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Low socioeconomic condition and the risk of dengue fever: A direct relationship

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ABSTRACT

This study aimed to characterize the first dengue fever epidemic in Várzea Paulista, São Paulo, Brazil, and its spatial and spatio-temporal distribution in order to assess the association of socioeconomic factors with dengue occurrence. We used autochthonous dengue cases confirmed in a 2007 epidemic, the first reported in the city, available in the Information System on Diseases of Compulsory Declaration database. These cases where geocoded by address. We identified spatial and spatio-temporal clusters of high- and low-risk dengue areas using scan statistics. To access the risk of dengue occurrence and to evaluate its relationship with socioeconomic level we used a population-based case-control design. Firstly, we fitted a generalized additive model (GAM) to dengue cases and controls without considering the non-spatial covariates to estimate the odds ratios of the occurrence of the disease. The controls were drawn considering the spatial distribution of the household of the study area and represented the source population of the dengue cases. After that, we assessed the relationship between socioeconomic variables and dengue using the GAM and obtained the effect of these covariates in the occurrence of dengue adjusted by the spatial localization of the cases and controls. Cluster analysis and GAM indicated that northeastern area of Várzea Paulista was the most affected area during the epidemic. The study showed a positive relationship between low socioeconomic condition and increased risk of dengue. We studied the first dengue epidemic in a highly susceptible population at the beginning of the outbreak and therefore it may have allowed to identify an association between low socioeconomic conditions and increased risk of dengue. These results may be useful to predict the occurrence and to identify priority areas to develop control measures for dengue, and also for Zika and Chikungunya; diseases that recently reached Latin America, especially Brazil.

1. Introduction

Dengue fever is the most important human arbovirus disease. It is especially concerning in tropical and subtropical regions, which require a complex management due to factors such as dynamic infections, morbidity, and mortality (Quintero et al., 2009; Resendes et al., 2010; WHO, 2012; Bhatt et al., 2013). Dengue fever incidence has increased globally in recent decades, especially in tropical countries where temperatures and humidity favor mosquito proliferation (Chaves et al., 2012, 2014; Wilke et al., 2017). According to the World Health Organization (WHO, 2012), over 40% of the world's population is at risk of dengue virus infection. Dengue fever is endemic in 115 countries, mainly in Southeast Asia and Latin America, and it is estimated that 390 million dengue infections occur annually worldwide, resulting in about 24,000 deaths (Bhatt et al., 2013). In 2014, the Brazilian Ministry of Health (MS, 2015) reported 600,000 cases resulting in 400 deaths. 35% of these deaths occurred in the state of São Paulo.

Some dengue determinants have been identified by many studies, including urbanization (Guha-Sapir and Schimmer, 2005; Wu et al., 2009), land use change (Nakhapakorn and Tripathi, 2005; Patz et al., 2008), population growth (Teixeira et al., 2002; Schmidt et al., 2011), massive migration to peri-urban areas with poor infrastructure (Thammapalo et al., 2008; Wilder-Smith and Gubler, 2008), environmental (Chowell et al., 2008; Patz et al., 2008; Thammapalo et al., 2008; Lowe et al., 2011; Restrepo et al., 2014; Delmelle et al., 2013, 2016), behavioral (Schmidt et al., 2011; WHO, 2013) and social factors

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(Braga et al., 2010; Hagenlocher et al., 2013; Delmelle et al., 2016). Nevertheless, the global increase in dengue fever incidence is not yet fully understood (Costa et al., 2013). The major dengue vector, *Aedes aegypti*, is also involved in the recent Zika and Chikungunya outbreaks in Latin America, mainly Brazil (Nunes et al., 2015; Faria et al., 2016). Moreover, Zika has been associated with the occurrence of microcephaly in newborns (Brasil et al., 2016). Dengue epidemiological situation and the recent Zika and Chikungunya outbreaks call for a better understanding of the disease dynamics in order to support controlling actions.

It is noteworthy the increasing use of Geographical Information Systems and spatial analysis in studies focused on *Ae. aegypti* and diseases related to it. Highlights investigation of the relationship between the occurrence of the diseases and the mosquito infestation levels (Carbajo et al., 2006; Barbosa et al., 2014; Moreno-Madriñán et al., 2014; Chiaravalloti-Neto et al., 2015; Vargas et al., 2015), aiming to identify socioeconomic, demographic and environmental risk factors that modulate its dynamics (Nakhapakron and Tripathi, 2005; Carbajo et al., 2006; Mondini and Chiaravalloti-Neto, 2008; Siqueira-Junior et al., 2008; Wu et al., 2009; Hu et al., 2012; Delmelle et al., 2013, 2016; Hagenlocher et al., 2013; Restrepo et al., 2014; Vargas et al., 2015; Teurlai et al., 2015) and disease clustering (Mammen et al., 2008; Wu et al., 2009; Yoon et al., 2012; Delmelle et al., 2013, 2016; Hagenlocher et al., 2013; Jeefoo et al., 2010). Eisen and Lozano-Fuentes (2009) also proposed that such techniques and tools could be used in controlling *Ae. aegypti* and diseases related to it.

Regression models is commonly used to identify determinants of dengue and other diseases related to *Ae. aegypti*. However, conventional models have the assumption of independence among cases per spatial unit. Nonetheless, dengue occurrence may be partly militated by its geographical location due to the heterogeneous spatial distribution of risk factors. In fact, it is possible to explain the spatial dependency through the addition of key risk factors in the model, avoiding, hence, violation of that assumption. However, most datasets do not allow such approach. A possible alternative is the use of regressions that explicitly consider the spatial structure of the dataset and also approaches that include geographically weighted regression (Lin and Wen, 2011). One good option is the use of generalized additive models (GAM) with a nonlinear spatial component (related to the geographical coordinates of the points) and linear components (the non-spatial covariates) (Bailey et al., 2007).

The present study aimed to characterize the first dengue fever epidemic in Várzea Paulista, São Paulo, Brazil, and its spatial and spatio-temporal distribution, assessing the association of local socioeconomic factors with dengue incidence. To reach these objectives, we used geographic information systems and spatial analyses techniques, shown in other studies to be appropriate tools to carry out studies on spatial understanding of dengue fever outbreaks (Bohra and Andrianasolo, 2001; Ali et al., 2003; Siqueira et al., 2004; Van Benthem et al., 2005; Lian et al., 2006; Vanwambeke et al., 2006; Mondini and Chiaravalloti-Neto, 2008; Honório et al., 2009; Hu et al., 2012; Teurlai et al., 2015).

2. Material and methods

2.1. Study design, population, and area

We conducted descriptive and ecological study in Várzea Paulista, São Paulo, Brazil (23°13′S and 45°49′W), distant 65 km from the state capital (São Paulo) (Fig. 1). The city has 34,807 km^2 and its estimated population is 107,089 inhabitants (IBGE, 2012). Local economy is mainly underpinned on trade and industries. The city's Human Development Index is 0.759. The mean annual temperature and annual precipitation is 20.3 °C and 1348 mm, respectively. To obtain population and also socioeconomic data of Várzea Paulista, we used 2010 census from the Brazilian Institute of Geography and Statistics (IBGE, 2012).

Ae. aegypti infestation was present in 2003, however, the first dengue epidemic only happened in 2007, when the first autochthonous cases were confirmed, likely caused by dengue virus serotype DENV-3. This serotype was first seen in Brazil in 2001 (Nogueira et al., 2005), associated to a 2007 epidemic that occurred in Campinas, a municipality near Varzea Paulista with more than one million inhabitants. Therefore, subsequent epidemics may be associated to any of the four DENV serotypes (probably with more than one serotype in each epidemic wave), since their circulation were identified in neighboring municipalities of Varzea Paulista (Fig. 2) (SES, 2011, 2013).

2.2. Data source

The São Paulo surveillance system gathers information about the suspected dengue cases in primary, secondary and tertiary health units, in both public and private services. This system uses serological, PCR tests, and clinical-epidemiological criterion to confirm the suspected dengue cases. All information is inserted in the Information System on Disease of Compulsory Declaration (SINAN). We used those secondary data available in SINAN database and 2010 population census from the Brazilian Institute of Geography and Statistics (IBGE, 2012) as a source of socioeconomic and demographic data, as cited before. We also used the list of the addresses of all visited premises during the Brazilian 2010 population census that was made available by IBGE (2011).

2.3. Data analysis

The SINAN confirmed 345 autochthonous dengue cases in Varzea Paulista in 2007. The first confirmed autochthonous case of 2007 epidemic showed symptom onset on 3rd of March, the last confirmed case was on 2nd of July. These cases were confirmed using serological test (294 cases, 85.2%) and clinical-epidemiological criterion (51 cases, 14.8%).

All 345 cases were geocodified using one of the three following methods: street map and TerraView software (version 4.2.2) in 69.3% (239) of the cases; retrieved coordinates from Google Earth in 15.9% (55) of the cases; and on-site acquisition in 14.8% (51) of the cases.

The 345 confirmed autochthonous dengue cases in 2007 were grouped in 165 of the 177 census tracts of Várzea Paulista (IBGE, 2012) using ArcGIS 10.1 tools, which allowed us to obtain the number of dengue cases per census tracts. The remaining 12 census tracts were excluded because they did not contain any population and correspond to a forest area. However, these tracts did not impact the spatial analysis strategies, once they were localized together in the southern part of the municipality (Fig. 3A).

We used the Kulldorf's scan statistic adjusting for age and sex to identify spatial and spatio-temporal clusters (Kulldorff et al., 2005; Kulldorff, 2015). We used a Poisson's discrete model and considered dengue cases on the centroids of the census tracts, circular (for spatial analysis) and cilindric (for spatio-temporal analysis) windows. We also considered the population exposed to the risk of getting dengue in each census tract, thus taking in account population density. The maximum cluster size was 50% of the exposed population and time window of spatio-temporal clusters was set between 3rd March and 2^{sd} July, respectively the symptom onset dates of the first and the last autochthone cases that occurred in 2007; precision of 1-day. The significance level was 0.05, which was assessed based on 999 Monte Carlo simulations.

To estimate dengue fever risk we used a population-based case-control design (Szklo and Nieto, 2014) and fitted a semiparametric GAM (Hastie and Tibshirani, 1990; Bailey et al., 2007) considering the point coordinates correspondent to the 345 autochthone confirmed cases during the 2007 dengue epidemic and 1380 controls as the outcome (four controls for one case). These models use the binomial distribution, with the logit as the link function and are adjusted to the points using a nonparametric bidimensional kernel. It is possible to incorporate in these models parametric components representing non

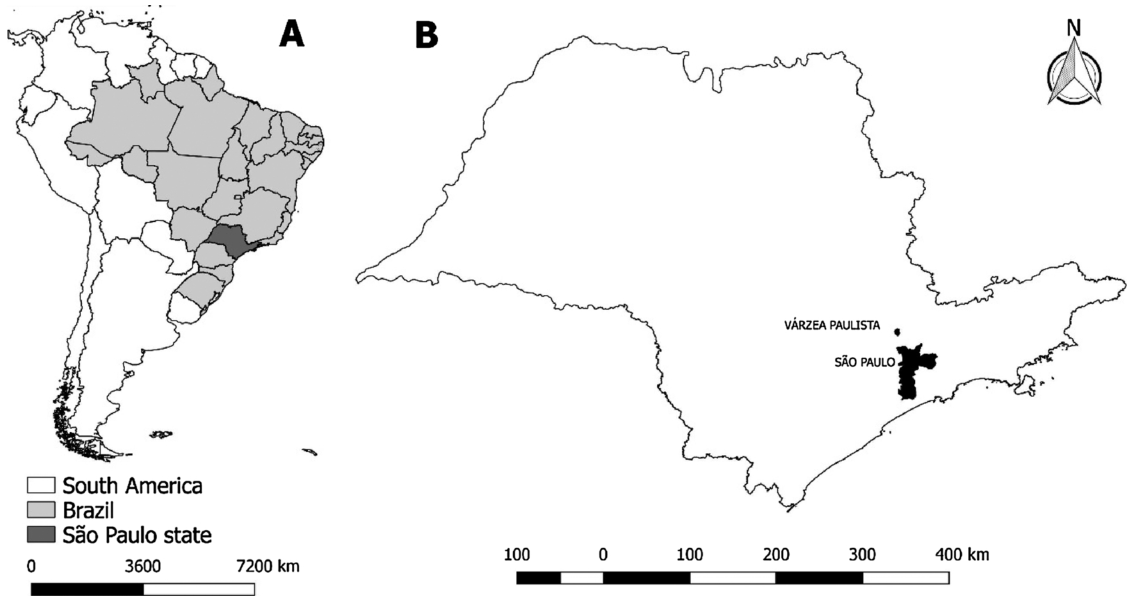

Fig. 1. São Paulo state, Brazil and South America (A); Municipality of Várzea Paulista and the São Paulo state capital (also named São Paulo), São Paulo state, Brazil (B).

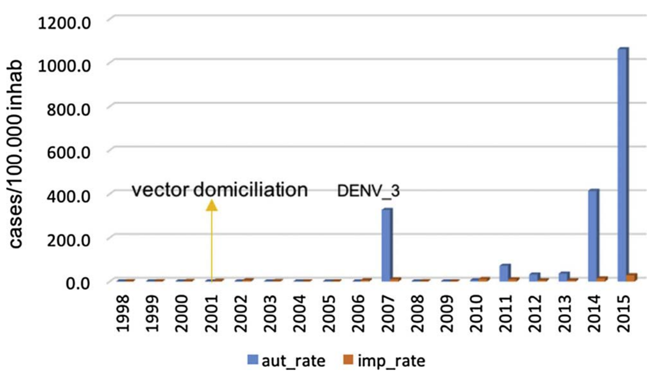

Fig. 2. Historical series of autochthonous (aut_rate) and imported (imp_rate) dengue cases per 100,000 inhabitants for the period 1998–2015, Municipality of Várzea Paulista, São Paulo, Brazil.

spatial covariates (Bailey et al., 2007).

We take into account that the spatial distribution of the source population of the dengue cases could be represented by the spatial distribution of the households of the study area to obtain the controls. Then, we took the controls through a simple random sample of 1380 households that was drawn from the IBGE address list considering our study area (the 165 census tracts of Varzea Paulista). We use the *AmostraBrasil* package (Cordeiro et al., 2016; Stephan and Cordeiro, 2016) of the R program (R Core Team, 2015) to obtain the household sample. This package makes automatic searches to the IBGE household address list and Google Earth databases and provide, limited to the study area, both the addresses of the sampled households and the respective geographic coordinates (Cordeiro et al., 2016).

Firstly, we adjusted the GAM model using only the point coordinates of cases and controls, without considering non-spatial covariates. The model's bandwidth was set at 500 m because it is the average of the minimum (100 m) and the maximum (900 m) cluster sizes found in studies that investigated dengue clustering behavior (Vazquez-Prokopec et al., 2010; Yoon et al., 2012). This analysis was performed in R version 3.0.2 using *epigam* package (R Core Team, 2015; Stephan et al., 2016).

Despite other studies have suggested different variables, we selected the following population health macrosocial determinants (the non-spatial covariates), as defined by the Pan-American Health Organization (PAHO) (PAHO, 1991), to test their association with dengue fever incidence: (1) percentage of household heads with an income between 2 and 3 monthly minimum wages; (2) percentage of female-head households; (3) mean income per member of household; (4) mean household income; (5) percentage of household heads with no income; (6) percentage of household heads with income equal to or less than 1 monthly minimum wage; (7) percentage of household heads with income equal to or greater than 20 monthly minimum wages; (8) percentage of families with household income equal to or less than 0.5 monthly minimum wage; (9) percentage of families with household income between 0.5 and 1 monthly minimum wage; (10) percentage of families with household income between 1 and 2 monthly minimum wages; (11) mean number of members per household; (12) percentage of households with 6 or more members; (13) percentage of households with 1 bathroom; (14) percentage of household members with 7 or more years of education; and (15) percentage of literate household heads. For each one of the 165 census tracts considered in this study, the values of these variables were obtained.

We used the principal component analysis (PCA) to reduce the complexity related to the 15 variables described above. PCA is a statistical technique for dimensionality reduction that produces principal components (PC) not correlated with other. These components, which are linear combinations of the original variables, retain all or part of the information of the original variables, depending on the number of components that are taken into account (Quinn and Keough, 2002).

After standardizing the 15 original variables, we use the *psych* package (Revelle, 2016) of R program (R Core Team, 2015) to obtain the PC and their respective eigenvalues, which were plotted against the PC. The number of retained PC were chosen using the Cattell Scree test (Kabacoff, 2015). Thereafter, we adopted the varimax procedure for the rotation of the chosen PC, obtained the scores that allowed us the calculation of the PC values for each one of the census tracts and categorized these PC values using quartiles (Kabacoff, 2015).

We assigned the categories of the PC of the census tract to the cases and controls based on their localization within the census tracts. Then, we adjusted the GAM using the point coordinates of cases and controls and the covariates representing the PC and obtained the effect of these components in the occurrence of dengue adjusted by the spatial localization of the cases and controls.

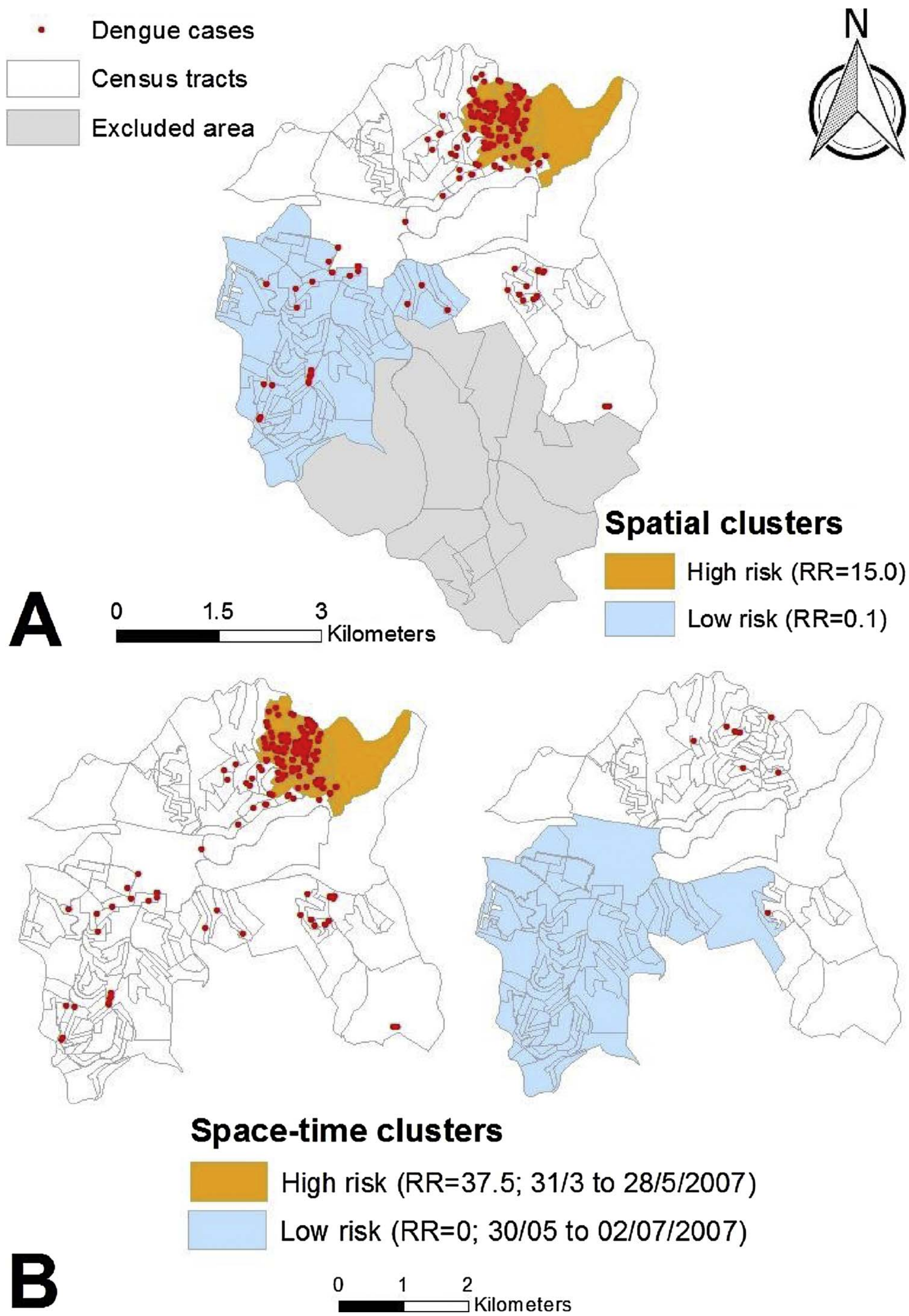

Fig. 3. Spatial (A) and spatio-temporal (B) clusters of dengue cases obtained using scan statistics and the respective relative risks (RR). Várzea Paulista, São Paulo, Brazil, 2007. The scale of markings that represent the dengue cases warrants that no individual could be identified.

2.4. *Ethical aspects*

This research study was submitted to and approved by the University of São Paulo School of Public Health Research Ethics Committee in accordance with Resolution CNS 196/96 (protocol number CAAE 08400212.5.0000.5421; November 23, 2012).

3. Results

345 cases were autochthonous with an incidence rate of 322.2 cases per 1000 person-years, out of the 392 confirmed dengue fever cases in 2007 in Varzea Paulista. Both first autochthonous case and first imported case were reported on the 13th epidemiological week (in the last week of March). April was the month with the highest number of cases (221) followed by May (117). Then the number of cases decreased until the 28th epidemiological week in July, when no more autochthonous cases were reported.

We identified a high-risk cluster (RR = 15.0), consisting of 25 census tracts, in the northeastern area and a low-risk cluster (RR = 0.1), consisting of 86 census tracts. We also identified a high-risk spatio-temporal cluster (RR = 37.5), consisting of 27 census tracts, in the northeastern area (Fig. 3A) between March 31st and May 20th; and a low-risk cluster (RR = 0.0) between May 30th and July 2^{sd} (Fig. 3B).

Fig. 4 shows representative images of environmental characteristics of high-risk spatial clusters and Fig. 5 shows representative images of low-risk spatial cluster. The first area is composed by houses with one or two floors (in general, with backyards) and apartments built in regularized areas with former license from the local government. The

Fig. 4. Representative images of a high-risk spatial cluster. Northeast area of Várzea Paulista, São Paulo, Brazil, 2014.

second area is named by IBGE (IBGE, 2012) as subnormal area and it is composed by self-constructed one floor houses built, in general, in invaded areas and without formal license (squatter settlements).

Fig. 6A shows the isoclines with the values of odd ratios (OR) and Fig. 6B displays areas were OR presented statistically significant values for dengue fever estimated by the GAM linked with coordinates of cases and controls. These results indicate that the northeastern area of Varzea Paulista has greatest risk of dengue occurrence, confirming the results of the spatial and spatio-temporal analysis.

The PC and their respective eigenvalues are presented in Fig. 7. We retained the two first PC using the Cattell Scree test with proportions of explained variance, after rotation, of 45.0% for the first component (PC#1) and 19.0% for the second (PC#2). Table 1 presents the correlation coefficients between the PC#1 and PC#2 and the original variables and the respective scores.

The PC#1 presented important negative correlation with variables representing better income and schooling conditions and positive with variables representing worse income and household conditions. The PC#1 values calculated for the census tracts were between a minimum of -2.25 and a maximum of 3.02, so that higher theirs values, lower the income and schooling and worse the household conditions. We named this component as socioeconomic index.

The PC#2 presented important negative correlation with the percentage of household heads with an income between 2 and 3 monthly minimum wages and positive with the percentage of household heads with no income and the percentage of female-head households. This component presented little or no correlation with schooling and household conditions. The PC#2 values calculated for the census tracts were between a minimum of -1.66 and a maximum of 3.32, so that higher theirs values, higher the proportions of household heads without income and female-head households, but without an important relationship with schooling and household conditions. We named this component as household head income index.

The values of the two PC were categorized by quartiles in four levels: A representing the census tracts with the best socioeconomic (PC#1) and household head income indices (PC#2); B and C with intermediate socioeconomic and household head income indices; and D, with the worst socioeconomic and household head income indices (Fig. 8).

Table 2 shows the GAM with the relationships between occurrence of dengue and the two PC adjusted for the spatial distribution of cases and controls. The B, C and D levels of the socioeconomic index (PC#1) significantly increased the dengue occurrence risk, mainly the D level with OR = 5.80 (CI 95%: 3.87–8.68). The C and D levels of the household head income index (PC#2) also increased the dengue risk, but with OR below the values obtained for B, C and D PC#1 levels.

Fig. 5. Representative images of a low-risk spatial cluster. Southwestern area of Várzea Paulista, São Paulo, Brazil, 2014.

Fig. 8A shows that almost all dengue cases occurred in census tracts classified in the C and D levels of the socioeconomic index. This map also agrees with the results obtained with the scan statistics and the GAM using only the cases and controls coordinates, showing the northeastern region of Varzea Paulista as the highest risk for dengue occurrence. From the 25 census tracts that constitute the spatial cluster of high risk (Fig. 3A), two (8.0%) were census tracts classified as C level and 23 (92,0%) as D level of PC#1. On the other hand, from the 86 census tracts that constitute the low risk spatial cluster, 66 (76.7%) were classified as A and B PC#1 levels. We can see in Fig. 8B that there is a relationship between the dengue occurrence and the PC#2, but not as strong as the relationship with PC#1. This is accord with the OR lower values obtained with the GAM for the PC#2 when compared with the PC#1.

4. Discussion

Cluster analysis and GAM agreed in the characterization of the northeastern area of Várzea Paulista as the most affected area during the first dengue fever epidemic in 2007 when the autochthonous cases were formally confirmed. The GAM also showed that household head income and, mainly, socioeconomic conditions were associated with dengue occurrence.

We named the PC1 as socioeconomic index, so that higher theirs values, lower the income and schooling and worse the household conditions (negative correlation). The high values of the socioeconomic index of the census tracts of the northeastern area (almost all census tracts of the high risk spatial cluster classified in the worst level of this index) are representative of the socioeconomic standards of the residents of this area. This index can be seen as a proxy of living conditions, purchase ability, access to health services, among others. Hence, its high values in the northeastern area suggest poor living conditions. Besides their related conditions, they also indicate area of informal urban settlement with substandard housing and poor sanitation, which favors mosquitos' proliferation. Therefore, the GAM was able to identify an association between unfavorable socioeconomic conditions and an increased risk of dengue fever.

The relationship between dengue occurrence and household head income index was not so strong as with the socioeconomic index, but was also identified. The main characteristic of this index is the representation of household head without income. It did not present or presented little correlation with years of education, literate household heads, household income, number of household members and number of bathrooms. This weaker relationship highlights the role of factors as schooling and house conditions, beyond the household head income, in the occurrence of this disease and shows the suitability of the

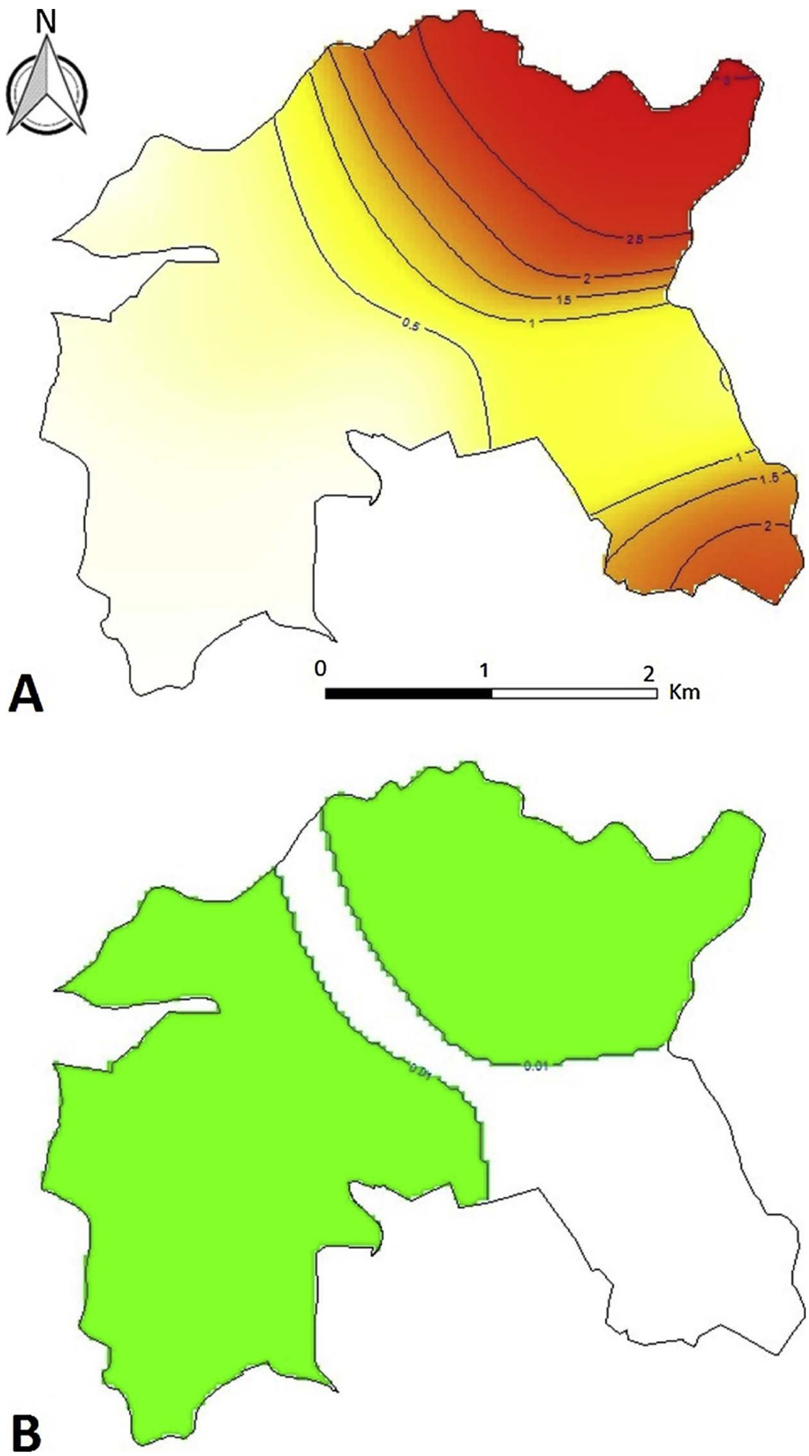

Fig. 6. Odds ratios (OR) for dengue fever estimated using a generalized additive model and considering only the geographic coordinates of cases and controls (A) and significance map of OR (B) (The p = 0.05 line is not shown because it was localized very close to the p = 0.01 line). Várzea Paulista, São Paulo, Brazil, 2007.

socioeconomic index to characterize the dengue risk.

An association between dengue fever incidence and unfavorable socioeconomic conditions have been verified in previous studies (da Costa and Natal, 1998; ; Mondini et al., 2009; Braga et al., 2010; Drumond et al., 2012, 2013; Costa et al., 2013; Delmelle et al., 2013, 2016; Hagenlocher et al., 2013; SES, 2013; Qi et al., 2015; Teurlai et al., 2015), yet other authors reported contrasting findings (Hu et al., 2012; Feldstein et al., 2015; Vikram et al., 2015; Gil et al., 2016). Some studies attribute the lack of correlation between cases and socioeconomic variables in that scenario due to the small size of the city, the widespread distribution of poverty and the high mobility of the inhabitants within the city (Gil et al., 2016). In contrast, those factors were not observed in our study area. In addition to these socioeconomic factors, dengue dynamics is also influenced by multiple factors as immunity, and entomologic, environmental, and behavioral factors (i.e., KAP – knowledge, attitude and practice (Guha-Sapir and Schimmer, 2005)), among others (Chiaravalloti-Neto et al., 2015; Teurlai et al., 2015) that interact in a complex way. Therefore, different studies may reach inconsistent conclusions when not evaluating similar factors. The contrasting findings in the literature about the association between socioeconomic conditions and dengue fever may be explained by the time of evaluation: socioeconomic variables could be mainly related with dengue incidence in a certain region at the time of the introduction or re-emergence of DENV serotype. Following the one ward of new

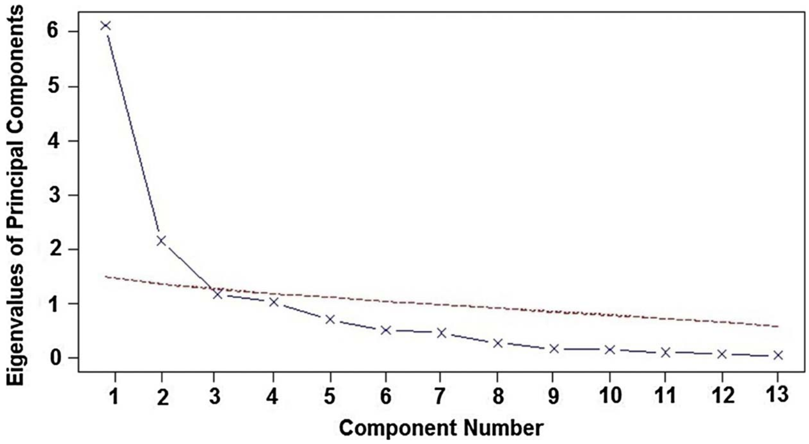

Fig. 7. Scree plot showing the number of the principal component and the respective eigenvalues.

epidemics caused by the same serotype, other areas within the same region with favorable socioeconomic conditions may also be affected, smothering the association between socioeconomic conditions and dengue fever (Mondini and Chiaravalloti Neto, 2007; Mondini et al., 2009).

We studied the first dengue fever epidemic in a highly susceptible population at the beginning of the outbreak, which may have allowed to identify an association between low socioeconomic conditions and increased risk of dengue fever. In such scenario, there were no confounding factors that could hidden this association, especially because it is most likely that the majority of human population was naïve to DENV infection. Studies carried out in another city in the state of São Paulo also showed a positive strong relationship between dengue cases and socioeconomic factors, which was related to the fact that the dengue epidemic was the first one caused by the DENV-1 (da Costa and Natal, 1998;) serotype in that city in a highly susceptible population. This is a common scenario in Brazil, where dengue epidemics have occurred after the introduction or re-emergence of specific virus serotypes (Teixeira et al., 2013).

The results achieved in this study could be useful to predict the occurrence and to identify priority areas to develop control measures for dengue. It may be also useful for Zika and Chikungunya control; diseases that recently reached Latin America, especially Brazil (Nunes et al., 2015; Brasil et al., 2016; Faria et al., 2016). Notwithstanding, it is important to discuss whether studies designed to identifying dengue risk areas and the ways dengue virus serotypes spread, in space and time, could produce important information to predict the occurrence of other arboviruses. The idea of using the results obtained here also to predict areas of Zika and Chikungunya occurrence is support for two main reasons: *Ae. aegypti* being one of the main vectors of these diseases and the fact that Zika and Chikungunya produce permanent immunity and, thus, their spatial distribution not be confounded for the presence of more than one viral serotype, as in the case of dengue. Once this information is correct, the results of this study could be a useful tool to support decision-making on control measure allocation for all these diseases: dengue, Zika and Chikungunya.

Let us discuss the plausibility of this hypothesis using the recent outbreak of Zika that reached São Paulo state as a case study. Two of the first three autochthones Zika cases that were confirmed by laboratory exams and, most likely transmitted by mosquitoes, occurred in Ribeirão Preto municipality (beginning symptoms on May 2015). 9 out of the 13 of autochthonous Zika cases confirmed by laboratory exams during 2015 were of the same city. Accordantly to Zika outbreak municipality list, between January and June 2016, the 12 highest incidence rates included Ribeirão Preto and municipalities of this region or neighbor regions (Barretos, Franca and Araraquara) (SES, 2016). The first dengue outbreak in São Paulo state began in 1990 (there was a previous occurrence in 1986 with the confirmation of only 46 cases in two municipalities (Pontes and Ruffino-Netto, 1994) was located in Ribeirão Preto (Pontes et al., 1991). Thereafter, this outbreak spread to the municipalities in neighbor regions; a similar behavior of Zika outbreak (SES, 1991; Pontes and Ruffino-Netto, 1994). These similarities in the dispersion pattern of both diseases, besides the same vector and these viruses belong to the same family (Flaviviridae) show the plausibility of the hypothesis raised: to use the results obtained here also to predict high-risk areas for Zika. Therefore, the results of the present study may contribute for both dengue control improvement and also for controlling other diseases, such as Zika and Chikungunya. Our research group is developing a study, having São Paulo state as study area, to test this hypothesis.

Table 1
Principal components #1 and #2 and the correlations coefficients with the considered variables and respective scores, Varzea Paulista, Sao Paulo state, Brasil, 2010.

Variables	Principal component #1		Principal component #2	
	Correlation coefficients	Scores	Correlation coefficients	Scores
Percentage of literate household heads	−0.82	−0.15	−0.05	0.04
Percentage of household members with 7 or more years of education	−0.81	−0.15	−0.01	0.05
Percentage of household heads with no income	−0.06	−0.08	0.93	0.42
Percentage of household heads with income equal to or less than 1 monthly minimum wage	0.66	0.12	−0.05	−0.07
Percentage of household heads with an income between 2 and 3 monthly minimum wages	−0.46	−0.03	−0.80	−0.32
Percentage of female-head households	−0.03	−0.07	0.84	0.37
Mean income per member of household	−0.75	−0.12	−0.22	−0.04
Percentage of families with household income equal to or less than 0.5 monthly minimum wage	0.91	0.16	0.15	0.00
Percentage of families with household income between 0.5 and 1 monthly minimum wage	0.61	0.11	−0.03	−0.06
Percentage of families with household income between 1 and 2 monthly minimum wages	−0.72	−0.11	−0.33	−0.09
Mean number of members per household	0.69	0.12	0.02	−0.04
Percentage of households with 6 or more members	0.76	0.13	0.10	−0.01
Percentage of households with 1 bathroom	0.73	0.13	0.07	−0.02

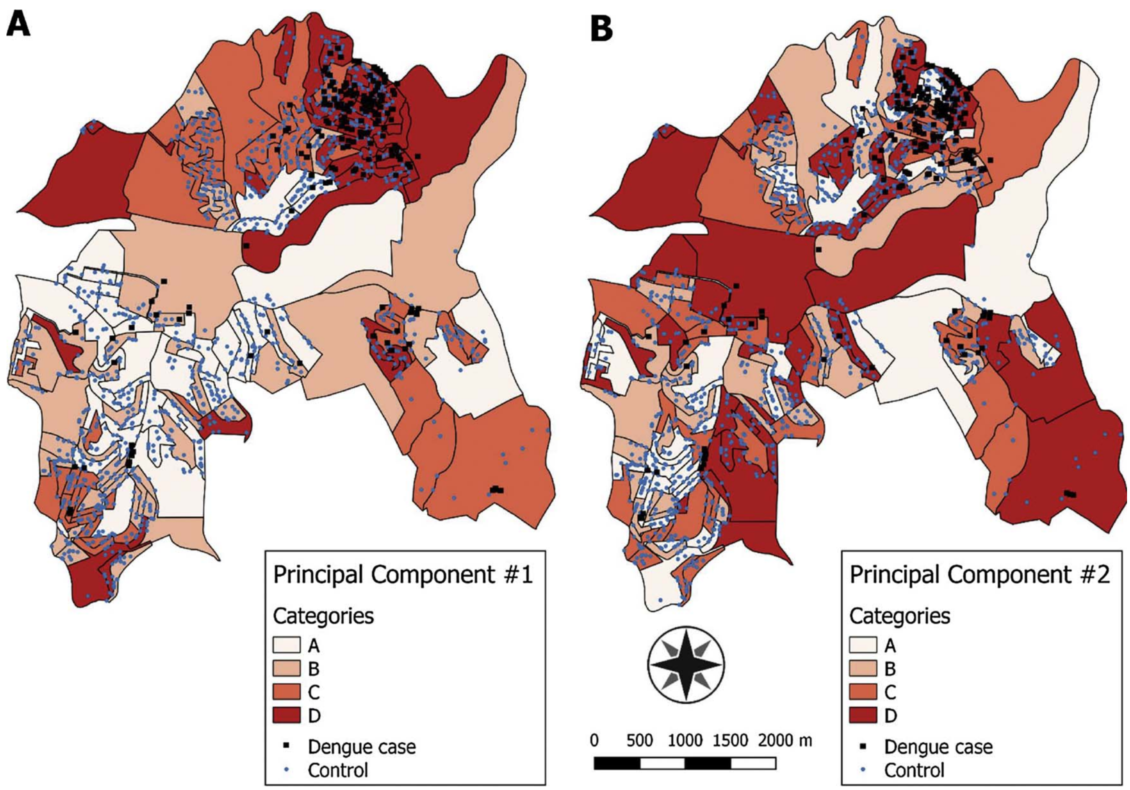

Fig. 8. Principal component # 1 categories (A) and principal component # 2 categories (B) by census tracts and dengue cases and controls, Varzea Paulista, São Paulo state, Brasil, 2007. The scale of markings that represent the dengue cases and controls warrants that no individual could be identified.

Table 2
Dengue risk estimated model for the two select principal components adjusted for the spatial distribution of the cases and controls, Varzea Paulista, São Paulo state, Brasil, 2007.

Principal Componentes (PC)	OR	95% CI	p-value
PC#1 – Categories			
A – Baseline	1.00		
B	2.07	1.24–3.47	0.0058
C	1.91	1.21–3.01	0.0053
D	5.80	3.87–8.68	0,0000
PC#2 – Categories			
A – Baseline	1.00		
B	0.53	0.39–0.74	0.0002
C	1.57	1.28–1.93	0.0000
D	1.49	1.21–1.83	0.0002

The main limitation of this study lies on the fact that all analyses were based on secondary dengue data obtained from local surveillance systems. We had no estimates of unreported dengue fever cases -underreporting is a common issue in Brazil due to confusion with other diseases or even absence of symptoms (Duarte and França, 2006). Reported and confirmed dengue cases were the only data available for this study. Another limitation is that no data was available to confirm the virus serotype causing the dengue epidemic in Várzea Paulista in 2007. Nonetheless, neighboring cities confirmed the presence of DENV-3 serotype in the 2007 epidemic, and, therefore, the epidemic in Várzea Paulista was most likely caused by the same serotype.

There is also an entomological limitation because we did not have access to data that could be used to characterize the differences in the entomological risk of the high and low risk clusters, but only for the entire municipality. The available Breteau index values for the period around the dengue outbreak of Varzea Paulista were 0.96 in December 2006, 1.21 in March 2007 and 3.25 in June 2007.

Even if the entomological information has not been incorporated in the modeling, it is possible to assume, especially taking into account that this was the first dengue epidemic in a totally or almost susceptible population, that the factors associated with dengue can also be related to vector infestation. In this way, both the socioeconomic and household head income indices, as well as the high-risk cluster identified, can be used to identify premises and priority areas for the development of vector control activities.

The well-known socioeconomic issues of the northeastern region stressed the need for interventions in Várzea Paulista. Indeed, the 2007 dengue fever epidemic and the recognized high vulnerability in the northeastern area of the city has led the local government to implement a re-urbanization program to improve sanitation and access to public health services. Acknowledging the major role played by socioeconomic factors in the spread of dengue fever is a way to promote the improvement needed in areas of poor sanitation worldwide.

5. Conclusions

This study characterized the first dengue fever epidemic in Várzea Paulista, São Paulo, Brazil, and its spatial and spatio-temporal distribution. GAM was able to identify an association between these unfavorable socioeconomic conditions and an increased risk of dengue fever. Most likely the association found was because we studied the first dengue fever epidemic in a highly susceptible population at the beginning of the outbreak. Cluster analysis and GAM are methodological approaches that allow identifying areas and times with an excess risk of disease transmission and related risk factors. Although each method uses specific procedures for estimating the risk, both were consistent in identifying the northeastern area of Várzea Paulista as the one with the highest risk and the southeastern area as the one with the lowest risk of dengue fever. The results achieved in our study could be useful to predict the occurrence and to identify priority areas to develop control measures for dengue. It may be also useful for Zika and Chikungunya control.

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