

Urbanization of Brazilian spotted fever in a municipality of the southeastern region: epidemiology and spatial distribution

Urbanização da febre maculosa brasileira em município da região Sudeste: epidemiologia e distribuição espacial

Jeanette Trigo Nasser^{III}, Rafael César Lana^{II}, Claudia Maria dos Santos Silva^I, Roberto Wagner Lourenço^{III}, Darllan Collins da Cunha e Silva^{II}, Maria Rita Donalísio^I

ABSTRACT: *Introduction:* Brazilian spotted fever is an emerging zoonosis notified mainly in the Southeast of Brazil, especially due to its high level of lethality. *Objective:* To analyze the epidemiological and spatial pattern of the disease in the municipality of Valinhos (106,793 inhabitants), São Paulo, Southeastern region of Brazil, in the period between 2001 and 2012. *Methods:* All laboratory-confirmed cases with likely site of infection in the city (n = 49) notified in the Brazilian Case Registry Database were studied. Sites were geocoded using the cartographic base of the city and Google Earth (geographic coordinates) with correction according to the Brazilian Geodetic System. We used the Kernel estimator to analyze the density of the cases on the map. Land cover and distance to basins of all cases were analyzed. Information about tick species and primary hosts were obtained from reports of the Superintendence of Control of Endemic Diseases. *Results:* Seasonality of the disease was observed with the highest incidence from June to November, and in 2005 and 2011. The most affected groups were men (79.6%) aged 20-49 years old (49%). Lethality was found to be 42.9%. Maps showed the progressive registration of cases in the urban area. Capybaras were reported as the main primary host, and *Amblyomma cajennense* was identified in probable sites of infection during field investigation. The likely sites of infection were mostly located near basins, dirty pastures, and bordering woods. *Conclusions:* The transmission pattern of Brazilian spotted fever in Valinhos is similar to that in other cities in the region, where capybara is the main primary host and an amplifier of *R. rickettsii*. Over the years, a higher occurrence of cases has been identified in the urban area of the city.

Keywords: Brazilian spotted fever. Spatial distribution. Epidemiology. Urbanization. *Rickettsia rickettsii*. *Amblyomma* ssp.. Capibara.

^ILaboratory of Spatial Analysis of Epidemiological Data, School of Medical Sciences, *Universidade Estadual de Campinas* – Campinas (SP), Brazil.

^{II}Department of Public Health of Valinhos, Secretariat of Health of Valinhos – Valinhos (SP), Brazil.

^{III}School of Environmental Engineering, *Universidade Estadual Paulista "Júlio de Mesquita Filho"* – Sorocaba (SP), Brazil.

Corresponding author: Maria Rita Donalísio. Laboratório de Análises Espaciais de Dados Epidemiológicos (Epigeo). Departamento de Saúde Coletiva da Faculdade de Ciências Médicas da Unicamp. Rua Tessália Vieira de Camargo, 126, Cidade Universitária, CEP: 13083-970, Campinas, SP, Brasil. E-mail: rita.donalisio@gmail.com

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RESUMO: Introdução: A febre maculosa brasileira é uma zoonose de caráter reemergente notificada principalmente na região Sudeste do Brasil, destacando-se pela sua alta letalidade. **Objetivo:** Analisar o padrão epidemiológico e espacial dessa enfermidade no município de Valinhos, São Paulo (106.793 habitantes), no período de 2001 até 2012. **Métodos:** Foram estudados todos os casos confirmados laboratorialmente (n = 49) com local provável de infecção no município, notificados no Sistema de Informação sobre Agravos Notificáveis. Os locais foram georreferenciados na base cartográfica usando o Google Earth (coordenadas geográficas) com correção de acordo com o Sistema Geodésico Brasileiro. Utilizou-se o estimador Kernel para a análise da densidade de casos no mapa. Cobertura do solo e distância a coleções hídricas foram analisados. A presença de espécies de carrapatos e hospedeiros primários foram obtidos de relatórios da Superintendência de Controles de Endemias. **Resultados:** Observou-se sazonalidade da doença com maior incidência entre junho a novembro, sendo os anos de 2005 e 2011 os de maior ocorrência. Houve predomínio de casos no sexo masculino (79,6%) e na faixa etária 20 a 49 anos (49%). A letalidade foi de 42,9%. Os mapas mostram o registro progressivo de casos na zona urbana da cidade. As capivaras foram notificadas como principal hospedeiro primário de *Amblyomma cajennense*, espécie identificada nas pesquisas acarológicas no local de estudo. Os locais prováveis de infecção estão localizados, na maioria, próximos às coleções hídricas, pastos sujos e mata ciliar degradada. **Conclusões:** O padrão de transmissão da febre maculosa brasileira em Valinhos é semelhante ao descrito em outras cidades da região, onde a capivara é o principal hospedeiro primário do vetor e amplificador da bactéria *R. rickettsii*. Com o passar dos anos foi identificada uma maior ocorrência de casos na área urbana do município.

Palavras-chave: Febre maculosa brasileira. Distribuição espacial da população. Epidemiologia. Urbanização. *Rickettsia rickettsii*. *Amblyomma* ssp.. Capivara.

INTRODUCTION

Brazilian spotted fever (BSF) is an infectious, febrile, and acute disease, with variable severity, which usually has an endemic character. It is transmitted by ticks¹. This disease can be difficult to diagnose, especially in early stages. For being multisystemic, spotted fever can have different clinical courses, ranging from classic pictures to atypical forms without exanthema. If not treated properly, lethality in the most severe cases reaches 80%².

The condition is also known as exanthematic typhus of São Paulo, Rocky Mountain spotted fever, or New World spotted fever³. BSF is caused by *rickettsia* from the spotted fever group (SFG), such as *Rickettsia rickettsii* and possibly *Rickettsia parkeri*. The latter is suspected to be the agent in charge of the milder cases of the disease in Santa Catarina^{4,5}.

This condition is transmitted by the *Amblyomma* ticks and has been more frequently notified in the Southeast of the country, especially the states of Minas Gerais and São Paulo⁶. In Brazil, the main vector of *Rickettsia rickettsii* is the *Amblyomma cajennense*¹ tick, and *Amblyomma aureolatum* is the vector of *R. rickettsii* in the metropolitan region of São Paulo⁷. Even though it is not totally proved, circumstantial evidence is available that in Brazil *Rhipicephalus sanguineus* may contribute to the transmission of *R. rickettsii* to humans^{8,9}. The clinical manifestations of the disease were first described in 1899 by Kenneth Maxcy,

in the United States (Rocky Mountain Spotted Fever). From 1906 to 1909, Howard Taylor Ricketts succeeded in transmitting this disease to guinea pigs, identifying the tick as the vector, and observed rickettsias in smears prepared from tick tissue¹⁰. In 1916, the bacteria were named *Rickettsia*¹¹.

In 1930, BSF was recognized for the first time in the state of São Paulo, by Piza et al.¹², apparently circumscribed to peri-urban areas of the capital. On that occasion, it was possible to distinguish spotted fever from other exanthematous diseases in Brazil, proposing the name *exanthematic typhus* of São Paulo for this new identified condition¹².

Since then, data have been recorded about the disease, which mainly occurs in individuals living in the rural zone of cities close to the capital, such as Mogi das Cruzes, Diadema, and Santo André¹³.

In 1985, three individuals living in the city of Pedreira, in the region of Campinas, São Paulo, presented with symptoms that were compatible with BSF, which was confirmed by clinical diagnosis^{14,15}. Up until that moment, there had been no records of the condition in the region¹⁶. From 1986 onward, cases of BSF have been confirmed in other cities of the region, with the progressive notification of cases after 1996 as well as the amplification of the transmission area; then it became a compulsory notification disease.

Nowadays, the region of Campinas is considered to be endemic for BSF in the state of São Paulo, as well as part of the Piracicaba river bay, which has the highest number of cases in the state. Valinhos stands out for presenting the second highest incidence of the disease in the metropolitan region of Campinas in the analyzed period¹⁷.

Capybaras have been associated with the cycle of this rickettsiosis for presenting positive serology and for being host of the *Amblyomma cajennense* ticks, which are the main vectors of the disease. They are frequently indicated as amplifying hosts of *R. rickettsii*¹⁸⁻²¹.

In the past 20 years, the number of capybaras has increased in the region. These mammals have presented larger population densities in anthropic environments than in natural ones. They move freely through large extensions of the riparian zones of the bay, which are often degraded, and invade inhabited spaces, thus intensifying the contact between ticks and human beings because they are highly infested by these parasites^{22,23}.

Georeferencing techniques and spatial analysis have been used to understand the distribution of diseases and are particularly useful in the study of zoonosis concerning its environmental features, the distribution and the ecology of vectors, reservoirs and their relationship with the landscape^{1,24-29}. Therefore, the objective of this study was to analyze the epidemiological profile of BSF, the presence of vectors and primary hosts in Valinhos, São Paulo, besides identifying tendencies and patterns of spatial distribution of the disease in the city.

METHODS

This is a retrospective epidemiological study with an ecological approach of BSF cases in the city of Valinhos, São Paulo, from 2001 to 2012. This city is located to the Southeast of

the state of São Paulo, 74 km away from the capital, in the metropolitan region of Campinas. The city has an area of 148.9 km² and its estimated population is of 106,793 inhabitants³⁰; of which 95% is urban population and 5% rural population. The vegetation in Valinhos is mainly composed of a mosaic of formations, with vestiges of semideciduous seasonal forests, *cerradão*, *cerrado* and *campinas*. Its territory includes rivers Atibaia and Capivari and streams Pinheiros, Bom Jardim, and Samambaia, belonging to the basins of rivers Piracicaba and Capivari. The subtropical climate is prevalent in its territory; there is no dry season and the temperature in the hottest month is always higher than 22°C (according to the climatic classification of Köppen)³¹. The totality of notified BSF cases (n = 49) from 2001 to 2012, available in the Notifiable Diseases Information System (SINAN) and in the Public Health Department of Valinhos, was investigated. The period of the study was divided into three quadrenniums (2001 – 2004, 2005 – 2008, and 2009 – 2012) to show the changes in the tendency of spatial distribution of the cases.

The first case of BSF in the city was confirmed in 2003, even though there had been confirmation of the disease since 1996. The inclusion criterion involved the case being laboratory confirmed and the probable site of infection (PSI) being in the city.

The geographic coordinates of the PSIs were obtained with Google Earth, being georeferenced by map rectification from the geometric correction of coordinate systems, based on map data for the city of Valinhos. Therefore, the correction was conducted according to the Brazilian Geodetic System (SGB) and the National Cartographic System (SCN) by SIRGAS2000, which is the reference system used for cartographic representations in Brazil. That stage allows minimizing or eliminating possible spatial positioning errors. The study of the relationship between the occurrence of PSIs and the type of coverage in the terrain was conducted using the generation of the matrix with percentages of soil use by treating satellite images. The images were taken from the Landsat 5 TM sensor, orbit point 219/76, from 2004, 2008, and 2012, together with the National Institute for Space Research (INPE). On the basis of that treatment, it was possible to identify the percentages of soil use in the analyzed period, every 4 years, and which types of soil use class coincided with the PSIs temporally. The distance between the PSIs and the hydrographic network was calculated.

The Kernel estimator was used for spatial analysis because it identifies places of larger density of cases in the study territory²⁶. The city contours in the rural and urban zones, in the study periods, were obtained from the cartographic base provided by the Secretariat of Planning and Environment, in Valinhos, in the different quadrenniums.

The epidemiological profile was studied according to the following variables: demographic features (sex, age), clinical progress, activity performed in the PSI, characterization of PSIs, monthly distribution of BSF cases, and spatial distribution of PSIs. The latter were defined as the place where the person became a host to the vector or the area this person attended in which there is the presence of ticks and/or favorable conditions for the transmission of the spotted fever³².

The areas were classified by the Superintendence of Control of Endemic Diseases (SUCEN), considering the acarologic study with identification of species, presence of primary hosts, and evaluation of environmental characteristics. The environmental data were obtained from SUCEN reports and by visits to the PSIs from the municipal health team and researchers.

The proportions of demographic and epidemiological variables were compared using the χ^2 test, considering a 5% significance level.

To elaborate the database and the descriptive analysis, the Epi Info software, version 6.04, was used; for spatial analysis, the chosen software was ArcGis 10.0 (ESRI, 2010). The study was approved by the Research Ethics Committee of the School of Medical Sciences of Universidade de Campinas, report n. 1192/2011.

RESULTS

Forty-nine cases reported during the study period (2001 to 2012) were analyzed. Figure 1 shows the distribution of cases and deaths caused by BSF from 2001 to 2012. Even though BSF has been notified since 1996 in the region, the uninterrupted record of the condition only took place after 2003; 2005 and 2011 recorded most of the cases.

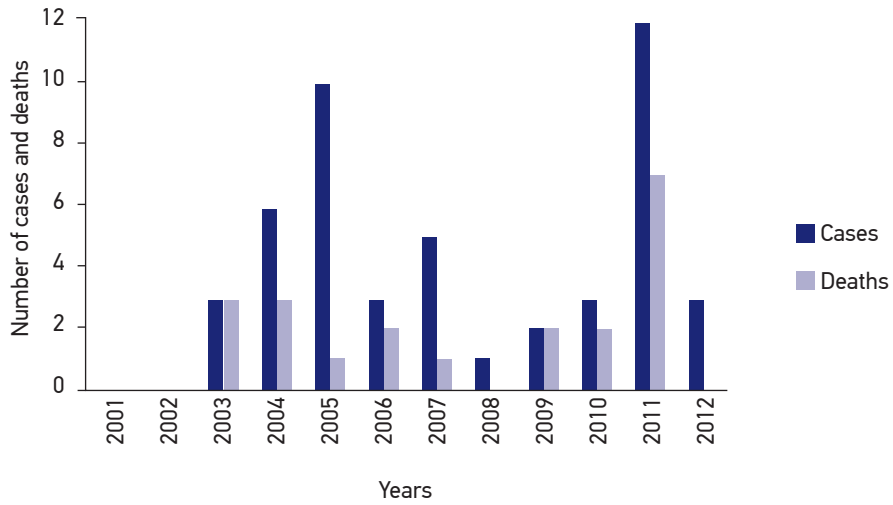
Figure 2 shows the seasonal pattern of the condition in the city during the study period. There have been more cases from June to November, when the nymph stage of *A. cajennense* is prevalent.

Table 1 shows the frequency of the variables associated with the notified cases. The disease was prevalent among male individuals, aged between 20 and 49 years old, in places with the presence of the capybaras, close to rivers and lakes. In 35 (71.4%) of the PSIs, the only notified primary host was the capybara, even though this host has also been found in 3 other sites (6.1%) in the equines. The higher notification of PSI in urban and peri-urban areas, as well as the high level of lethality of the disease (42.9%), stands out. In 2011, there were 12 cases and 58.3% of lethality in the PSIs in an urban zone, and no deaths in the rural zone.

SUCEN recorded the presence of *A. cajennense* in 12 (24.5%) and *Amblyomma dubitatum* in 6 (12.2%) of the PSIs and of both species in 22 sites (44.9%). The difference was found to be statistically significant using the χ^2 test for the variables gender, primary host, and hydric resources.

Figure 3 presents the percentages of PSI of the cases and the different types of soil use obtained in the processing of satellite images. It is observed that more than 37% cases occurred in urban regions and 49% were located in regions of pasture and woods.

The distribution of PSIs of BSF cases regarding the distance from the closest hydric collection, from 2001 to 2012, is shown in Figure 4. Most PSIs (67.3%) occurred less than 100 m away from the margin of the hydric body whereas 28.6% took place in the interval from 100 to 300 m.



Source: SINAN, SMS Valinhos.

Figure 1. Annual distribution of cases and deaths by Brazilian spotted fever in Valinhos, SP, 2001 to 2012.

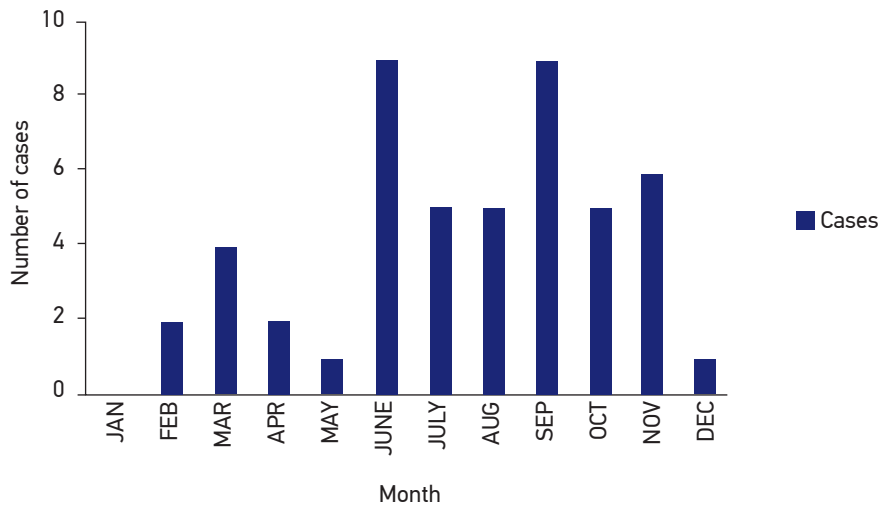


Figure 2. Monthly distribution of Brazilian spotted fever cases in Valinhos, SP, 2001 to 2012.

The spatial distribution of the PSIs of the BSF cases in Valinhos, from 2001 to 2012, is shown in Figure 5. It is worth mentioning that the number of observed spots is inferior to 49 because some cases have had more than one registered case. In the

Table 1. Demographic and epidemiological characteristics of Brazilian spotted fever cases, Valinhos, SP, 2001 to 2012.

Variables	n	%
Sex		
Male	39	79.6
Female	10	20.4
Age group (years)		
< 19	10	20.4
20 – 49	24	49.0
50 – 69	14	28.6
≥ 70	1	2.0
Clinical evolution		
Cure	28	57.1
Death	21	42.9
Activity in the PSI		
Leisure	19	38.8
Work	10	20.4
Household	20	40.8
PSI location		
Rural	20	40.8
Urban/peri-urban	29	59.2
Primary host		
Equine	7	14.3
Capybara	35	71.4
Capybara and equine	3	6.1
Not informed	4	8.2
Hydric resources in the PSI		
Rivers, streams, lagoons	42	85.7
No hydric resources	7	14.3
Ticks in the PSI *		
<i>Amblyomma cajennense</i>	12	24.5
<i>A. dubitatum</i>	6	12.2
<i>A. cajennense</i> and <i>A. dubitatum</i>	22	44.9
<i>Amblyomma</i> spp.	6	12.2
Not informed	3	6.1

PSI: probable site of infection; *The not informed ones were not included in the analysis.

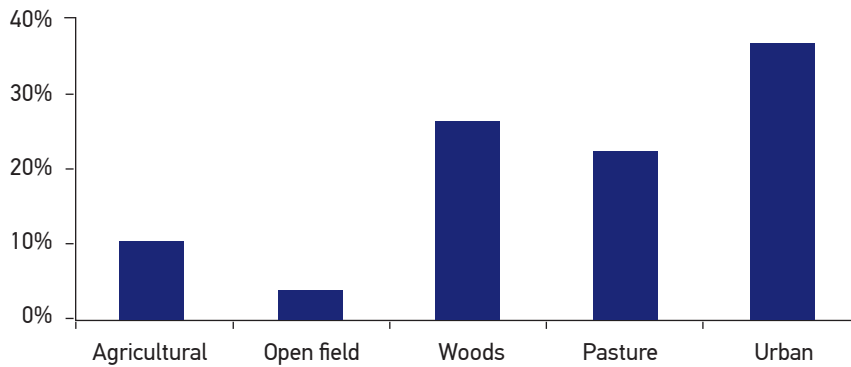


Figure 3. Percentage distribution of probable sites of infection of Brazilian spotted fever and different soil uses, Valinhos, SP, 2001 to 2012.

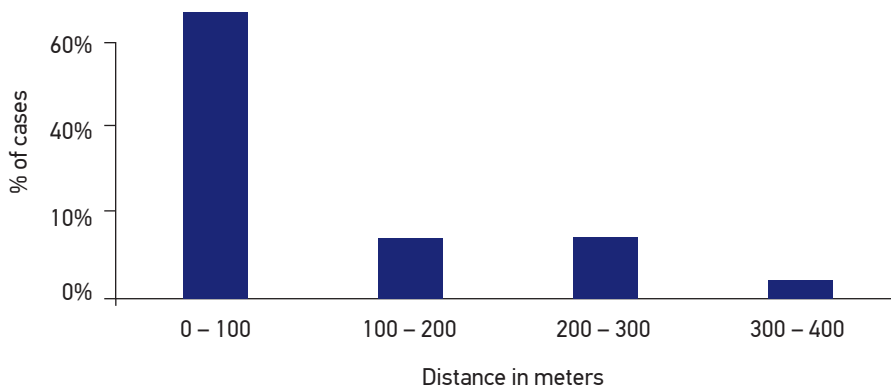
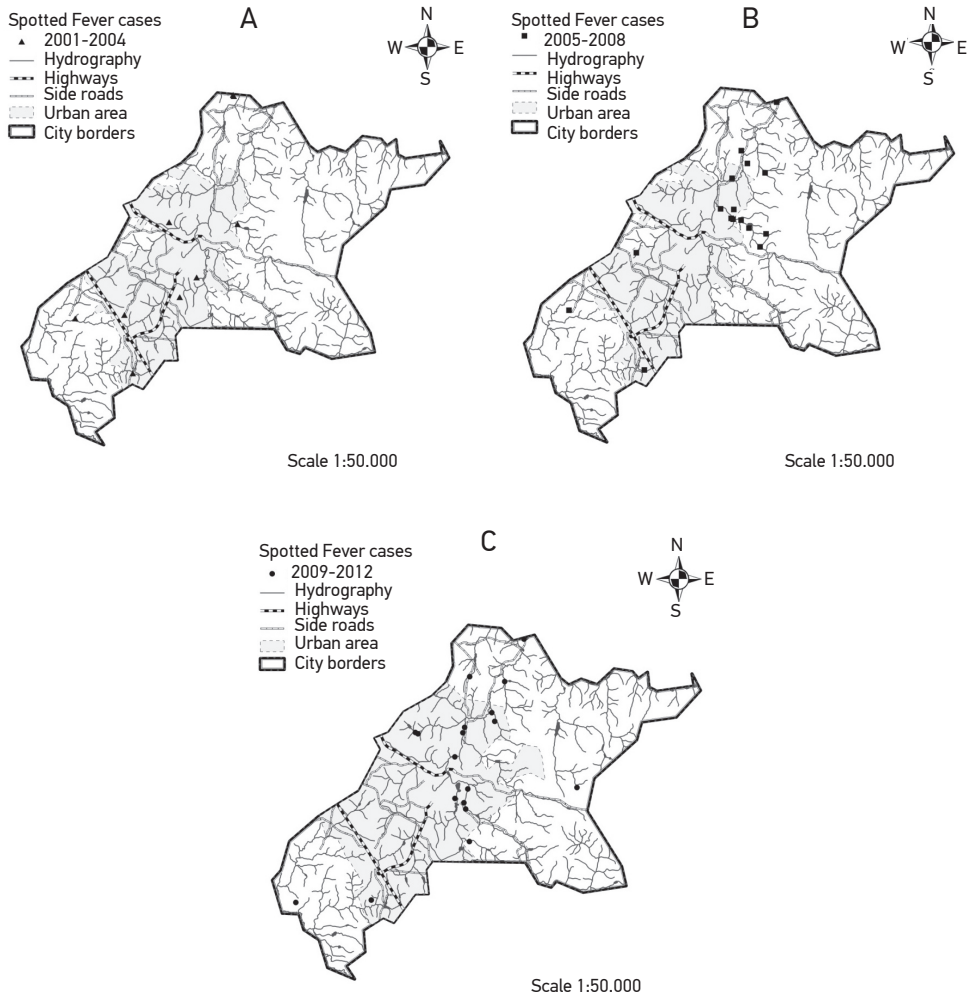


Figure 4. Percentage distribution of Brazilian spotted fever cases (probable sites of infection) regarding the distance from hydric collections, Valinhos, SP, 2001 to 2012.

maps, it is possible to observe that the location of the PSIs is close to the hydrographic network of the city.

Figure 6 presents the spatial distribution and the places of higher density of cases from 2001 to 2004. Two regions are seen with transmission in the rural zone, in which there were five cases (55.6% of the total in the period and 10.2% of the cases in the city until 2012), and other regions of transmission in the suburbs. Figure 6B represents the spatial distribution of 19 cases that occurred from 2005 to 2008, when it was possible to register a single cluster of cases of BSF in the consolidated urban area, and 11 cases (57.8% of

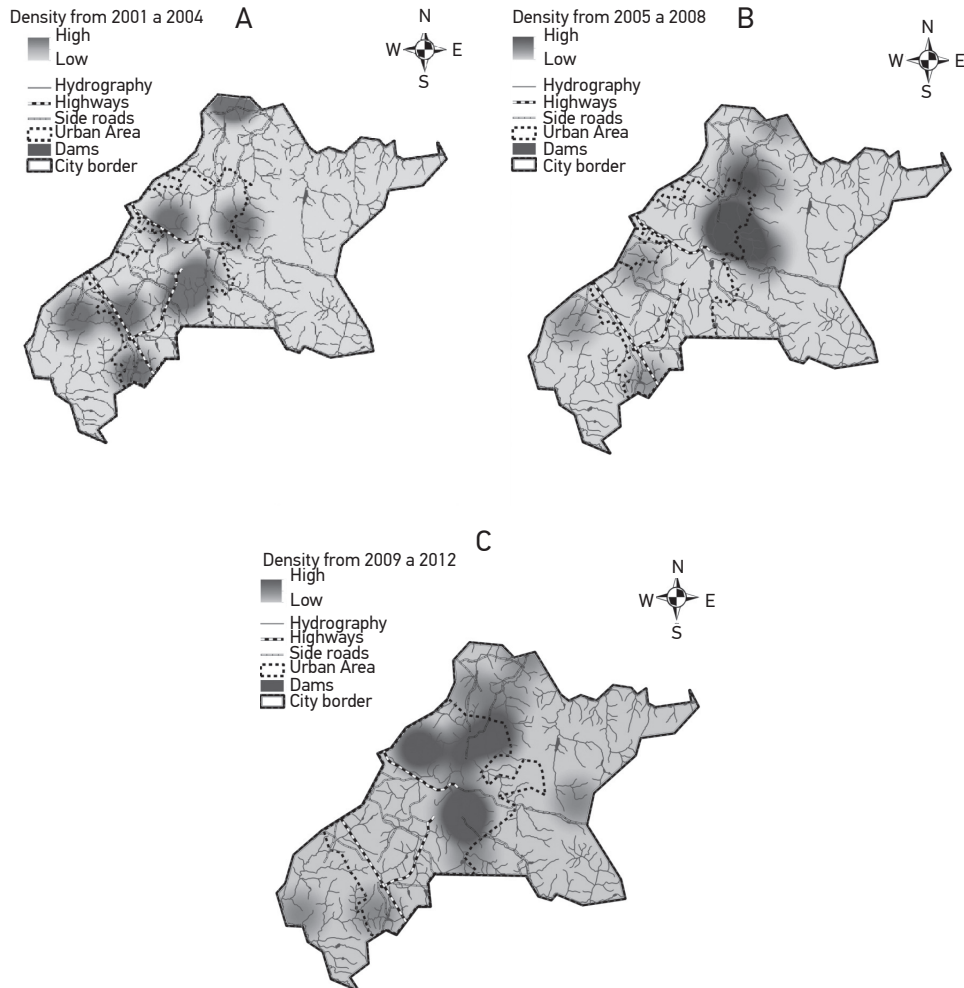


Source: IBGE Carta do Brasil – Scale 1:50.000.

Figure 5. Map of Valinhos, SP, with delimited urban area, hydrography, and cases of Brazilian spotted fever. (A) From 2001 to 2004, (B) from 2005 to 2008, and (C) from 2009 to 2012.

the cases in the period and 22.5% of the total until 2012) reaching urban areas, without significant expression in the rural areas of the city.

The density of cases (21) that occurred from 2009 to 2012 constitutes 42.9% of the total. Three clusters are seen to be located in a consolidated urban area and in expanding urban area (Figure 6C).



Source: IBGE Carta do Brasil – Scale 1:50.000.

Figure 6. Density map of probable sites of infection of Brazilian spotted fever, by the Kernel estimator, Valinhos, SP. Density of probable sites of infection (A) from 2001 to 2004, (B) from 2005 to 2008, and (C) from 2009 to 2012.

DISCUSSION

The results of this investigation showed the occurrence of more and more cases in the urban area, the frequent presence of the capybara as a primary host in the city, and the constant proximity of PSIs to hydric collections.

In many regions of the country, studies have shown the supposed urbanization of the BSF and that this condition has been occurring in regions that had not been considered as a risk for transmission. It is no longer restricted to rural and forest areas, and it often occurs

in peri-urban and urban areas, including public parks^{18,33,34}. The results found in this study corroborate these observations and also suggest the adaptation of the disease cycle to the peri-urban and urban environment.

The role of the capybaras as the primary host in Valinhos becomes clear by the high percentage of sites (77.5%) in which these mammals were present, alone or together with the equines, and by the proximity of hydric resources in the PSIs (85.7%).

According to Souza et al.^{18,19}, in the region of Campinas, most cases of BSF are related to the population growth of the capybara, one of the main primary hosts for all of the developmental stages of the *A. cajennense* tick¹⁹.

According to Ferraz et al.³⁵, the increasing agricultural production and the decreasing number of natural predators are the two main factors that contribute to the increase and the expansion of the capybara population, besides the prohibition of hunting and the high reproductive capacity of this species.

Besides the capybaras, the equines are also primary hosts of ticks transmitting the spotted fever³⁶. Because the equines meet the criteria established for sentinel animals³⁷, they have been used for this purpose; once they are prone to BSF, they present good immunological response and are not amplifiers of the agent^{38,39}. The use of sentinel animals may provide information about the changing incidence of a disease with time, its propagation, and the risk factors associated with it³⁷.

In the analyzed PSIs, it was possible to observe the prevalence of sites in which both *A. cajennense* and *A. dubitatum* could be found; these are the most common ectoparasites found in capybaras (*Hydrochoerus hydrochaeris*) in the Southeast of Brazil⁴⁰.

The higher the density of the capybara, the higher the availability of hosts for the adult stage of *A. cajennense*, which increases the growth rate of the tick exponentially⁴¹.

The seasonal distribution of the disease in Valinhos, where cases are prevalent between June and November, coincides with the period in which the nymph phase of *A. cajennense* is prevalent, and that has been observed in other endemic areas of São Paulo and Minas Gerais^{36,42-44}. This could be partly explained by the fact that stings from immature forms are less painful and are not noticed by humans, unlike the sting from an adult, which is painful; therefore, the person can rapidly notice it and remove the ixodid from the body, so it is not attached for too long and there is no time to transmit the bacteria³³.

By analyzing the distribution of the 49 cases throughout the period, the prevalence of cases among men aged from 20 to 49 years old was observed, as verified in sites of BSF transmission involving the vector *A. cajennense*, as observed in Minas Gerais⁴⁵.

In the state of São Paulo, two species of ticks are implied in the transmission of *Rickettsia rickettsii* to humans, *A. cajennense* and *A. aureolatum*; the latter occurs in places where the Atlantic Forest prevails^{7,46}, so it does not occur in the analyzed city, in which the Cerrado bioma. The identification of the vector species helps in understanding the specificities of its biological cycle and its relationship with the hosts. Of the PSIs in urban and peri-urban areas, 59.2% were registered, being 40.8% transmitted in the domiciliary and peridomiciliary environments. Possible factors involved in these findings were the advance of houses and

condos in forest areas, the proximity of parks, the increasing population of capybaras, and the absence of predators, thus making it easier to expose humans to hosts and vectors of the disease.

The coefficient of lethality found in this study, 42.9%, is higher than that recorded in the state of São Paulo from 1985 to 2011, with 38.4%³³. The high lethality of the disease can be a reflex of a low diagnostic suspicion, with possible delay in the onset of treatment, besides the low notification and the detection of the most severe cases.

It is important to point out for the need of permanent strategies of education in health and environmental management with the control of hosts^{47,48}, including methods of population control for the capybaras in urban areas.

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