ORIGINAL RESEARCH

Differences in the association of dengue and leptospirosis incidences with respect to socio-sanitary vulnerability in the city of Santa Fe, Argentina

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Introduction

Leptospirosis is a zoonotic disease caused by pathogenic bacteria belonging to the genus Leptospira. Various species of domestic and wild mammals can act as a reservoir, shedding the bacteria into the environment through urine (1). The main form of transmission to humans is through contact with water and/or soil contaminated with the bacteria (1,2). On the other hand, dengue is a viral disease transmitted by mosquitoes of the genus Aedes, mainly Aedes aegypti. The vector inhabits the home and peridomicile of humans, and lays its eggs in rigid-walled reservoirs with clean or semi-clean water (3). Both leptospires and dengue virus can cause asymptomatic infections or cause mild or severe disease and can sometimes lead to death.

In relation to the distribution of these diseases, leptospirosis is present in all continents (except Antarctica), being more frequent in areas with tropical and subtropical climates and in floodable areas (4), with peaks occurring in the months corresponding to the rainy season. Dengue, on the other hand, is a disease that has a wide distribution in the tropical countries of the world due to the fact that the temperature allows the mosquito vector to reproduce, being more frequent in America and the Caribbean (5). Currently, its incidence is moving to temperate zones (6).

Certain environmental conditions are favorable for the occurrence of both diseases, such as high temperatures and humidity. However, there are conditions linked more to the risk of one or the other disease. Historically, leptospirosis has been characterized as a rural disease; however, the behavior of leptospirosis in recent years indicates an increase in urban areas (7). Although this disease occurs in a wide spectrum of social conditions, it is considered to be a disease that mainly affects the most marginalized sectors of the population (6, 8, 9).

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Due to the limited influence of these sectors in politics and the invisibilities produced by structural imbalances in access to power and resources, the diseases that affect them are often neglected in public health priorities and are therefore considered neglected diseases (9, 10).

The evidence establishing dengue as a poverty-related disease is still under discussion (11). If we consider that mosquitoes are efficient vectors that can move to different sectors of the territory and transmit the virus effectively, it is to be expected that the population affected by dengue is larger and more heterogeneous than that affected by leptospirosis. The spread of leptospires increases when the bacteria are mobilized from environmental reservoirs (soil and bodies of water) by rainfall or flooding (12). However, the contact of people with flooded areas is greater for vulnerable social groups (13).

The urban territory is usually characterized by great environmental and socioeconomic heterogeneity. Socio-economic characterization can be defined with respect to the level of social inclusion. The level of inclusion is usually represented in relation to different variables such as access to drinking water and sewage systems, proximity to the public transport network or to health centers (14). These variables have an impact on the health conditions of the population and, therefore, could determine the degree of vulnerability of the population to leptospirosis and dengue.

The level of social inclusion or exclusion is a field of debate, discussion and construction of public policies (15, 16, 17). Therefore, knowing to what extent the level of social inclusion is associated with one or the other disease can contribute to the planning of governmental actions.

In the city of Santa Fe, Argentina, there is a clear zoning of quality of life in relation to both the socioeconomic and environmental dimensions (16). In addition, due to its geographical location, the city has characteristics that make it vulnerable to river floods, heavy rains or a combination of both phenomena (17). This water-pluvial context, together with the warm temperatures of the region, generates optimal conditions for the occurrence of leptospirosis and dengue epidemics. Previous studies based on predictors of environmental and socioeconomic suitability for the occurrence of leptospirosis show that it is higher in the peri-urban areas of the city of Santa Fe and in nearby small towns (18).

The planning of public health interventions (mainly prevention and monitoring) is conditioned by the geographical, socioeconomic and environmental context in which both diseases can occur in the city. When these epidemics occur simultaneously, knowing the similarities and differences of these contexts is extremely relevant for decision making.

The aim of this study was to detect geographical areas of the city with a higher incidence of each disease, and to find and compare patterns of association between the incidences of dengue and leptospirosis with socio-environmental descriptors related to social and health inclusion.

Materials and methods

A retrospective, cross-sectional, ecological, observational analytical epidemiological study was conducted. With pooled data on the incidences of both diseases and indicators of social and health vulnerability, to assess the presence of associations.

The study area was the city Santa Fe de la Vera Cruz, capital of the province of Santa Fe, Argentina (Fig. 1; 31°38′0″ S, 60°42′0″ W). It has a total population estimated in the 2010 census - of 391,164 inhabitants and an area of 268 km2. The climate is temperate with an average daily temperature of about 19.5°C and an approximate annual precipitation of 990.4 mm (17). Santa Fe has a flat topography and is crossed by the Salado River to the west and the Paraná floodplain to the east (including the Colastiné River and Setúbal Lagoon). The predominant vegetation types in the area are characterized by the confluence of the phytogeographic provinces Paranaense (Interior Atlantic Forest) and Espinal. The vegetation is strongly influenced by the floodplain of the Paraná River, which is composed of subtropical rainforest and gallery forest and different types of flooded savannas and wetlands (rivers, streams, lagoons and estuaries) (19, 20). Due to its abundance of

humidity, temperature conditions, and flooding levels (21), the city has an incidence of both diseases (17).

Fig. 1. Location of the city of Santa Fe, Argentina.

Epidemiological database

Data on leptospirosis cases recorded in Santa Fe corresponds to the period between 2010 and 2019. In that period there were only two dengue outbreaks, a minor one in 2016 (with 55 cases) and a major one in 2019 (with 352 cases). It was not possible to access information associated with the 2016 cases that would allow their georeferencing, so the major outbreak was included in this work. These data were obtained from the National Health Surveillance System database. Geographic coordinates were assigned to the cases with detailed descriptions of the domiciles using Google Earth.

The following socio-environmental indicators based on census data were considered: households with unsatisfied basic needs (HNBI), socioeconomic stratum (ESE), educational level (NE) (22) and health vulnerability index (IVS) (23). HNBI is a continuous and aggregated variable, which indicates the proportion of households that have at least one unmet basic need, such as drinking water, material floor, flush toilet, etc. NE is a continuous and aggregated variable, which indicates the proportion of households whose heads of household have not completed primary education. ESE is an index that standardizes and integrates data on unsatisfied basic needs at the household level, type of house construction, educational level attained by the head of household, and access to material goods, using 7 levels or strata, being 1= upper class and 7= indigence, it is a discrete and global variable. Finally, SVI is an index that varies between 0 and 1, and refers to the relationship of the socioeconomic strata and indexes with the real, or effective, access to public health, taking into account the distance to universal health centers, among others (24). It is a continuous and aggregated variable.

These indicators were obtained from the "Poblaciones.org" (25) platform, which depends on an agreement between the National Council for Scientific and Technical Research and the Social Debt Observatory of the Argentine Catholic University.

Data analysis

The incidence of cases was calculated for both diseases in each census unit, which is formed by census radii, which in turn form census fractions. The Moran index (M) was applied to determine global spatial autocorrelation, and the local autocorrelation index was analyzed for both diseases using the packages "tmap", "spgwr", "grid" of R and R Studio (26). Linear regressions were used to evaluate the association of the different variables with the incidence of each disease and with the incidence adjusted for population density. The latter is due to the differences found between the areas of the territory and the population size of each census unit. Evaluations were performed at both the radius and census tract level. Correlations were performed using Past software (27). For the linear regressions, since the distributions of dengue and leptospirosis incidences did not follow a normal distribution, we used logarithmic transformations to achieve normalization (28).

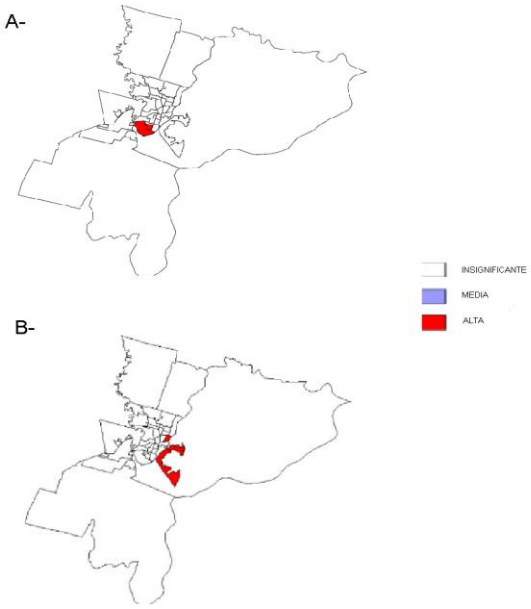
Results

Between 2010 and 2019, a total of 167 cases of leptospirosis were recorded in the city of Santa Fe. In the 2019 outbreak in the same city, 352 cases of dengue fever were recorded, being the most important outbreak in the period.

Evidence of spatial autocorrelation was found in the study area for dengue ($M=0.2$, $p=0.002$), but not so for leptospirosis ($M= -0.02$, $p>0.05$). Regarding the local autocorrelation index, two zones were identified for each disease with statistically significant spatial

autocorrelations. For dengue, the incidence was higher in the southwestern area of the city (Barrio Chalet, San Lorenzo, and surrounding areas), and a central-western area (Barrio Barranquitas, Fomento 9 de Julio and surrounding areas; Fig. 2). For leptospirosis, the area with significant autocorrelations corresponds to the southeastern area (Alto Verde area and surroundings), and a central-eastern area, adjacent to the former Belgrano railroad (Fig. 2).

Fig. 2 - Areas with significant local spatial autocorrelation for dengue (A) and leptospirosis (B) cases registered in the city of Santa Fe.



The linear regression of dengue incidence by census radius and HNBI was negative (r^2=0.090, p=0.003, d.f.=89; Fig. 3) indicating that as the proportion of households with at least one unmet basic need in the census radii increases, the incidence of dengue decreases. There was also a significantly negative association between dengue incidences at the census tract level and SVI (r^2=0.175, p=0.041, d.f.=22; Fig.4). The rest of the associations evaluated were non-significant (p>0.05).

For the incidence of leptospirosis adjusted for population density by census tract, a positive and statistically significant association was found with SES (r^2=0.536, p<0.001, d.f.= 26; Fig. 5), indicating that in census tracts with a higher proportion of households with lower socioeconomic levels (high SES), the incidence of leptospirosis is higher. A positive and significant association was also obtained with NE (r^2=0.343, p=0.001, d.f.= 26; Fig. 6), indicating that in census fractions with a high proportion of households whose heads of household have not completed primary education the incidence of leptospirosis is higher. Finally, a positive association was also obtained with SVI (r^2=0.610, p<0.001, d.f.=26; Fig. 7). The rest of the associations were not significant (p>0.05).

Fig. 3 - Linear regression between the Logarithm of dengue incidence by census radius and the Households with Unsatisfied Basic Needs Index (HNBI) - City of Santa Fe (2019).

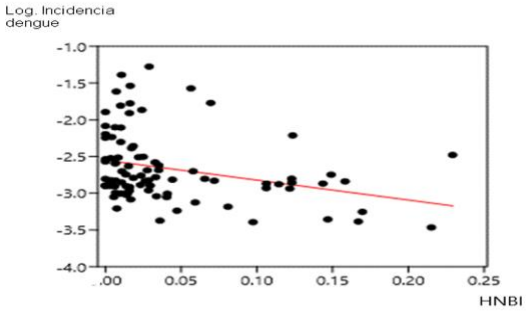


Fig. 4 - Linear regression between the Logarithm of dengue incidence by census fraction and the Health Vulnerability Index (SVI), city of Santa Fe (2019).

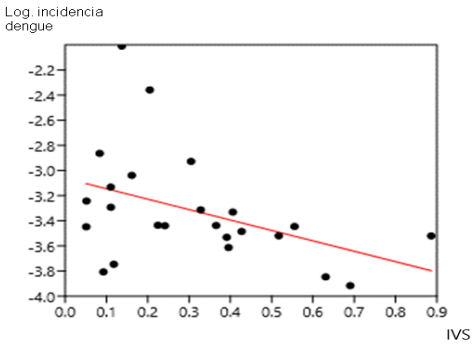


Fig. 5 - Linear regression of the logarithm of leptospirosis incidence adjusted for population density and socio-economic stratum, city of Santa fe (2010 - 2019).

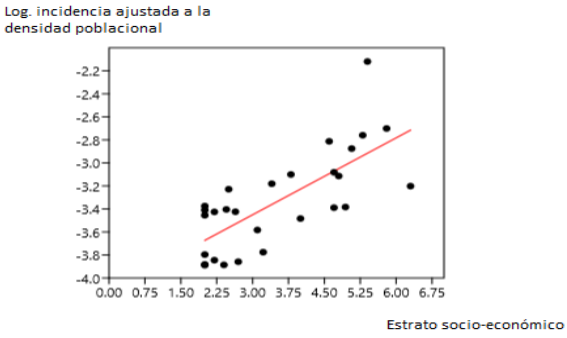


Fig. 6 - Linear regression of the logarithm leptospirosis incidence adjusted for population density and Educational Level, city of Santa fe (2010 - 2019).

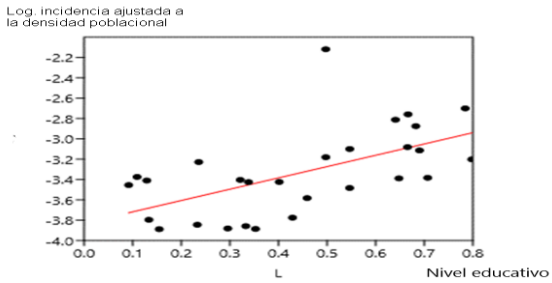
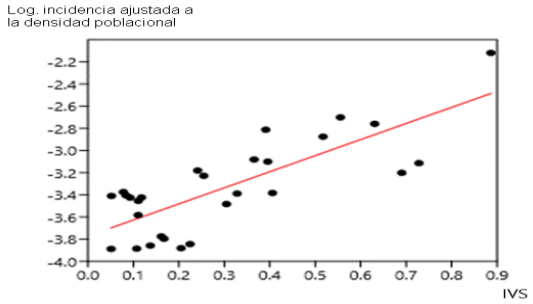


Fig 7 - Linear regression of the Logarithm of the incidence of leptospirosis adjusted for population density and the Health Vulnerability Index (SVI), city of Santa Fe (2010 - 2019).



Discussion

The results indicate that the higher the degree of vulnerability or social and health exclusion, the higher the incidence of leptospirosis, while the opposite is true for dengue cases. The results also suggest that there are two sectors with a higher incidence of dengue, one located in the central-western area of the city and the other in the southwest, both urban sectors with greater social inclusion and health accessibility. On the other hand, leptospirosis has its highest incidence in peripheral neighborhoods of the city located in the islands and the river coast, with high vulnerability indexes. Likewise, a conglomerate of cases was observed in areas near the former Belgrano railroad tracks, where some settlements with high social and sanitary vulnerability indexes are also located.

In contrast to this work, Vanlerberghe (29), based on studies carried out in Cali, Colombia, suggests that dengue incidences are higher in more unprotected sectors of the population. Based on a worldwide meta-analysis, Muligan et al. (11) suggest that the relationship between social marginalization or lack of protection variables and the incidence of dengue is under discussion. In the city of Santa Fe, dengue epidemics have been associated with the occurrence of imported cases (5), and these are generally people who have traveled to countries where dengue is endemic. Therefore, it is more likely that dengue epidemics are initiated in sectors of Santa Fe society with a certain purchasing power that allows for travel outside the country. The results of this study indicate that in Santa Fe we found a lower incidence of dengue in sectors with high socio-sanitary vulnerability indicators, coinciding, in this sense, with the studies of Muligan et al (11).

In relation to leptospirosis, the results coincide with those found by different researchers (6, 18, 30, 31) who describe this disease as more likely to happen amongst marginalized sectors of society. Three of the variables analyzed showed this pattern. We observed an increase in the incidence of leptospirosis as socioeconomic conditions deteriorated, which was also reflected in the spatial analysis of the determinants of the disease in Greater Santa Fe (18). Peri-urban and suburban sectors present the greatest

environmental and socioeconomic susceptibility for the occurrence of leptospirosis (18).

Finally, we also found that the incidence increased with higher proportions of households whose heads of household did not complete primary education. In a study carried out in neighborhoods of the city of Santa Fe and nearby localities, we observed an influence of the educational level achieved by people in their ability to adopt practices to prevent the disease (32). We also found a higher incidence of leptospirosis the higher the degree of health vulnerability, which could be related to the fact that cases of leptospirosis with detectable or severe symptomatology usually occur. Although leptospirosis has been considered a neglected disease at international level (6), some countries have not developed public policies aimed at improving its prevention. Martins and Spink (8) consider that in Brazil leptospirosis is a doubly neglected disease, because the epidemiological surveillance system in that country does not have data that would allow an efficient characterization of the populations that are mainly affected, so that its impact and the profile of the people affected remain invisible. When comparing it with dengue, Martins and Spink (8) attribute the differences in the sectors of the population affected by these diseases to the characteristics of the vectors/reservoirs that transmit them. Although Aedes aegypti mosquitoes have an area of action of approximately 300 m, they can easily disperse throughout the territory. Moreover, females lay their eggs in containers with rigid walls, which are not necessarily exclusive to more unprotected areas (6). Leptospira transmission, on the other hand, involves their excretion in the host's urine, persistence in the environment and entry into a new host. The main reservoir of leptospires are rats (Rattus sp.). These animals proliferate in urban environments with inadequate basic services, such as waste collection, closed storm drainage systems, and well-maintained green spaces. Thus, for example, rats are associated with micro-dumps, ditches, and unweeded areas. On the other hand, conditions that favor the persistence of the bacteria in damp soils are also often found in marginal neighborhoods with poorly maintained dirt roads and open canals (1). Thus, poorer living conditions increase the chances of contracting leptospirosis in an urban context (8). These could be the mechanisms that result in the increased incidence of leptospirosis that we observed in the city of Santa Fe as the socioeconomic stratum index increases toward less favorable conditions.

It should be emphasized that the number of cases of these diseases may be underestimated due to underreporting in the National Health Surveillance System. This may be due to the fact that these diseases in some cases produce mild symptoms, for which some people do not seek health care. In other cases, these diseases may be under-diagnosed due to lack of access to adequate health care or deficiencies in the health system's ability to diagnose these diseases.

It is necessary to take into account that the location of the dengue data from the 2016 minor outbreak could not be accessed, and that the type of study applied does not allow us to conclude on individual associations and could fall into an ecological bias. The patterns found are general and the resulting associations allow guiding new studies that search for more specific variables and with greater explanatory power, with the aim of avoiding possible confounding biases

In recent years, great emphasis has been placed on public policies aimed at controlling dengue fever, with variable results (33), while leptospirosis prevention campaigns are scarce. We consider that these results constitute an advance and a contribution to the analysis of how these diseases are distributed in the city of Santa Fe, with the aim of guiding the development of public policies that will make it possible to adequately address invisible diseases, such as leptospirosis.

In general terms, this work coincides with the statement made by Dr. Mike Begon (pers. comm.) that leptospirosis is such a neglected disease that it did not even make it to the WHO list of neglected diseases (34). In the case of Santa Fe, leptospirosis is neglected, underdiagnosed and underestimated in relation to Dengue. It is also, coinciding with Martins and Spink (8), invisibilized. And this is related to the sectors it affects, unlike dengue.

Inequity, marginality, low educational level and vulnerability based on the social structure are elements that promote the deterioration of health in cities (35). Health does not obey an exclusively individual order, but is a process that depends on how societies produce and

reproduce themselves (36, 37). Public policies must be equitable and comprehensive, with a high degree of social relevance, and must not respond only to an ahistorical and decontextualized biological perspective (38). Public policies aimed at disease prevention should cover the totality of conditions without excluding any material, social, educational, cultural or economic context.

This would make it possible to achieve an improvement in the overall quality of life, especially if participatory inclusion is promoted in the construction of a dignified community future. When public policies aimed at improving economic conditions or strengthening social protection are implemented, there are usually positive repercussions on the health of the population (39,40).

It is essential to address the problems associated with zoonoses in a transdisciplinary manner, considering the "One Health" concept. There cannot be human health if there is no animal health, and both cannot exist if the environment is not healthy; if it is deteriorated, if it is not sustainable (41, 42). Applying the One Health concept to the case of leptospirosis and dengue, we can expect that a healthy environment that has good garbage and vacant land management and minimizes rainwater accumulation will present fewer opportunities for mosquitoes, rodents and leptospires to survive and reproduce. In turn, in a more diverse animal community, including rodent and mosquito predators, and with a low dominance of reservoir species, there will be less transmission of these pathogens. Finally, an empowered human population with basic needs met and with broad access to education and health care will have greater capacity for prevention, detection and treatment of these zoonoses. Therefore, taking into account all of the above, we consider that it is necessary to advance in unraveling the socio-environmental roots of the health problems generated by this system of accumulation and segregation (37) in order to move towards healthier relationships, with citizen protagonism, which shed light on the invisible diseases that affect invisible populations and subjects.

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