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Temporal and Spatial Analysis of Vector-Tick Borne Spotted Fever in the State of São Paulo

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Simple Summary

Brazilian spotted fever (BSF) is a tick-borne acute febrile disease that can be lethal to humans, caused by *Rickettsia rickettsii*. This is a temporal study with secondary data on confirmed human BSF cases of vector-tick borne in the State of São Paulo. In *Amblyomma sculptum* areas, incidence and mortality increased significantly between 2007 and 2015 (p-value < 0.05). In *Amblyomma aureolatum* areas, incidence decreased (p-value < 0.05), but mortality remained stable. Lethality was higher in *A. aureolatum*-associated cases. Most patients were hospitalized near the probable site of infection. Patterns varied markedly by vector tick species, with substantially higher mortality in *A. aureolatum* areas. These results reinforce the need for vector-specific BSF surveillance and regionally tailored public health interventions in São Paulo.

Abstract

Brazilian spotted fever (BSF) is a tick-borne acute febrile disease that can be lethal to humans, caused by the bacterium *Rickettsia rickettsii*. In the State of São Paulo, transmission occurs mainly through two tick species: *Amblyomma sculptum* and *Amblyomma aureolatum*. We analyzed trends in BSF incidence and mortality in relation to the spatial distribution of these vector species in the State of São Paulo from 2007 to 2017 and evaluated clinical outcomes according to hospitalization location. In *A. sculptum* areas, incidence and mortality showed significant increasing trends between 2007 and 2015 (p-value < 0.05). In contrast, *A. aureolatum* areas exhibited a significant decrease in incidence (p-value < 0.05), while mortality remained stable throughout the study period. Lethality was substantially higher in cases associated with *A. aureolatum* than in those linked to *A. sculptum* (67.1% versus 55.0%, p-value = 0.037). Most patients received care in hospitals located near the probable site of infection. Incidence and mortality patterns differed sharply between vector-specific areas, with notably higher mortality in *A. aureolatum*-related cases. These findings highlight the importance of incorporating vector distribution into surveillance, prevention, and clinical management strategies to better address the distinct epidemiological contexts within the State of São Paulo.

Keywords: Brazilian spotted fever; temporal series analysis; spatial distribution; epidemiology; incidence; mortality; information systems

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1. Introduction

Brazilian spotted fever (BSF) is caused by *Rickettsia rickettsii*, a highly virulent Gram-negative, obligate intracellular bacterium. Human infection results from the bite of infected ticks, and the disease often presents as a severe acute febrile illness with potentially fatal outcomes [1]. Since 2014, all suspected or confirmed BSF cases must be reported to the Notifiable Diseases Information System (Sinan) within 24 h [2–4].

BSF is endemic in several regions of Brazil, particularly in the State of São Paulo, where transmission occurs primarily through ticks of the genus *Amblyomma*. Among them, *Amblyomma sculptum* and *Amblyomma aureolatum* are recognized as the most important vectors [1,5,6]. Their ecological differences directly influence the epidemiology and spatial distribution of BSF [1,5,6].

The *A. sculptum* tick is widely distributed across the Cerrado and Atlantic rainforest biomes. Capybaras and horses serve as major hosts, and the seasonal activity of this tick is well characterized [7,8]. Most BSF cases associated with *A. sculptum* occur during the winter, when nymphs exhibit heightened activity and aggressiveness in human parasitism. This period also corresponds to increased bacterial replication within the tick, contributing to enhanced transmission potential [4,9,10]. In endemic areas, capybaras act as key amplifier and maintenance hosts for *R. rickettsii*, supporting the long-term persistence of the pathogen in *A. sculptum* populations [4,9,11]. Efficient horizontal transmission generally requires an infected tick to remain attached to a host for four to six hours [12].

In contrast, *A. aureolatum* is the predominant vector in the São Paulo Metropolitan Region. This species is strongly associated with high-altitude (>700 m) remnants of Atlantic rainforest and relies primarily on domestic dogs as hosts [4,13–15]. Unlike *A. sculptum*, *A. aureolatum* does not exhibit a clear seasonal pattern. Dogs can be parasitized throughout the year, with lower infestation levels between February and May [4,13,16,17]. Although infections in dogs are typically asymptomatic, clinical manifestations may include fever (>39.5 °C), anorexia, neurological signs, gastrointestinal disturbances, and prostration within 5–11 days after tick attachment [4,18].

Clinically, BSF is a severe multisystemic disease with an incubation period of 2–14 days (mean 7 days). Early symptoms are nonspecific—high fever, chills, intense myalgia, headache, and general malaise—often followed by nausea, vomiting, diarrhea, and other gastrointestinal disturbances [4,19,20].

The absence of pathognomonic signs during the initial phase frequently leads to diagnostic confusion with dengue, viral hepatitis, encephalitis, leptospirosis, *Mycoplasma pneumoniae*, salmonellosis, and malaria [4,21]. Because of the rapid progression and high lethality of untreated cases, timely therapy is crucial. Doxycycline is the treatment of choice for all suspected cases and should be initiated within the first three days of symptoms to reduce mortality [4,10]. Fever typically subsides within 24–72 h after treatment initiation, and therapy may be discontinued 2–3 days after defervescence [22]. For severe cases, intravenous doxycycline is preferred; however, it remains unavailable in Brazil. Intravenous chloramphenicol, alone or combined with oral doxycycline, may be used as an alternative, though with reduced efficacy [10].

Understanding the ecological and epidemiological distinctions between vector species is essential for improving BSF surveillance. Classifying cases by vector and identifying spatial patterns can provide public health authorities with more precise information for risk assessment and targeted interventions. In this context, the present study aimed to analyze the incidence and mortality rates in relation to the spatial distribution of hospitalized BSF cases according to the implicated vector species in the State of São Paulo from 2007 to 2017.

2. Materials and Methods

Anonymous records of confirmed BSF cases by Sinan between 2007 and 2017 were provided from the databases of the epidemiological surveillance center of the São Paulo State Health Department.

The State of São Paulo spans an area of 248,219.481 km^2 and comprises 645 municipalities [3] (Figure 1).

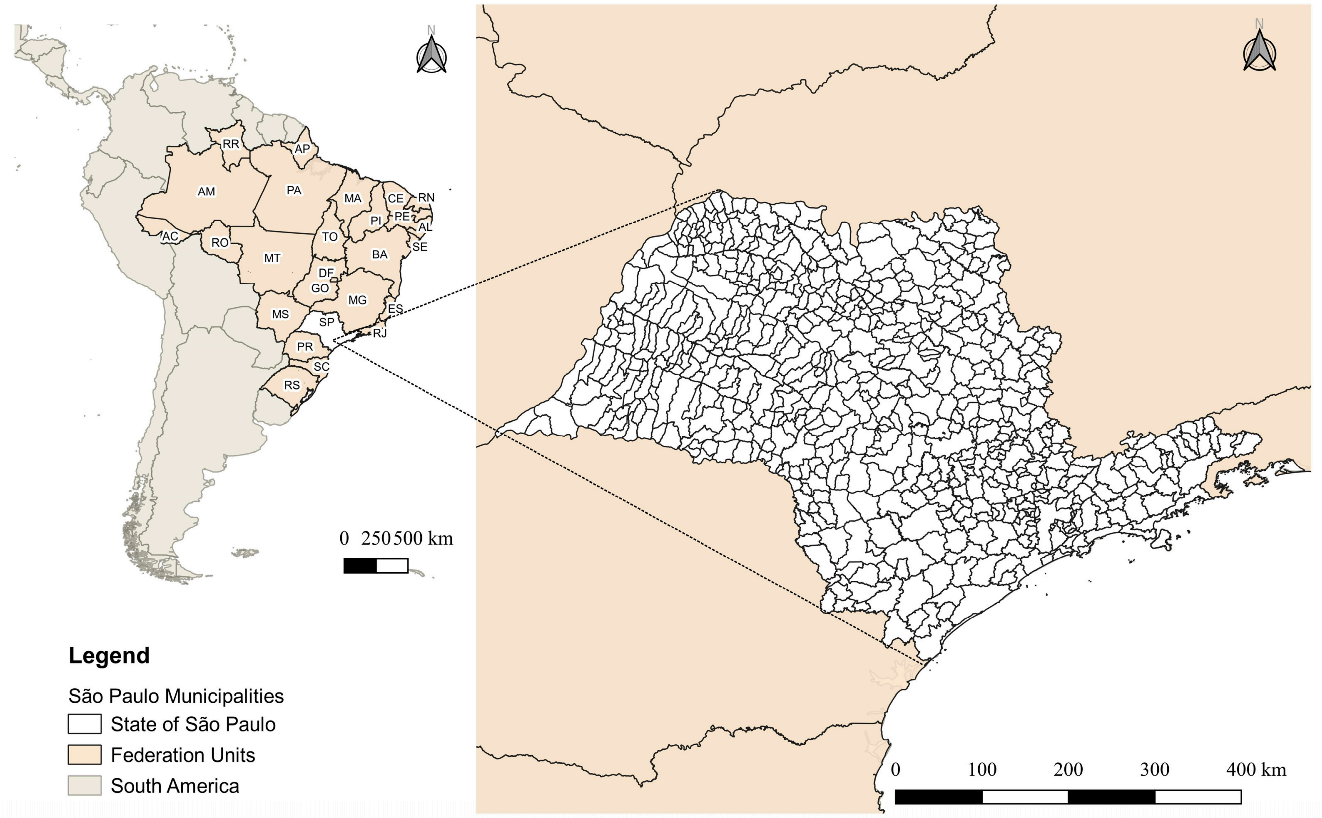

Figure 1. Map of study region. State of São Paulo.

Inclusion criteria were as follows: (1) confirmed cases by clinical, epidemiological or laboratory criteria; (2) São Paulo State residents and with probable site of infection (PSI) located within São Paulo State territory.

Cases involving the tick species *Amblyomma ovale* were excluded from the analysis, as this vector is responsible for transmitting *Rickettsia parkeri* strain Atlantic rainforest, which causes a distinct disease characterized by a milder clinical presentation compared to infections caused by *R. rickettsii*.

Information of the most probable vector-tick species per area was obtained from the Superintendence of Endemic Disease Control, based on long-term ecological records and historical endemicity [10].

Two approaches were used: (a) temporal series study considering all patients; (b) georeferencing of hospitalized cases was performed using the addresses of the hospitals where patients were admitted.

Age-standardized incidence and mortality rates per 100,000 people were calculated through direct method using Segi Standard World Population [23] and data provided by Fundação SEADE [24].

The direct method is a widely used age-standardization technique in Epidemiology for calculating and comparing incidence or mortality rates across populations. Using an international standard population minimizes the influence of differences in age structure between groups, enabling more direct and robust comparisons across periods, regions, and populations—an approach particularly valuable in the analysis of transmissible and zoonotic diseases [25].

For temporal trend analysis, regression models were used considering the tick species observed in the PSI area (*A. sculptum* or *A. aureolatum*) and the outcome of the disease via software Joinpoint Regression Program software [26], version 4.2.0 to assess the Annual Percent Change (APC) with confidence interval of 95% and significant if p-value < 0.05. The APC method enables the identification of periods of increasing or decreasing disease rates, providing a detailed analysis of the temporal dynamics of the condition.

For the spatial distribution analysis, addresses of sites of hospitalization were obtained from National Health Care Facilities Register (CNES), and geographical coordinates were determined via Google Earth Engine. Shapefiles were obtained from the Instituto Brasileiro de Geografia e Estatística [27]. Theme maps were prepared via QGIS software, version 3.16.

3. Results

A total of 736 BSF cases were reported to Sinan in the State of São Paulo from 2007 to 2017. From those, 46 cases (6.3%) have not matched inclusion criteria, and 24 cases (3.3%) were associated with *A. ovale* vector-tick.

Five reported cases held unknown disease outcome: their results were used for determining incidence rate only.

A total of 581 human BSF cases were associated with *A. sculptum* tick as the most probable vector; from those, 467 were men (80.4%). Within the same period, 85 cases were associated with *A. aureolatum* tick, and 48 of them were men (56.5%).

Lethality rate was significantly lower among cases associated with *A. sculptum*, when compared with those associated with *A. aureolatum* cases at 55.0% and 67.1%, respectively (p-value = 0.037) (Table 1).

Table 1. Clinical outcomes of human Brazilian spotted fever cases associated with *Amblyomma sculptum* and *Amblyomma aureolatum* infestations in São Paulo, 2007–2017.

	***Amblyomma sculptum* Tick**	***Amblyomma aureolatum* Tick**
Cure (n)	259	28
Death (n)	317	57
Total number of cases (n)	576	85
Lethality rate (%)	55.03	67.06
Hospitalization (n)	478	82
No hospitalization (n)	98	3

The temporal series analysis of incidence rate indicated an upward trend in areas of tick species *A. sculptum* occurrence between 2007 and 2015 (APC 11.1; 95% CI 5.3 to 17.2, p-value < 0.05) (Figure 2A) and a downward trend in tick species *A. aureolatum* areas within the entire period of study (APC −5.2; 95% CI −9.9 to −0.3, p-value < 0.05) (Figure 2B).

In turn, temporal series analysis of mortality rate showed an upward trend in tick species *A. sculptum* areas between 2007 and 2015 (APC 23.1; 95% CI 15.8 to 30.9; p-value < 0.05) (Figure 2C) and a stability of trend in tick species *A. aureolatum* areas throughout the period analyzed (APC 0.1; 95% CI −6.6 to 7.3) (Figure 2D).

A total of 560 individuals (84.1%) required hospital care, including 82% of *A. sculptum* cases and 96.5% of *A. aureolatum* cases. Among those who were hospitalized, no difference in lethality rate was observed for tick species *A. sculptum* and *A. aureolatum* related cases 62.7% and 67.1%, respectively (p-value = 0.44) (Figure 3).

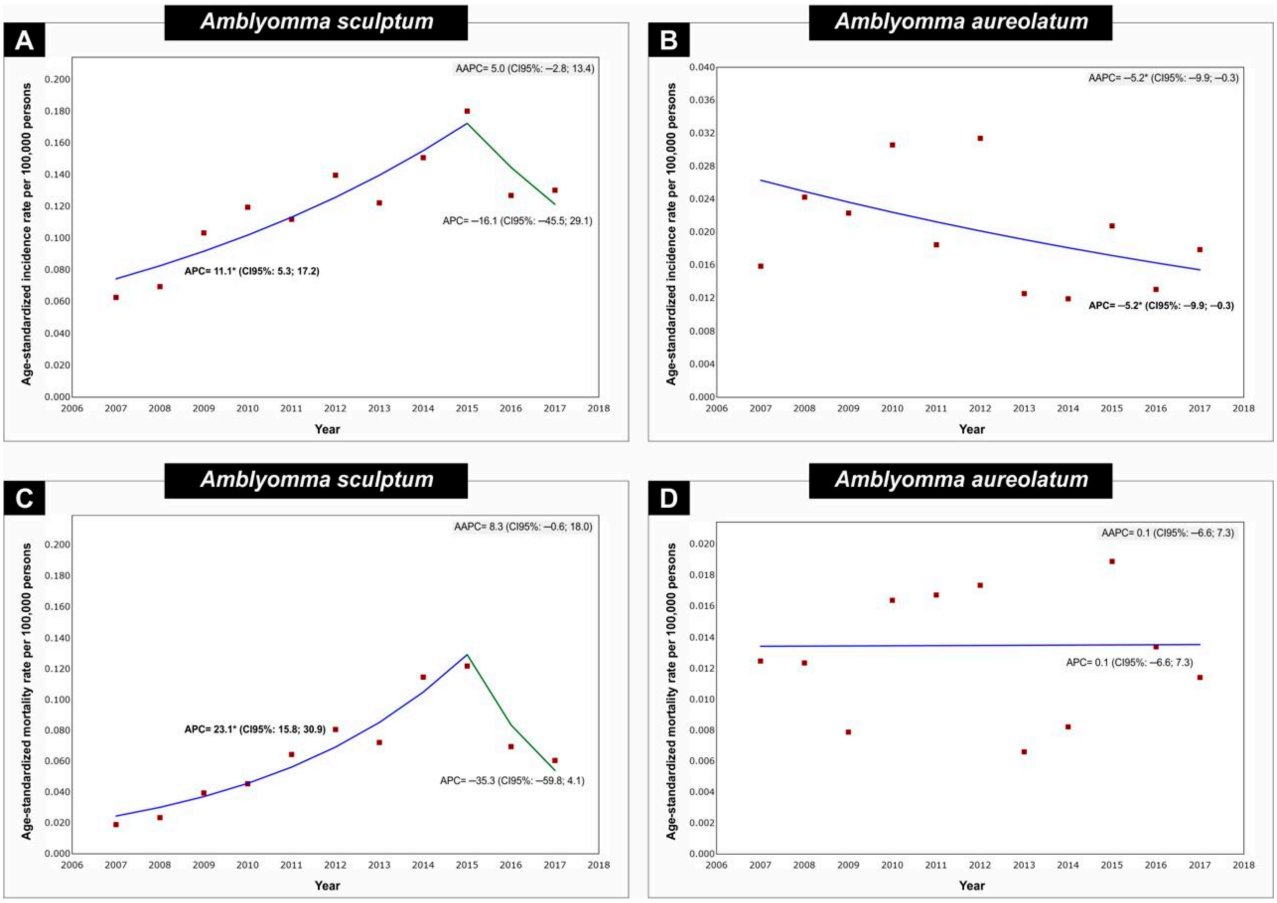

Figure 2. Incidence and mortality trends of Brazilian spotted fever (BSF) associated with *Amblyomma sculptum* (**A**,**C**) and *Amblyomma aureolatum* (**B**,**D**), São Paulo State, Brazil, 2007–2017. Note: APC: Annual Percent Change; AAPC: Average Annual Percent Change; *—Statistically significant.

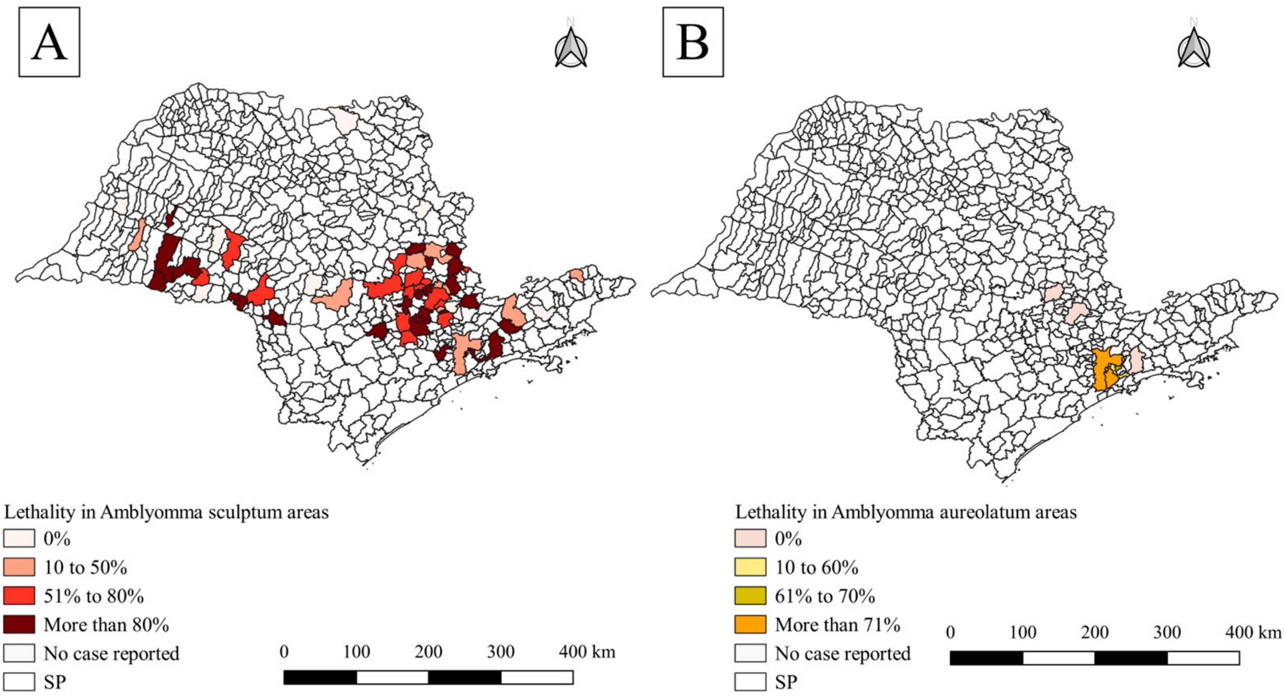

Figure 3. Spatial distribution and lethality of hospitalized cases in areas of occurrence of *Amblyomma sculptum* (**A**) and *Amblyomma aureolatum* (**B**) per municipality. State of São Paulo, 2007 to 2017.

Hospital location were reported for 531 cases (94.5%). 528 cases with known outcome were georeferenced.

The municipalities in which human BSF cases related to tick species *A. sculptum* were hospitalized are listed in Figure 4 (Figure 4A: cases cured, Figure 4B: fatal outcome). During the study period, the majority of hospitalizations occurred in the Campinas region, with Campinas, Piracicaba, and Valinhos exhibiting the highest number of recovered cases and deaths.

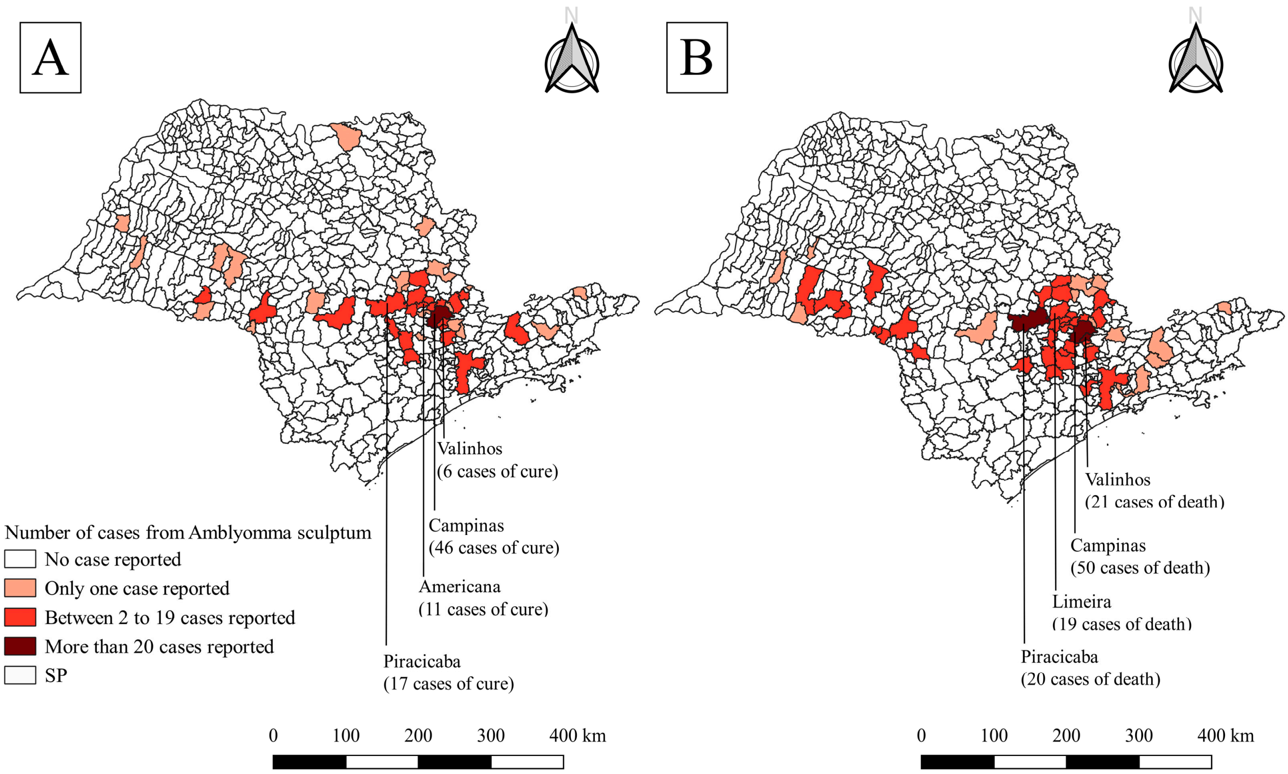

Figure 4. Spatial distribution of human cases of Brazilian Spotted Fever (BSF) linked to *Amblyomma sculptum* by hospital location. (**A**) Cured cases, (**B**) Deaths per municipality. São Paulo, Brazil, 2007–2017.

In most cases reported from those localities, the PSI was associated with parks or forested areas. It is worth pointing out that cities of São Paulo, Mogi das Cruzes, Santo André, Diadema, and Cotia, places with occurrence of tick species *A. aureolatum*, presented 10 cases notified imported from tick species *A. sculptum* areas of occurrence, and seven of them resulted in death. There was no difference in lethality rate among cases treated inside and outside the PSI area, 62.4% and 70.0%, respectively (p-value = 0.62).

The primary hospital locations for human BSF cases related to the tick species *A. aureolatum* are shown in Figure 5. Cities of Santo André, São Paulo, São Bernardo do Campo, and Diadema reported the highest number for both outcomes (Figures 5A and 5B, cure and death, respectively).

In most cases, infection probably occurred inside or nearby their residences. Two patients from the São Paulo Metropolitan Region (tick species *A. aureolatum* area) were hospitalized in the cities of Campinas and Limeira, both areas associated with tick species *A. sculptum* presence, and both were cured. Among the cases related to tick species *A. aureolatum*, the lethality rate observed was 68.0% for those cases hospitalized in the same municipality of the PSI area; there was no comparison among groups since only two hospitalizations were reported outside the PSI area.

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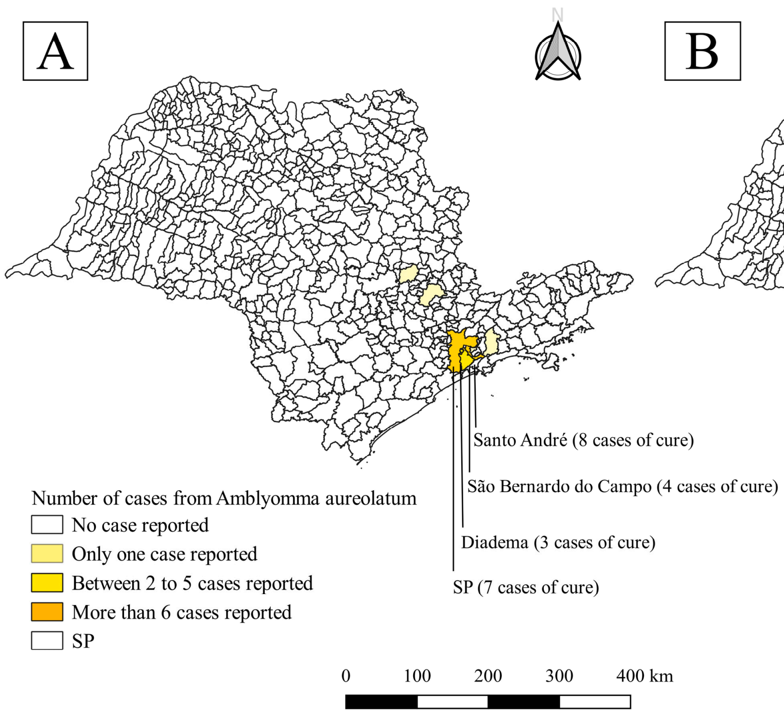

Figure 5. Spatial distribution of human cases of Brazilian Spotted Fever (BSF) linked to *Amblyomma aureolatum* by hospital location. (**A**) Cured cases, (**B**) Deaths per municipality. São Paulo, Brazil, 2007–2017.

4. Discussion

As far as we know, this is the first study on human BSF cases using a stratified approach based on areas the areas of occurrence of tick species *A. sculptum* and *A. aureolatum*, integrating trends in incidence and mortality rate with the spatial distribution of patient hospital care and clinical outcomes. This method revealed distinct epidemiological and ecological patterns between the two vector species.

A stratified analytical approach provides a valuable framework for risk zoning, epidemiological surveillance, and targeted intervention strategies for BSF. By incorporating ecological, temporal and vector-specific differences—such as the constrasting transmission dynamics of *A. sculptum* and *A. aureolatum*, their associated hosts, and environmental niches—this method enables the identification of localized high-risk areas and periods of increased transmission. Such stratification enhances public health decision-making by improving the precision of preventive measures, early diagnosis efforts, and resource allocation. Similar stratified models have been recommended for other vector-borne diseases, given their ability to capture complex spatial–temporal patterns and support evidence-based control measures [28,29].

The identification of vector species in our analysis was based on the historical endemicity of each area rather than direct acarological confirmation, according to official data. This choice is supported by long-term surveillance and ecological studies consistently showing stable vector presence—*A. sculptum* in rural regions with abundant capybaras and *A. aureolatum* in forest-fragmented metropolitan areas near São Paulo [11].

Our results corroborate previous findings by Angerami et al. [30], showing that human infections associated with *A. aureolatum* progress more severely than those linked to *A. sculptum*. Despite an overall downward trend in BSF lethality across the state, mortality associated with *A. aureolatum* did not change over time. Even though incidence decreased, the unchanged mortality trend indicates a proportional increase in lethality in these areas.

The higher mortality risk associated with *A. aureolatum* appears independent of municipality or hospital location. Several hypotheses may explain this pattern. First, infections transmitted by *A. aureolatum* may involve higher bacterial loads, as this species transmits *R. rickettsii* through adult ticks that begin inoculating the pathogen immediately at the onset of blood feeding. Experimental evidence shows that *A. aureolatum* may likely transmit a load proportional to feeding duration [31]. Second, emergency care teams in metropolitan areas may have lower clinical suspicion of BSF, delaying diagnosis and early treatment—an established factor associated with fatal outcomes. Studies from São Paulo demonstrate that prolonged time from symptom onset to doxycycline initiation is the strongest predictor of death [10]. International guidelines, including the Centers for Disease Control and Prevention, emphasize that treatment must begin within the first 72 h, even without laboratory confirmation [32,33].

Differences in incidence between areas dominated by each vector species cannot be explained solely by human behavioral factors. Environmental conditions, host availability, vector biology, and the size of the exposed population play crucial roles. In *A. sculptum* areas, the expansion of sugarcane cultivation since 2007 has increased food availability for capybaras. This has likely boosted capybara survival and reproduction, consequently increasing populations of infected *A. sculptum* ticks [34–36], and may explain the rise in incidence of BSF cases. Conversely, the decline in incidence after 2015 may reflect severe environmental disturbances, including the water shortage in 2014–2015, which affected southeastern Brazil [37,38]. Reduced water volumes may have disrupted the life cycle of *A. sculptum* and lowered capybara birth rates, decreasing the number of infected immature ticks—key drivers of *R. rickettsii* amplification [9,12,39,40].

The ecology of BSF transmission varies sharply between rural and peri-urban settings. In rural areas, capybaras act as amplifying hosts for *A. sculptum*, increasing tick abundance and sustaining pathogen circulation [9,11]. In contrast, in Atlantic Forest remnants, dogs are the primary hosts of *A. aureolatum*, transporting infected ticks from forested environments to households, especially in metropolitan regions [17]. These ecological differences determine distinct human exposure patterns: *A. sculptum* transmission follows a marked seasonal pattern associated with nymphs in winter, whereas *A. aureolatum* transmission can occur year-round due to dog movement between forest fragments and residential areas.

Although human occupation has increasingly altered the biophysical environment in *A. aureolatum* regions, particularly in the São Paulo Metropolitan Region [14,41], BSF incidence linked to this vector has declined. This reduction may reflect effective public campaigns promoting tick-control collars and restricting dog access to forest areas, which reduce human exposure to infected tick.

Important knowledge gaps remain. The absence of systematic data on capybaras and dogs populations limits the ability to model transmission risk accurately. Few studies integrate land-use change, forest fragmentation, microclimate, and vector dynamics, despite their relevance for understanding spatial heterogeneity in disease occurrence, which limited a more ample environmental and sociodemographic analysis. Additionally, although *R. rickettsii* genotyping has been performed in Brazil [8,42], systematic integration of molecular data with clinical and epidemiological findings is still lacking and could identify potential differences in strain virulence.

Structural limitations in the national surveillance system also affect interpretation of BSF patterns. Although Sinan is the primary database for BSF notifications, it suffers from delays, underreporting, incomplete fields, and variability in diagnostic capacity across municipalities [3]. These issues may introduce information bias in temporal and spatial analyses, as well as mortality analysis, and must be considered when interpreting findings.

The number of human BSF cases linked to *A. aureolatum* who sought care outside their municipality of residence was low, restricting some comparative analyses. Moreover, because this study analyzed hospitalized patients, results may not represent the full spectrum of disease severity.

Our findings highlight the need for public health strategies tailored to local ecological scenarios, particularly those defined by vector-tick species. Continuous acarological surveillance remains essential. Strategies should include communication campaigns for visitors and residents in forested areas, mechanisms to deter capybara access in *A. sculptum* areas, and reinforcement of responsible pet ownership—including permanent use of leashes and anti-tick collars—in *A. aureolatum* areas. Broader discussions on sustainable land use and occupation are also needed to prevent environmental degradation. Finally, permanent education programs to improve early reporting, investigation, diagnosis, and treatment of BSF are strongly recommended across the State of São Paulo.

This regionalized approach revealed several epidemiological and ecological patterns that were not detectable when BSF was analyzed as a single grouped disease, underscoring the importance of vector-specific stratification in understanding and controlling BSF transmission.

5. Conclusions

Our stratified analysis revealed distinct epidemiological patterns between *A. sculptum* and *A. aureolatum* transmission areas, underscoring the need for regionalized education programs for health professionals and population. Incidence and mortality rates were markedly different depending on the vector-tick involved and higher lethality associated with *A. aureolatum*. These findings show that effective BSF control requires region-specific, vector-focused strategies.

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Institutional Review Board Statement: The study was conducted and approved in accordance with the Ethics and Research Committee, of Faculdade de Saúde Pública da Universidade de São Paulo (opinion number 2,961,082 approved on 15 October 2018) followed by the consent from Secretaria de Estado da Saúde de São Paulo.

Informed Consent Statement: Not applicable.

Data Availability Statement: The datasets presented in this article are not readily available due to institutional restrictions and Brazilian data protection and confidentiality regulations. Requests to access the datasets should be directed to Secretaria de Estado da Saúde de São Paulo.

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Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

BSF	Brazilian Spotted Fever
PSI	Probable site of infection
AAPC	Average Annual Percent Change
APC	Annual Percent Change

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