Prospective Study About the Influence of Human Mobility in Dengue Transmission in the State of Rio de Janeiro

Bruna C. dos Santos, Larissa M. Sartori, Claudia Peixoto, Joyce S. Bevilacqua and Sergio M. Oliva

Abstract Dengue is a human arboviral disease transmitted by Aedes mosquitoes and it is currently a major public health problem in which around 2–5 billion people are at risk of infection each year. Climate changes and human mobility contribute to increase the number of cases and to spread the disease all around the world. In this work, the influence of human mobility is evaluated by analyzing a sequence of correlations of dengue incidence between cities in southeastern Brazil. The methodology initially identifies the cities were the epidemy begins, considered as *focus* for that epidemic year. The strength of the linear association between all pairs of cities were calculated identifying the cities which have high correlations with the focus-cities. The correlations are also calculated between all pairs considering a time lag of 1, 2 or 3 weeks ahead for all cities except the focus ones. Centred differences of the notification number are used to detect the outbreaks. The tests were made with DATASUS-SINAN data of the state of Rio de Janeiro, from January 2008 to December 2013. Preliminary results indicate that the spread of dengue from one city to another can be characterized by the development of the sequence of shifted correlations. The proposal may be useful to consider control strategies against disease transmission.

Keywords Dengue · Human mobility · Correlation · Rio de Janeiro

B. C. dos Santos (✉) · L. M. Sartori · C. Peixoto · J. S. Bevilacqua · S. M. Oliva
Instituto de Matemática e Estatística, Universidade de São Paulo,
Rua do Matão, 1010, São Paulo, Brazil
e-mail: brunacs@ime.usp.br

L. M. Sartori
e-mail: larissa@ime.usp.br

C. Peixoto
e-mail: claudiap@ime.usp.br

J. S. Bevilacqua
e-mail: joyce@ime.usp.br

S. M. Oliva
e-mail: smo@ime.usp.br

A. A. Pinto and D. Zilberman (eds.), *Modeling, Dynamics, Optimization and Bioeconomics III*, Springer Proceedings in Mathematics & Statistics 224,
https://doi.org/10.1007/978-3-319-74086-7_21

1 Introduction

Dengue virus infects each year about 300 million people worldwide and nearly 90 million of them develop the classic symptoms of the disease, such as fever, headache and nausea. Currently, dengue is endemic in more than 100 countries in Africa, America, Asia and Oceania [9]. In Brazil, the first documented occurrence was in Roraima, 1981–1982, and the first huge epidemic was in Rio de Janeiro city, 1986 [17]. The largest outbreak in Brazil occurred in 2013, accounting for around 1.5 million of notified cases [13]. Dengue is transmitted primarily by *Aedes* mosquitoes, particularly *Aedes aegypti*. The disease manifests in tropical and subtropical areas, which climatic conditions favor the development of eggs into larvae and mosquitoes. In Brazil circulate four strains of the virus, known as DEN-1, DEN-2, DEN-3 and DEN-4 of the family Flaviviridae, *genus Flavivirus* [3].

Factors such as population growth, global warming, rural-urban migration, environmental deterioration and the quality of basic sanitation, are some of the causes for the increase in infectious disease transmitted by vectors [12, 22]. Although there are not a consensus about disease's persistence, recent studies suggested the human mobility may be responsable for the emergence and reemergence of some diseases, in both the direct and indirectly transmitted [1, 17, 21]. Chikungunya and Zika outbreaks in Brazil are examples of diseases that have emerged in the country lately, and until recently, Chikungunya had only been detected in Africa, East Asia and India [10, 15].

Adams and Kappan [1] indicate that the spread of influenza and SARS (Severe Acute Respiratory Syndrome), from national to continental scale has been supported by the growth of airline transport network. In both global and local scales exist a daily traffic of people who move to work, tourism, etc. In the case of dengue, many people are asymptomatic then this scenario may be even more pronounced, because people may be spreading the disease to other places without even known they are infected [1, 4, 21]. The study developed in [1] highlights the role of human movement for the disease's persistence by establishing a dynamic on a hypothetical network. The authors observed that the understanding of human mobility can be used to map risk areas and provide targets for intervention and prevention. Stoddard et al. [21] investigated the relevance of human movement associated with vector behavior and how these two factors can increase the risk of exposure to disease due to human movement.

In general, most people have the same habit of daily mobility, in this work we analyze if the spread from one city to another can be explained by human mobility. Correlations between all pairs of cities were calculated considering that the beginning of the disease in each pair may be synchronized or not. The methodology is applied to a region composed by the municipalities of Rio de Janeiro State and all the border cities of Sao Paulo, Minas Gerais e Espirito Santo.

2 Materials and Methods

The state of Rio de Janeiro is located in southeastern Brazil, has a total population of 16.627.880 inhabitants [16]. About 96% of its population live in urban areas. The climate is tropical with an average temperature of 25 Celsius degrees throughout the year. Rio de Janeiro is one of the most visited place in Brazil, receiving tourists from all over the world during all seasons. These conditions, along with climate changes and increasing urbanization, ensure the mosquitoes proliferation and the disease maintenance [9].

Our analysis is based on data obtained from database of Notifiable Diseases Information System (Sistema de Informação de Agravos de Notificação - SINAN) an entity of Federal Government. In our study, the data considered were the weekly cases of dengue incidence from 2008 to 2013 for all cities of Rio de Janeiro and also the surrounding cities, totaling 130 cities [19]. The raw data were normalized by the urban population of each city [16].

The incidence considered significant was based on epidemiological alert thresholds defined by the Ministry of Health, therefore, there were excluded from the study, cities with incidence below than 300 cases per 100.000 inhabitants [13].

Defining a period of 52 weeks the methodology initially identify the cities that had outbreak, for instance, the cities which the number of notifications is equal or greater than 300 cases per 100 thousand inhabitants. Among this subset of cities a second cut is done excluding the cities which the total size of the population is less than 50 thousand inhabitants. After these two filters we selected the cities that first reach the incidence of 300 cases and define them as focus of the infection. Centred differences of the notification numbers were used to detect the outbreaks.

The correlations between all pairs of cities were calculated for the whole region with Pearson coefficient for two cases: Case 1: for all cities the period of analysis is defined from week 1 to week 52; Case 2: except by the focus, the period for the other cities is defined with a delay of 1, 2 or 3 weeks. A high correlation with delays between two cities (C_j, C_k), $j, k = 1, \cdots, m$, where m is the total number of cities being analyzed, suggests that the outbreaks have a time lag of n-weeks, which may indicate that the disease migrates from city C_j to city C_k. We define that the correlation is significant if its value is greater than 0.8 and the significance $p - value$ is less than 0.05. Our hypothesis is that dengue spread from one city to another and it could be verified by the evolution of the sequence of n time lag calculated correlations.

We aimed to test essentially if the disease initiates at the same time all over the state. We were inspired by the work of Saba et al. [18] that used the correlation between the occurrences of cases of dengue between cities in the state of Bahia to build a network of mobility [11, 14]. The authors considered that the existence of correlation between cases of dengue in two cities corresponds to an edge of the graph. It is possible to see through the graphs of incidence that there is a time lag between the epidemic curves, then we considered reasonable to verify the hypothesis of human mobility in the spread of the disease through the development of correlations.

3 Results

The year 2008 was chosen for presentation of results due to the high incidence of reported cases and by present a well-defined qualitative behavior compared to other years, however, the whole period from 2008 to 2013 was analyzed. We defined the epidemiological year considering the period from January to December, because we are assuming that the disease is the same in the whole state.

Considering the two filters described by the methodology, among the 130 municipalities analyzed, 18 of these are part of the metropolitan area of Rio de Janeiro (MARJ), 3 of these are part of Baixada Litorânea, 3 of these are part of the Médio Parnaíba, 2 of these are part of the northwest region, 1 of northern region and one of Região da Costa Verde. From the incidence data observed for this year, the cities Angra dos Reis, Campos dos Goyatacazes, Niterói, Nova Iguaçu, Rio de Janeiro and Seropédica, were chosen as focus of the disease because they were the first cities to achieve 300 cases per 100.000 inhabitants.

Table 1 shows in the first column the pairs of cities with high correlation presented without delay, the second and third columns are the correlations with n-weeks of delay $n = 1, 2$. Correlation nn', $n' >= n$, $n, n' = 0, 1, 2, 3$, means that the correlation is evaluated between the time series of two cities shifted, respectively, by n and by n' weeks from the first week of the period of one year. If $n = 0$ and $n' > n$, the focus cities were fixed in the first position with no delay, and the other cities were shifted by n-weeks, giving Correlation 00, 01, 02 and 03. Intermediate correlations as Correlation 12, 13, 23 were calculated in order to try to explain some cases of high-type correlations between cities that are geographically distant.

Table 1 Pairs of Cities in the Rio de Janeiro State with correlation above 0.8. Correlation 00 means correlation between the cites C_j and C_k without delay. Correlation 01 is the correlation between the cities C_j and C_k with the city C_k shifted by one week. Correlation 12 means the city C_j shifted by one week correlated with the city C_k shifted two weeks

	Correlation 00	Correlation 01	Correlation 12
1	Nova Iguaçu - Niterói	Niterói - Itaboraí	Itaboraí - Cachoeiras de Macacu
2	Seropédica - Duque de Caxias	Duque de Caxias - Itaboraí	Itaboraí - Cachoeiras de Macacu
3	Rio de Janeiro - Duque de Caxias	Duque de Caxias - Magé	Magé - Rio Bonito
4	Niterói - Araruama	Araruama - Saquarema	
5	Niterói - Duque de Caxias	Duque de Caxias - Magé	Magé - São Pedro da Aldeia
6	Niterói - Rio de Janeiro	Rio de Janeiro - Magé	Magé - Rio Bonito
7	Campos dos Goyatacazes - Araruama	Araruama - Saquarema	
8	Cantagalo - Cordeiro	Cordeiro - Sto Ant. de Padua	Sto Ant. de Pádua - Porciúncula

From Table 1 is possible to observe that dengue begin simultaneously in the pairs presented in the first column of the Table 1, because high correlation was found with no delay. On the other hand, high correlations between nearby and distant cities with delay of 1 or 2 weeks were found (second and third columns of the Table 1), when one of the city of the pair is a focus.

Examples in which appear high correlation between dengue time series with relatively distant cities, could be an indicative of the role of human mobility in spreading the disease. According to Farias [6] is possible to highlight two types of commuting in the state of Rio de Janeiro: daily flows of short distance and greater frequency, mainly associated with trade and manufacturing industries (intra-regional level); and not daily flow of great distance and low frequency, associated with mining and construction industry inter-regional level.

In fact, such commutings may explain some of the correlations. The state has significant flow rates primarily concentrated in the metropolitan area of Rio de Janeiro, MARJ for short [7], explaining the high correlations independent of the existence of the delay between the cities of MARJ region, respectively, lines 1, 2, 3 and 6 of the Table 1.

On the other hand, intercensual analysis from 2000 to 2010 indicate a decentralization of the pendulum movement inside MARJ. A significant growth of the pendularyity outside MARJ was observed concentrated mainly between the northern regions and the coast. During the first decade of this century some urban centers in the state, especially Macaé, expanded its area of influence to the northern region, in particular to Itaperuna and to Baixada Litorânea. This movement could be observed in the pairs presented in the lines 4 and 7 of the Table 1.

The correlation between Magé and São Pedro da Aldeia in the line 5, may not necessarily be explained by human mobility, since there are few signs of mobility between these two cities. In especial, we see a great migration from São Pedro da Aldeia to Macaé and other cities that make up the region of OMPETRO [5]. As it is generally known, dengue is influenced by several factors such as climate, temperature, basic sanitation or public health policy, and in these cases it is not ruled out the hypothesis that the epidemic curves for these two cities have obtained correlation because the events may have occurred simultaneously but in an isolated manner. For these cases, we address that mobility is not responsible for high correlation.

In addition, for a more complete analysis, we also calculated the correlations including those cities which had urban population smaller than 50000 and greater than 10000, and that also reached more than 300 cases per 100 thousand inhabitants in 2008. About 66 cities were selected, the focus was Cantagalo that reached more than 300 cases in the fifth epidemiological week.

Cantagalo is characterized as an independent pole and correlates with other cities of the mountainous region of north and northwest parts of Rio de Janeiro State [2]. It has obtained correlation between Porciúncula and Santo Antônio de Padua with one and two weeks delay showed in Table 1, line 8. Although the 2010 census data indicates that exists considerable migration between metropolitan cities and the mountainous northwestern region of Rio de Janeiro, we did not find sufficient evidence to suggest that human mobility has been responsible for this association.

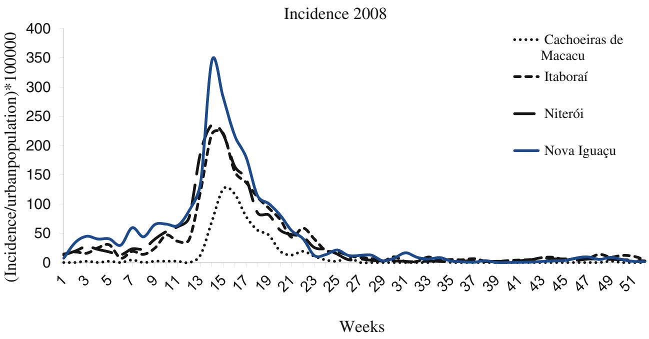

Fig. 1 Incidences of dengue cases in 2008 for cities that have correlation with Nova Iguaçu

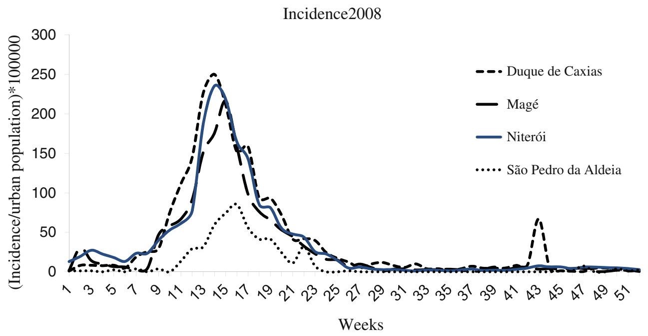

Fig. 2 Incidences of dengue cases in 2008 for cities that have correlation with Niterói

Figures 1, 2, 3 and 4 show the incidence data of DATASUS-SINAN observed in 2008. In Fig. 1 is presented the correlations obtained in line 1 of the Table 1. Nova Iguaçu was chosen as focus because this city was the first one to achieve the 300 cases (tenth epidemiological week). Nova Iguaçu and Niterói have high correlation with no shift (line 1, column 2); Itaboraí has higher correlation with Niterói with a shift of 1 week and finally Cachoeiras de Macacu has higher correlation with Itaboraí with a shift of 2 weeks.

In Fig. 2 are presented the correlations obtained in line 5 of Table 1. Niterói was chosen as focus because this city was the first one to achieve the 300 cases (tenth epidemiological week). Niterói and Duque de Caxias have high correlation with no shift (line 5, column 2); Magé has higher correlation with Duque de Caxias with a shift of 1 week and finally São Pedro da Aldeia has higher correlation with Magé with a shift of 2 weeks.

In Fig. 3 are presented the correlations obtained in line 3 of Table 1. Rio de Janeiro was chosen as focus because this city was the first one to achieve the 300 cases (tenth epidemiological week). Rio de Janeiro and Duque de Caxias have high correlation with no shift (line 3, column 2); Magé has higher correlation with Duque de Caxias

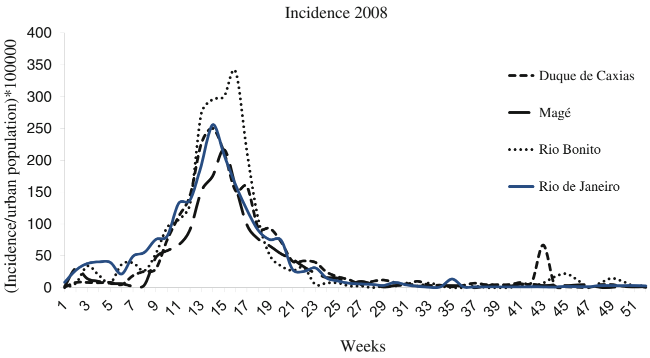

Fig. 3 Incidences of dengue cases in 2008 for cities that have correlation with Rio de Janeiro

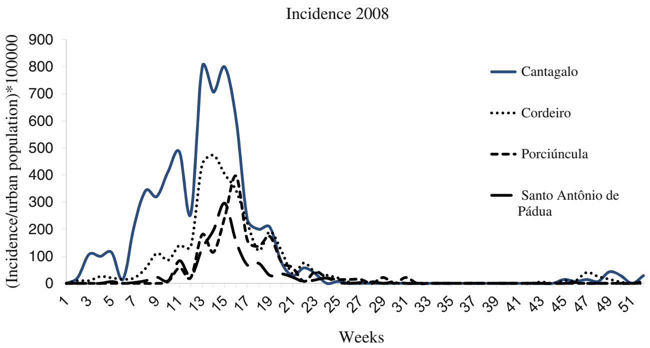

Fig. 4 Incidences of dengue cases in 2008 for cities that have correlation with Cantagalo

with a shift of 1 week and finally Rio Bonito has higher correlation with Magé with a shift of 2 weeks.

In Fig. 4 are presented the correlations obtained in line 8 of Table 1. Cantagalo was chosen as focus because this city was the first one to achieve the 300 cases (fifth epidemiological week). Cantagalo and Cordeiro have high correlation with no shift (line 8, column 2); Santo Antônio de Padua has higher correlation with Cordeiro with a shift of 1 week and finally Porciúncula has higher correlation with Santo Antônio de Padua with a shift of 2 weeks.

4 Conclusions

The hypothesis of an association between the occurrence of dengue cases between different cities in the state of Rio de Janeiro and surrounding areas was tested. The proposed methodology identified significant correlation between cities without delay, this results suggests that the dengue epidemic occurred simultaneously in both cities, while correlations with delay may provide evidence that the mobility of people may be responsible for the spread of the disease among the regions of the state.

Using the proposed methodology, we identified the cities: Nova Iguaçu, Niterói, Rio de Janeiro, Seropédica, Campos dos Goytacazes and Cantagalo as focus of the disease in the year 2008. Then we calculate the correlations with n-delay, $n = 0, 1, 2, 3$ for the focus cities with the other cities that were selected. We were able to justify part of the significant correlations between various cities through the pendular mobility among regions of the state. The correlations that we can not explain could be independent events or characterize one diffusive process.

This information could provide an efficient control framework to guide health authorities in decision making. Once verified that dengue does not emerge at the same time in all state, and that there exist cities with potential for further spread (due to the concentration of industrial activities, market, turism, etc.) the control services could concentrate resources in a more efficient way in cities that are potential sources of spread.

Based on the identification of the propagation cascade of dengue from the focus into the other municipalities, the next step is the construction of a topological network, representing these spread dynamics coupled with human mobility data.

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