy herds and bTB was reported by several authors from Brazil and other countries. This is primarily due to the prolonged time of production and the agglomeration of the animals for the milking procedures, factors that contribute to the persistence and propagation of bovine tuberculosis (BAHIENSE et al., 2016; BARBIERI et al., 2016; GALVIS et al., 2016; GRISI-FILHO et al., 2011; QUEIROZ et al., 2016; ROCHA et al., 2016; SILVA et al., 2016; VELOSO et al., 2016; DAWSON et al., 2014; PEREZ et al., 2002; PORPHYRE et al., 2008; ZENDEJAS-MARTÍNEZ et al., 2008).

One of the risk factors associated with bTB was the number of adult females in a herd, i.e., bigger herds were more likely to be infected (Table 5). Farmers owning big herds tend to purchase more cattle, the strongest factor associated with an increased bTB risk (SKUCE et al., 2012). Moreover, larger the bovine population, greater is the probability of introduction and persistence of the infection (HUMBLET et al., 2009), which is in agreement with the known epidemiological pattern of bTB (RAMÍREZ-VILLAESCUSA et al., 2010). The same risk factor was observed in the Brazilian states of Paraná, Santa Catarina, and Bahia e Espírito Santo (GALVIS et al., 2016; BAHIENSE et al., 2016; SILVA et al., 2016; VELOSO et al., 2016).

Dairy and mixed herds also emerged as risk factors (Table 5). As mentioned before, the association between dairy farms and tuberculosis is very well documented in the literature. Furthermore, the sophistication of the milking process, use of milking parlors, or mobile milking machines, also increased the risk for bTB (Table 5). The higher production stress associated with intensive dairy management has been associated with increased risk (GRIFFIN et al., 1996).

Sharing of pastures with other herds was also identified as a risk factor for bTB in the present study (Table 5). The possibility of close contact between animals from different farms may have favored the spread of the infection. Even a short duration contact may have been sufficient to maintain the disease (COSTELLO et al., 1998; BROOKS-POLLOCK; KEELING, 2002; HUMBLET et al., 2009).

Conclusion

São Paulo has the highest prevalence of bTB among the Brazilian states studied. The disease occurs all over the state, especially in dairy farms using milking parlors or mobile milking machines, but is more concentrated in the northern region of the state, a traditional dairy production area in the country. The spread of bTB among farms in the state is mainly associated with the purchase of animals and the sharing of pastures. Considering these findings, the state of São Paulo should implement a surveillance system to detect bTB infected herds and certify them as free, preferably incorporating elements of risk-based surveillance. In addition, anefficient animal health education program that educates the farmers to test replacement animals for bTB, prior to introduction in their herds and to avoid pasture sharing with farms of unknown sanitary conditions, should be implemented.

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