Environmental influence on the hantavirosis incidence in the federal district, Brazil

Influência ambiental na incidência da hantavirose no distrito federal, Brasil

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ABSTRACT
Most of studies dealing with hantaviruses have focused on people affected by this disease. Few studies have dedicated in the role of the land use and land cover (LULC) type in the hantavirus occurrences. The objective of this study is to analyze the influence of environmental factors in the incidence of hantavirus in the Federal District of Brazil. Probable sites of infection were identified based on the global Moran index (Moran I), local Moran index, and Getis-Ord Gi* spatial statistics analysis. Results showed that the Paranoá, Planaltina, and São Sebastião administrative regions are the critical regions in terms of occurrence of hantaviruses in the study area. altitude, categories of transition, LULC type, and geomorphology were the most important parameters related to the occurrence of the hantavirus disease. This study provides information on the effects of landscape and climatic factors on the incidence of hantavirus. The information can be used to better understand how hantavirus cardiopulmonary syndrome (HCPS) behaves in the Federal District, providing assistance for public health monitoring strategies and epidemiological surveillance.

Keywords: Zoonosis, rodent, land use and land cover, landscape, geospatial analysis, environmental modeling.

RESUMO
A maioria dos estudos que lidam com hantavírus tem se concentrado em pessoas afetadas por esta doença. Poucos estudos têm se dedicado ao papel do uso e cobertura da terra (LULC) nas ocorrências de hantavírus. O objetivo deste estudo é analisar a influência de fatores ambientais na incidência de hantavírus no Distrito Federal do Brasil. Os locais prováveis de infecção foram identificados com base no índice Moran global (Moran I), índice Moran local e análise estatística espacial Getis-Ord Gi*. Os resultados mostraram que as regiões administrativas de Paranoá, Planaltina e São Sebastião são as regiões críticas em termos de ocorrência de hantavírus na área de estudo. altitude, categorias de transição, tipo LULC e geomorfologia foram os parâmetros mais importantes relacionados à ocorrência da doença de hantavírus. Este estudo fornece informações sobre os efeitos de fatores paisagísticos e climáticos na incidência de hantavírus. As informações podem ser utilizadas para entender melhor como a síndrome cardiopulmonar...
1 INTRODUCTION

The genus *Hantavirus* of the family *Bunyaviridae* causes severe diseases in humans, as is the cases of hemorrhagic fever due to the renal syndrome (HFRS), hantavirus pulmonary syndrome (HPS), and hantavirus cardiopulmonary syndrome (HCPS). Rodents are the main hosts of hantavirus. Transmission occurs by inhaling aerosols containing the virus or through contact with blood or excreta of infected rodents. HFRS is more frequent in Europe and Asia and is caused by at least four antigenically and genetically different viruses classified by serotypes: *Hantaan*, *Seoul*, *Dobrava/Belgrade*, and *Puumala* (Schmaljohn et al., 1985). The HPS, on the other hand, has a higher incidence in America and is associated with sigmodontine, such as the *Sin Nombre virus* in North America and the *Andes virus* in South America (Nichol et al., 1993; Manigold and Vial, 2014). HFRS and HPS are heavily lethal: up to 15% for HFRS and up to 50% for HPS (Avsic-Zupanc et al., 2019). Concerns about the hantavirus infections are growing in the public health sector because of the annual incidence of approximately 30,000 cases in humans and an increasing distribution in the world (Watson et al., 2014).

The first HFRS outbreak occurred in the 1950s among Americans soldiers in mission in the Korean War. They had contact with rodents and other soldiers who resided outdoors (Sheedy et al., 1954). HPS was first recognized in 1993 in the Four Corners region of the United States, a region encompassed by the states of Colorado (southwest), Utah (southeast), Arizona (northeast), and New Mexico (northwest), as well as in South America (Nichol et al., 1993). In Brazil, the first case of disease was also reported in 1993 in the São Paulo State (municipality of Juquitiba). In the Federal District (DF) of Brazil, the first case of disease occurred in 2004. The outbreaks in São Paulo and DF were due to the deforestation of rodents’ native habitats (Ferreira, 2003). Among the 27 Brazilian federative units, DF has the highest fatality rate (Dusi et al., 2016).

Precipitation is the most studied climatic predictor of HCPS outbreaks. Several authors have indicated positive relation between rainfall and rodent density (Donalisio et al., 2011). However, this positive relation may apply only in environments with water
deficiency for native vegetation growth (Guterres & Lemos, 2018). Food availability and temperature are other key environmental drivers pointed out by Monchatre-Leroy et al. (2016). Besides these climate parameters, the land use pressure accelerates the introduction of new pathogens such as the hantavirus into native ecosystems, reducing the resilience of these environments. Thus, efforts to detect disease outbreaks should also focus on analyzing the influence of disturbed landscapes, primarily, agricultural areas (Goodin et al., 2006).

Dusi et al. (2016) described the main epidemiological aspects of hantavirus cases in the DF during the period 2004–2013, including field surveillance of age, sex, month and year of occurrence, clinical symptoms, syndromes and outcomes, and probable transmission place. In this period, the authors found 126 cases of hantavirus, predominantly from April (end of wet season) to August (peak of dry season). At least 75% of the cases were autochthonous. Acute respiratory failure was reported in 48% of cases, and the fatality rate was 40%. This study aims to analyze the environmental influence of the hantavirus incidence in the DF between 2004 to 2017. The purpose is to generate information on critical areas of DF that may be the center of future epidemics in the capital of Brazil.

2 MATERIAL AND METHODS
2.1 STUDY AREA

DF is located in the middle-west region of Brazil, extends between 15.50° and 16.50° of south latitude and 47.31° and 48.29° of west longitude and occupies an area of 5802 km² (IBGE, 2004). The topography is flat to hilly, with altitudes ranging from approximately 950 m to approximately 1400 m. Dominant form of relief evolved by the erosion process is the plateaus (CODEPLAN, 2017). In this region, we find the headwaters of three largest Brazilian basins – the Maranhão River (tributary of the Tocantins Basin), the Rio Preto River (tributary of the São Francisco Basin) and the São Bartolomeu and Descoberto rivers (tributaries of the Paraná Basin).

The region's climate is humid tropical savanna with strong climatic seasonality (dry winters and rainy summers), with an average annual temperature between 20 °C and 22 °C (Silva et al., 2008). The historical precipitation series recorded by the Embrapa Cerrados automatic meteorological station, located in the Planaltina administrative region (south latitude: 15.35°; west longitude: 47.42°; period: 1974-2019) indicates an average annual precipitation of 1323 mm. The natural vegetation of DF is typical from Cerrado,
that is, a mosaic of grasslands, shrublands, and forestlands in different proportions, depending on the region (Ribeiro and Walter, 2008). DF is composed of 33 administrative regions (ARs), which are the official political divisions of the DF, created by the Federal Law no. 4.545 of 1964 (Figure 1).

The estimated population of 3.06 million inhabitants and a demographic density of 444.66 inhabitants per km². It is similar to the division of the Brazilian states into municipalities and was created for the purpose of administrative decentralization and coordination of public services at local scale. The total number of inhabitants in the 1960-2010 period in FD increased from 142 thousand in 1960 to 2.0 million in 2000 and then to 2.6 million in 2010. Approximately 97% of the inhabitants are in urban areas (Brasília city and satellite cities such as Ceilândia, Gama, Planaltina, Samambaia, and Taguatinga) (country average is 82%). The population density is 444 inhabitants/km² (country average = 22 inhabitants/km²), with an average of 3.3 people per household (same as the national average). The Human Development Index (HDI) of the DF was 0.824 in 2010 (national average = 0.727) (CODEPLAN, 2013).

Figure 1. Map of 33 administrative regions (RAs) of the Federal District (A). The RA identifications in the orange square in (A) are shown in (B). The background image corresponds to the Landsat 8 image acquired in April 8, 2015. The RA identification are given in Roman numerals; however, for clarity purposes, we used Arabic numerals in this figure.
2.2 DATA SETS

The geographical coordinates (latitude and longitude) of the 108 possible infection sites (PIS) and 43 home addresses of confirmed hantavirus cases in the DF were obtained from the Disease Notification Information System (SINAN) available in the Environmental Surveillance System of the Federal District for the periods 2004–2017 and 2007–2017, respectively. The geographical coordinates of the home addresses were obtained through the high spatial resolution satellite images available in the Google Earth™ platform.

2.3 METHODOLOGICAL APPROACH
2.3.1 Spatial statistics
The sites of hantavirus occurrences in the DF were analyzed using the Moran's global and local indices (index (I), a spatial statistic that analyzes the spatial autocorrelation and observed spatial data similarity in addition to quantitatively investigating the characteristics of spatial distribution in spatial units (Moran, 1948). The main goal of the global Moran index (I) is to verify the degree of spatial autocorrelation of the data, whether the distribution is grouped or randomly distributed (Anselin, 1995). Positive values (between 0 and +1) show direct correlation and negative values (between 0 and −1) show inverse correlation (Marques et al., 2010). The local Moran index (Ii) measures the correlation between an observation and its neighborhood (Anselin, 1995). High and positive Ii values indicate presence of clusters of similar values, whereas low values indicate dissimilarity within a specific region. The results are expressed as clusters of high (HH) and low (LL) values or as outliers of high values surrounded by low values (HL) or low value surrounded by high values (LH) (Zhang and Lin, 2016). The results of the Moran’s indices were obtained by the ESRI ArcMap geographical information system package (level of significance < 0.05 and 999 simulations).

We also analyzed the hantavirus occurrences through the Getis-Ord Gi* (G) spatial indicator (Getis and Ord, 1995). High positive values of G indicate that there is a cluster of high values of the variable analyzed with reference to their average. High negative values of G mean the existence of a group of low values relative to the average of the variable analyzed. The results of spatial statistics (I, Ii, and G) were masked with the conservation unit map of the DF.

2.3.2 Environmental modeling

We used the Dinamica EGO software, a non-commercial platform developed by the Federal University of Minas Gerais for environmental modeling (Soares-Filho et al., 2009) to determine which variables most contributes to the occurrence of hantavirus in the DF between 2004 and 2017. The following nine variables were selected as the input parameters (Table 1): elevation, drainage network, road network, conservation units, soils, PIS, land use pressure, average precipitation, and average temperature. We generated Euclidian distance maps for drainage network, urban area, road network, conservation units, and PIS to understand the relevance of these factors in terms of proximity with the hantavirus occurrences.

Table 1. Characteristics of the input parameters selected for the environmental modeling of the hantavirus occurrences in the Federal District of Brazil through the Dinamica EGO software.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data Format</th>
<th>Year</th>
<th>Data Source</th>
</tr>
</thead>
</table>

We analyzed the spatial association between the explanatory variable with presence of hantavirus, using the method of weights and evidence. In this phase, we used the initial disease (2) and the final disease (1) as input data considering the absence of the disease and the incidence sites as the final landscape. The variables were weighted. Each variable received a favorable weight (W+) or not favorable (W-) to the probable site of infection. This allowed the calculation of the probability of hantavirus occurrence in the Federal District as well as identifying which factors mostly influence the proliferation of the disease.

The distributions of the weights of evidence by categorical variable were as follows: land use and land cover transition: 03 - Forest Formation, 04 - Savanna Formation, 12 - Country Formation, 15 - Pasture, 33 - River, Lake and Ocean, 300 - Mining, 303 - Forest Formation for Forest Formation, 304 - Forest Formation for Savanic Formation, 309 - Forest Formation for Savanic Formation, 312 - Forest Formation for Campestre Formation, 315 - Forest Formation for Pasture, 319 - Forest Formation for Annual and Perennial Culture, 324 - Forest Formation for Urban Infrastructure, 325 - Forest Formation for Another Non-Vegetated Area, 330 - Forest Formation for Mining, 333 - Forest Formation for River, Lake and Ocean, 400 - Savanica Formation, 403 - Savanica Formation for Forest Formation, 404 - Savanica Formation for Savanic Formation, 409 - Savanica Formation for Planted Forest, 412 - Savanica Formation for Campestre Formation, 415 - Savanica Formation for Pasture, 419 - Savanica Formation for Annual and Perennial Culture, 424 - Savanica Formation for Urban Infrastructure, 425 - Savanica Formation for Another Non-Vegetated Area, 430 - Savanica Formation for Mining, 433 - River, Lake and Ocean, 903 - Planted Forest for Forest Formation, 904 - Planted Forest for Savanna Formation, 909 - Planted Forest for Planted Forest, 912 - Planted Forest for Country Formation, 915 - Planted Forest for Pasture, 919 - Planted Forest for Annual and Perennial Culture, 924 - Planted Forest for Urban Infrastructure, 1200 - Country Formation, 1203 - Country Formation for Forest Formation, 1204 -

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<th>Source</th>
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<td>MAPA</td>
</tr>
<tr>
<td>Drainage network</td>
<td>Vector</td>
<td>2017</td>
<td>SIEG</td>
</tr>
<tr>
<td>Road network</td>
<td>Vector</td>
<td>2017</td>
<td>Open Street Map</td>
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<tr>
<td>Conservation units</td>
<td>Vector</td>
<td>2017</td>
<td>IBRAM</td>
</tr>
<tr>
<td>Soils</td>
<td>Vector</td>
<td>2006</td>
<td>SIEG</td>
</tr>
<tr>
<td>Probable infection sites</td>
<td>Vector</td>
<td>2004–2017</td>
<td>DIVAL; DIVEP; Federal District</td>
</tr>
<tr>
<td>Land-use pressure</td>
<td>Vector</td>
<td>2001–2016</td>
<td>MapBiomas</td>
</tr>
<tr>
<td>Average rainfall (mm)</td>
<td>Raster</td>
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<td>WorldClim 2</td>
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<tr>
<td>Average temperature (°C)</td>
<td>Raster</td>
<td>1970–2000</td>
<td>WorldClim 2</td>
</tr>
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</table>
Culture, 3324 - River, Lake and Ocean for Urban Infrastructure, 3325 - Rio, L ago and Ocean to Another Non-vegetated Area, 3330 - River, Lake and Ocean for Mining, 3333 - River, Lake and Ocean to River, Lake and Ocean.

Distribution for the geomorphological categories: 7 - Alluvial Strip (FA), 15 - Water mass, 27 - Fluvial Plain with Meandriform Pattern (PFm), 34 - Regional Planing Surface IIA with dimensions between 900 and 1100 m, with strong dissection, developed on Precambrian rocks (SRAIIA (fo)), 35 - Regional Planing Surface IIA with elevations between 900 and 1100 m, with weak dissection, developed on Precambrian rocks (SRAIIA (fr)), 36 - Superficie Regional of Planing IIA with elevations between 900 and 1100 m, with medium dissection, developed on Precambrian rocks (SRAIIA (m)), 65 - Receding Erosion Zone with very strong dissection, related to the generation of SRAIIA and erosion dominant to SRAIIA: Associated with hills and with Strong Structural Control (ZER-SRAIIA-MC-FCE / IIA (mfo)), 92 - Retreating erosion zone with strong dissection, dominating erosion (SRAIIA ZER / IIA (fo)).

3 RESULTS
3.1 SPATIAL ANALYSES

During the period 2007–2017, the hospitals in the DF received 838 patients with suspected contamination by hantavirus. Six hundred and eighty cases were excluded, 95 were undetermined, and 63 confirmed. Among the 63 cases, 43 were autochthonous (residents in the DF). The administrative regions of São Sebastião (8 cases), Planaltina (7 cases), and Paranoá (6 cases) presented the highest number of occurrences. The administrative regions with the highest incidence rate for every 100,000 inhabitants were Paranoá (13.34), Fercal (12.07), and Varjão (11.83).

The majority of human hantavirus cases are located less than 1 km apart from the potential habitat of hantavirus (land occupation in grasslands, natural grasslands, managed pastures, reforestation, forestlands, public forests, and conservation units (virus reservoirs) (Figure 2).

Figure 2. Location of 43 hantavirus confirmed cases in the Federal District of Brazil in the period 2007-2017, overlaid with the land use and land cover map produced by the MapBiomas project (see Figure 1 for administrative region identification).
According to the Global Moran index (z-score of 4.93), there is less than 1% probability that this high cluster pattern is random. In other words, there is positive autocorrelation between the observed distance values, that is, there is proximity between the residence of infected patient's and the rodent habitat (Figure 3).

**Figure 3.** Global Moran’s index.

According to the GI coefficient (z-score of 4.06), there is less than 1% probability that this high cluster pattern is random, which means high confidence that there is positive
autocorrelation between the observed distance values; that is, the proximity of the infected patient’s residence with the wild rodent habitat is related to the contraction of the disease (Figure 4).

Figure 4. GI coefficient.

In the Paranoá administrative region (AR VII), the number of infected people is high and is surrounded by administrative regions that are also above the average. Thus, the high number of hantavirus incidence probably influences the neighboring administrative regions. In the Taguatinga administrative region (AR III), the number of hantavirus incidence is also high, but it is surrounded by values below the number of infected in the neighboring regions (Figure 5).

Figure 5. Statistics Anselin Local Morans I for the number of people infected by hantavirus for the years 2007 to 2017 in the administrative regions of the Federal District, Brazil.
In the Paranoá administrative region (AR VII), there was a trend to form homogeneous groups. The homogeneous also occurs, although with less reliability in the following administrative regions: VI, XIV, II, IV, III, XII, and XV. In the XVII, XI, XVIII, and XXIII administrative regions, there is low probability of the formation of homogeneous groups of confirmed cases, with a minimum confidence of 90% probability (Figure 6).

**Figure 6.** Hotspots and couldspot statistics (Getis-ord* statistics) for the number of people infected by hantavirus for the period 2007–2017
3.3 ENVIRONMENTAL MODELING

The analysis of weights and evidence shows the relationships between the variables and the transitions according to the occurrence, or not, of the disease. We noticed that all the variables presented classes of retraction and attraction to the disease, except for the variable distance of highways and back roads that indicated only refraction. The disease is more likely to occur at elevations of 1134 m and less likely at altitudes of 1292 m. Concerning hantavirus, it is likely to occur in places close to natural habitats, close to watercourses, and likely places of infection; however, the drainage distance and likely places of infection are characteristics that are seen only in the first meters of analysis. Regarding the average temperature and average precipitation, the actual data are given in lower temperatures and precipitations, with retraction in higher temperatures and precipitations.

Categorical variables demonstrated well-defined behavior. About land use and land cover transitions, most of them are refractory to the occurrence of the disease, the most influential being: river and lake environments, forest formation for savanna formation and field formation for annual and perennial culture, and annual and perennial for annual and perennial culture. The transitions that indicated more attraction were: another non-vegetated area for savanna formation, another non-vegetated area for pasture, urban infrastructure for pasture, annual and perennial culture for pasture. The analysis of the geomorphological variable showed retraction for all categories, except the area of Receding Erosion Zone with strong dissection, predominantly eroding the (SRAIIA ZER / IIA (fo)) which presented attraction.

For more efficient analysis of the model, we studied the correlation between the variables to reduce duplicate information in the research. The matrix generation (Crammer's criterion) (Table 2) showed for most variables a data correspondence with low inter-correlation, which pointed to independent elements. Exceptionally, the altitude and temperature variables showed a correlation of 73% among themselves, which shows a significant relationship.
Table 2. Correlation obtained between variables used by the Crammer criterion.

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<td>0.064</td>
<td>0.132</td>
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<td>0.063</td>
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Legends: Geom. – Geomorphology; Dist. Drain. – Distance of drainage network; Dist. habitats – Distance of habitats; Dist. PIS – Distance of probable infection sites; Dist. roads – Distance of roads; LC trans. – Land use and cover transitions; Rain – Average rainfall; Temp. – Temperature.

4 DISCUSSIONS

The I index showed a significant autocorrelation between the confirmed cases of hantavirus and the natural habitats of wild rodents. This result suggests that infected people possibly live near rodent habitats. The *Necromys lasiurus* can live close to urban areas, agricultural expansion, rural settlements and condominiums in the DF (Oliveira et al., 2013). This rodent can adapt to small fragments of vegetation in areas of interface with wild environment, rural environment, and home environment (plantations), therefore, the importance of analyzing the risk of possible infections in urban and peri-urban areas (Pereira, 2006).

The Ii analysis showed the formation of homogeneous groups in the Paranoá administrative region, which shows high occurrences of the disease. It is noticed that this scenario can be influenced by the regions of Planaltina and São Sebastião, which are neighboring regions with strong spatial dynamics. These regions have diversified agricultural activities, rural settlements and areas with a transition from rural to urban areas. The proximity of residences to areas of native forest and pasture facilitates contact with reservoir rodents that move in search of new spaces to obtain food (Penna, 2003). In Taguatinga, there was also a significant occurrence of hantavirus. However, the surrounding regions did not present relevant data. It can be assumed that the contagion in the Taguatinga region is a problem mainly due to internal environmental issues within its perimeter.
We observed that the spatial statistics in the Gi* algorithm shows a behavior similar to the Moran index, since the Paranoá region has statistically relevant clusters, determining a pattern of distribution of hantavirus in the Federal District. The central areas of the Federal District did not present outliers in the model. However, according to the map, we observed that this central area is surrounded by areas that present cases of hantavirus infections or areas of favorable habitats for rodents carrying hantavirus.

In the analysis of weights and evidence, we noticed that the results confirm the spatial statistics results. We observed that the risk of the disease occurring is more likely in places of natural habitats of the rodent that hosts the hantavirus. It can be seen that infection risk increases with the non-length of the minimum distance of 40 meters for the construction of houses, silos, pigsties, farms, waterfalls, sheds, garages and others in these environments, which perform the natural function corridors, facilitating the entry of rodents in urban environments. According to Santos (2011), cities' natural expansion has promoted the construction of houses towards rural, agricultural, and wild regions that surround the municipalities. In the Federal District, the natural growth of the urban area leads to the emergence of new condominiums and satellite cities, which are usually located in old farms. These land invasions of areas with abandoned planting or stretches of wild vegetation, which are habitats of the rodent, allow occasional contact with man, with the possibility of transmitting the disease to humans.

Considering the analysis of categorical variables, the relation of land use and land cover transitions, the areas that showed the greatest significance for the disease's occurrence were the transition areas for pastures. In the Federal District, the cultivation of grasses of the *Brachiaria* species is conventional, in which beef cattle breeding in acidic and low-fertility soils is prevalent, predominant in the Cerrado region (Papini, 2009). According to Pereira (2006), in field studies 70.3% of the catches occurred in the area of *Brachiaria* grass. It is noticed that the rodent *Necromys tarsiurus* is adapted to live inside the *Brachiaria* pasture, in which it feeds on the seeds and water of its roots, mainly during the dry periods, which promotes the maintenance of the high-density rodent population (Alvin and Xavier, 2002). The only geomorphological category that showed attraction was those of Receding Erosion Zones (ZER), which present irregular relief, strongly dissected, less favorable to agriculture and pasture practices, where high rates of arboreal and forest strata are located (Carvalho et al., 2002).

Altitude and temperature, as examined by Crammer's criterion, showed a significant correlation for the occurrence of hantavirus. The climate in the Federal District...
is predominantly tropical in altitude, according to the Köppen classification, where there are two well-defined seasons: hot and humid, and cold and dry (Cardoso et al., 2014). We found in the study that the variables are more representative when analyzed together with other parameters. The model confirmed Santos (2011) observations that pointed out the relationship between average temperature and average precipitation in the incidence of the disease in the Federal District, where the cases are concentrated in the dry season (from April to September). The regions of rainy weather with dry winter, as in the case of the Federal District change agricultural production dynamics. These changes can make food available in large quantities in naturally limited periods, interfering with the rodent population's dynamics and abundance (Klemba, 2009). Generalist species, such as *Necromys lasiurus*, adapt better to anthropized habitats. The reproduction period of these rodents occurs between October and January, reaching adulthood around March. Adult rodents are the significant agents of transmission of hantavirus, due to the increased probability of exposure to the virus, contracted in fights and disputes, a fact observed in several species associated with hantavirus (Childs, 1995). In the dry season (from May to October), *Necromys lasiurus* presents its highest density, which corresponds to the harvest period (Vieira, 1997).

5 CONCLUSIONS

The expansion of urban areas and agricultural activities in the DF contributes to the increase of rodent’s reservoirs of hantavirus. Therefore, continuous monitoring of land use and land occupation is mandatory to track the dynamics of hantavirus incidences in the DF. The growing transmission of this disease in humans may be related to the increasing cultivation of grains in farms located near natural areas or higher production of wastes such as the leftover foods in the residences, attracting wild rodents. The spatial statistics (e.g., Moran index and Getis-Ord Gi*), combined with the environmental modeling approach such as provided by the Dinamica EGO software, can assist the risk analysis of hantavirus and other zoonosis such as the leishmaniasis and rabies or promote strategies for epidemiological surveillances in the field.
REFERENCES


