Geospatial analysis applied to epidemiological studies of dengue: a systematic review

Análise geoespacial aplicada em estudos epidemiológicos de dengue: uma revisão sistemática

Abstract

A systematic review of the geospatial analysis methods used in the dengue fever studies published between January 2001 and March 2011 was undertaken. In accordance with specific selection criteria thirty-five studies were selected for inclusion in the review. The aim was to assess the types of spatial methods that have been used to analyze dengue transmission. We found twenty-one different methods that had been used in dengue fever epidemiological studies in that period, three of which were most frequently used. The results show that few articles had applied spatial analysis methods in dengue fever studies; however, whenever they were applied they contributed to a better understanding of dengue fever geospatial diffusion.

Keywords: Dengue. Spatial analysis. Geographic information systems. Geographic mapping. Time series studies. Medical geography

Maria Aparecida de Oliveira[I]

Helena Ribeiro[I]

Carlos Castillo-Salgado[II]

[I]Department of Environmental Health, School of Public Health, *Universidade de São Paulo* – São Paulo (SP), Brazil.

[II]Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University – Baltimore (MD), USA.

Corresponding author: Helena Ribeiro. Departamento de Saúde Ambiental, Faculdade de Saúde Pública, Universidade de São Paulo. Avenida Doutor Arnaldo, 715, Cerqueira César, CEP: 01246-904, São Paulo, SP, Brazil. E-mail: lena@usp.br

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Resumo

Foi realizada uma revisão sistemática dos métodos de análises geoespaciais que têm sido utilizados em estudos de dengue nos artigos publicados entre janeiro de 2001 a março de 2011. Depois de seguir critérios específicos de seleção, trinta e cinco estudos foram selecionados para inclusão na revisão. No total o presente estudo identificou vinte e um métodos diferentes que têm sido utilizados em estudos epidemiológicos de dengue, três dos quais foram utilizados com maior frequência.

Os resultados apontam um número pequeno de artigos, que aplicaram métodos de análise espacial em estudos epidemiológicos de dengue. No entanto, estes métodos contribuem para melhor compreensão da difusão geo-espacial da dengue.

Palavras-chave: Dengue. Análise Espacial. Sistema de informação geográfica. Mapeamento geográfico. Estudos de séries temporais. Geografia médica

Introduction

People, place and time are the basic elements of epidemiological investigations. According to Moore and Carpenter[1], the development of the Geographic Information System (GIS) has, over the last twenty years, boosted the development of the analysis of spatial patterns and processes in public health.

A general interest in spatial data analysis has developed rapidly over the last few decades, mainly because of the need for better public health tools. Greater interest and the subsequent improvements made have enabled researchers to tackle new urban diseases such as the dengue fever.

Geographical factors and information from different sources and formats can be spatially combined by GIS, both in epidemiology and public health — as, for example, in the studies of Briggs[2], Albert et al.[3], Aron et al.[4], Elliot et al.[5] and Khan et al.[6].

With the growing number of studies such as these in public health research, new methods of geospatial analysis have been developed specifically for applications in epidemiological studies and have been incorporated in different analytical software packages around the world. Moreover, currently, it is possible to access several innovative geospatial analysis tools via Internet.

The objective of this review was to provide an overview regarding the types of geospatial methods that have been used to analyze epidemiological data for dengue transmission over the ten years quoted.

Methods

Selection of studies

In order to yield the largest number of articles utilizing spatial analysis, searches using the PubMed (http://www.ncbi.nim.nih.gov/pubmed), SciELO (http://www.scielo.br) and LILACS (http://lilacs.bvsalud.org/) databases were conducted using, in the first search, the keyword “spatial analysis”. In the following searches, the keywords: “spatial autocorrelation dengue”, “spatial clustering dengue", and "spatio-temporal clustering dengue" were used because they had appeared in the articles found in the first search.

We selected every article published between January 2001 and March 2011 that contained the keywords at some point in it. We selected studies published in English or Portuguese that focused on dengue fever and used spatial analysis methods. First, each abstract was appraised to determine whether the article could be included in the review. The criterion of inclusion was that the articles should have applied methods of spatial analysis to dengue data. The criteria adopted are presented in Figure 1.

The analysis focused on papers according to the unit of analysis of data, typology of representation, spatial methods applied, and the main results of the analysis of spatial data.

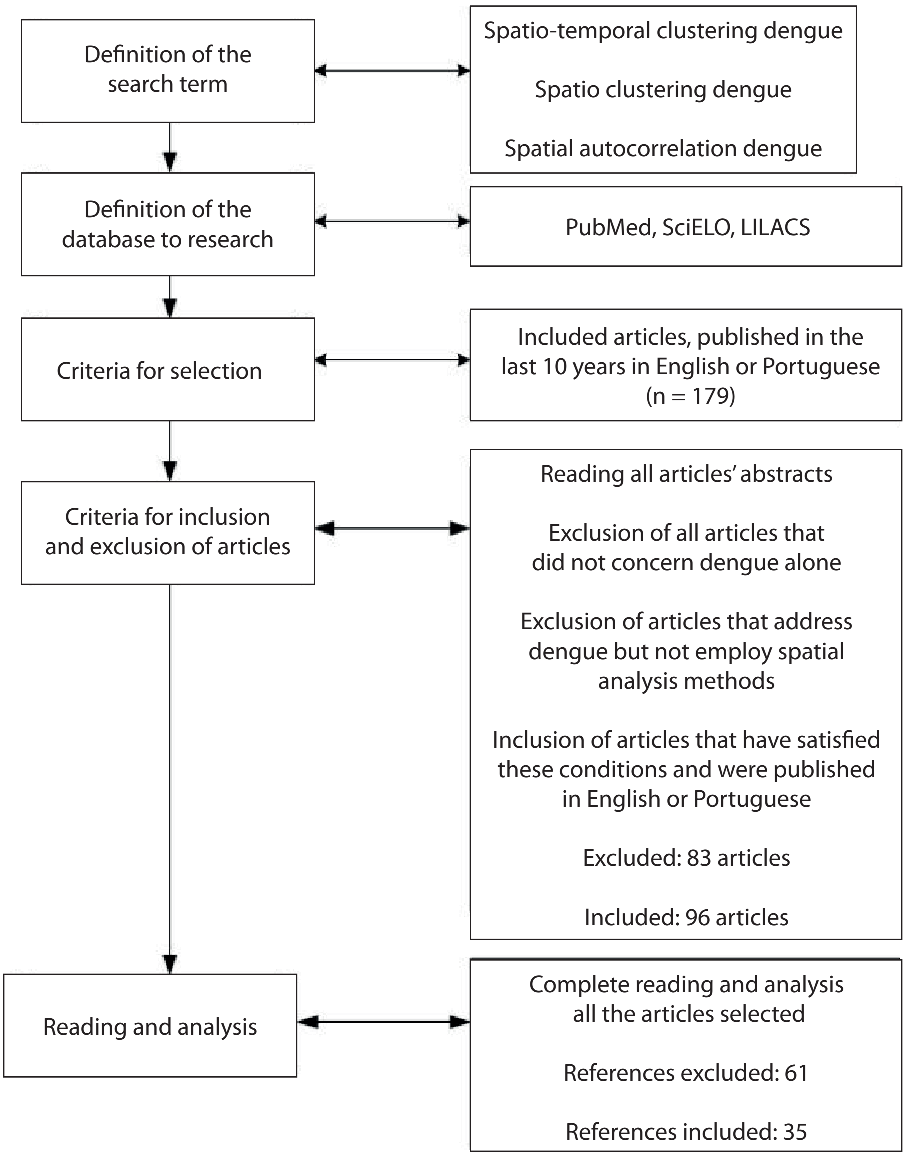

Figure 1 - Selection process used in a systematic review of Geospatial analysis applied to dengue epidemiological studies, 2001 – 2011.
Figura 1 - *Processo de seleção utilizado na revisão sistemática dos métodos de análise geoespacial aplicados em estudos epidemiológicos da dengue, 2001 – 2011.*

Results

Initially, 179 articles, published in either English or Portuguese, between 2001 and 2011, were selected. After reading the abstracts, 83 articles were excluded because they did not satisfy the inclusion criteria. Only 35 of the other 96 articles were found to meet the review criteria.

We found that some authors cited spatial analysis in the abstract but did not use a spatial method to analyze the data. For example, some articles had incorporated the term "spatial" but referred to micro-scale as it applies to genetics. A comparison of the spatial analysis methods used in the selected articles is given in Table 1.

Table 1 - Review of the spatial analysis method used in the selected articles.
***Tabela 1 -** Métodos de análises espaciais utilizados nos artigos selecionados.*

Reference	Spatial Method	Objectives of spatial analysis
7	Cuzick and Edwards Nearest neighbor tests and Monte Carlo simulation (49)	To identify spatial clusters of dengue cases.
8	Global K-functions, Getis-Ord Gi* (44)	To identify spatial clusters of dengue cases.
9	Knox test (43)	To detect spatiotemporal clustering.
10	Spatial average and Standard Deviational Ellipsis [SDE] (48)	Identification of spatial diffusion patterns.
11	Kulldorff Spatial scan statistic (47)	To investigate how dengue varies over space and time.
12	Ripley's K statistic (44)	To detect clustering of dengue cases.
13	Spatial operations to calculate the distances	To investigate the association of environmental, entomological, socio-demographic factors with dengue cases.
14	Local Indicators of Spatial Association, Monte Carlo Test (54)	To identify spatial clusters of dengue cases.
15	Knox test (43), Fourier Harmonic Analysis	To detect spatiotemporal clustering.
16	Kernel Intensity(55)	To identify the pattern of spatial diffusion of dengue fever cases.
17	Getis-Ord Gi* (44)	Identification of hot-spot areas of dengue cases.
18	Moran Global Index (54)	To test hypotheses of spatial autocorrelation of dengue fever cases.
19	A Generalized Additive Model (49)	To identify potential high-risk intra-urban areas of dengue.
20	Spatial operations to calculate the distances	To test the hypothesis that DENV transmission is spatially and temporally focal.
21	Moran Global Index (54) and The nearest-neighbor statistic (55)	To test hypotheses of spatial autocorrelation of dengue fever cases.
22	Local Indicators of Spatial Association (54) , Ripley's K-function (44)	To identify spatial clusters of dengue cases. To analyze spatial-temporal-spatial patterns of dengue.
23	Local Indicators of Spatial Association and the Moran Global Index (54)	To identify spatial clusters of dengue cases and to test hypotheses of spatial autocorrelation of dengue fever cases.
24	Just calculated distances between events.	To investigate the efficacy of Insecticide-treated bednets in reducing Aedes aegypti populations and dengue transmission.
25	Thematic maps	To identify spatial patterns of dengue.
26	Local Indicators of Spatial Association (54) and Kernel Intensity (55)	To identify spatial clusters and the pattern of spatial diffusion of dengue fever cases.
27	K-means clustering (48)	To determine the strength of spatial structure in both DENV-1 and DENV-3.

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Table 1 - Continuation.
***Tabela 1 -** Continuação.*

Refence	Spatial Method	Objectives of spatial analysis
28	Inverse Distance Weighting (45)	To define geographical barriers to gene flow.
29	Generalized Additive Model (49)	Analysis of individual and spatial factors associated with dengue seroprevalence.
30	Moran Global Index and Local Indicators of Spatial Association (54)	To analyze spatial patterns of dengue.
31	Kernel Intensity (55)	To identify the pattern of spatial diffusion of dengue fever cases.
32	Global K functions (48) and the local Getis-Ord Gi* (44)	To define the temporal and spatial patterns and clustering of dengue fever.
33	Maxent algorithm (50)	To investigate conditions associated with suitable areas for Dengue fever occurrence in 2008 in three municipalities
34	Kernel Intensity (55), Kulldorff's spatial scan statistic (48)	To identify the pattern of spatial diffusion and the spatial and temporal occurrence of dengue fever.
35	The kernel estimator (55)	To identify the pattern of spatial diffusion of the dengue cases.
36	Thematic maps.	To describe the process of dissemination of dengue in the state of Bahia.
37	Local Indicators of Spatial Association (54)	To identify spatial clusters of dengue cases.
38	Cluster analysis (55)	To assess the spatial pattern of dengue fever in 2003.
39	Local K-function (48), angular wavelet analysis of the spatial clustering (51), Knox test (43)	Analyzed the spatio-temporal pattern of denguevirus-2 outbreak during the 25 weeks of the outbreak.
40	Moran Global Index and Local Indicators of Spatial Association (54), Standard Deviational Ellipsis (48), Getis-Ord Gi* (44) and Spatial Empirical Bayes smoothing (46)	To analyze spatial patterns of dengue, spatial diffusion patterns and hotspot identification.
41	Moran Global Index and Local Indicators of Spatial Association (54), Spatial empirical Bayes smoothing (46)	To test hypotheses of spatial autocorrelation of dengue fever cases, To analyze spatial patterns of dengue and dynamic dispersion of dengue incidence.
42	Moran Global Index (54)	To test hypotheses of spatial autocorrelation of dengue fever cases.

Year of studies and publication

Variations were reported in the period studied. Most published studies involved an analysis of data covering two years or more. Generally, the articles used data that had been collected four to ten years before publication. About 48% of the studies published used data collected for fewer than three years. Furthermore, more than 52% of the studies were published just four years after the event occurred, and only 8.5% of the studies used data collected less than one year before publication.

Not many papers using spatial analysis[6-15] were published between 2001 and 2006, but since 2006 the number of papers based on geospatial studies has increased. Approximately 72% of the relevant papers were published after 2008[16-42] (Table 2).

Most of the studies were undertaken by Brazilian or American investigators. These countries are responsible for 50% of all the studies developed, followed by Thailand and Australia. However, it is noteworthy that, in the case of Brazil, the studies were carried out with the Brazilian database for dengue fever in Brazilian institutions. In the United

States, on the other hand, the studies were undertaken using other countries' databases.

The articles were published in the various journals listed in Table 3, most of them being published in just four journals: *PLoS Neglected Tropical Diseases*, *Cadernos de Saúde Pública*, *Revista de Saúde Pública* and *Revista Brasileira de Medicina Tropical*. These journals published 78% of the articles which used spatial analysis methods in the investigation of dengue fever transmission.

Nine of the studies included in this review applied spatial methods to analyze epidemiological and entomological information[7,8,10,20,21,24,26,35,36], and 23 others just analyzed epidemiological information[9,11-19,22,23,25,27,30,31,33,34,37-41]. Three articles included analysis of entomological information only[29,32,42].

In terms of the geometric or shape representation of data, the studies primarily used polygons and points. The polygons were used to represent administrative frontiers, such as neighborhoods, districts, census tracts, or other administrative frontiers, and the points were used to represent cases of dengue, households, schools, or vector traps.

There is no predominant type related to the topology utilized because it was common to use more than one type in the articles. For example, often data are collected at household level, but for analysis purposes they are aggregated into areas.

Spatial units

In the articles selected, nine different primary units of analysis were identified. The most-used primary unit of analysis was the household, which was applied in ten articles, or around 28% of the published studies[7,8,11-13,19,20,24,29,30].

The dengue case as primary unit was used in five studies[9,15,16,27,33], and census tracts were used in four studies[10,23,24,31]. Some studies used more than one unit of spatial analysis; for example, census tracts and cases were used in five studies[10,22,34,37,39]. Four studies[18,25,36,38] used the cities as the unit of analysis. Other studies used the block analysis unit[21,35,41]. In two studies, districts were used[26,30].

Table 2 - Total articles by year and periodical.
Tabela 2 - *Total de artigos publicados por ano e periódicos.*

Year	Number of articles	Periodical
2001	01	Tropical Medicine and International Health
2003	01	American Journal Tropical Medicine Hygiene
2004	01	Emerging Infectious Diseases
2005	01	Revista Brasileira de Medicina Tropical
2006	04	International Journal of Health Geographics, Tropical biomedicine, Science of total environment; British Medical Journal
2007	01	Acta Tropica
2008	09	Epidemiology and Infection, Cadernos de Saúde Pública, PLoS Medicine, BMC Public Health, Revista de Saúde Pública, Tropical Medicine International Health
2009	9	PLoS Neglected Tropical Diseases, Cadernos de Saúde Pública, Journal of Virology, Revista de Saúde Pública, International Journal of Environmental Researches and Public Health.
2010	5	PLoS Neglected Tropical Diseases, Revista Brasileira de Medicina Tropical, International Journal Infectious Diseases, Epidemiology and Infection
2011	3	PLoS Neglected Tropical Diseases, Epidemiology and Infection, International Journal of Environmental Research and Public Health

Towns or cities were applied in two cases[28,40], administrative districts were used in one[17], and the planning unit was used in one[41].

Methods of spatial analysis applied in dengue fever studies

Twenty-one different spatial methods used to analyze dengue data were found in the articles. However, some were more common than others. The methods used in selected papers are listed according to the topology of the data used.

Spatial analysis of points

In the analysis of point data, the method used most frequently, in 6 papers[16,19,26,31,34,35], was kernel density estimation. The Knox method43 was applied in three papers[9,15,39]. The local Gi* statistic[44] was used in three papers[8,17,32]. Three papers[13,20,36] used only the distance operations[45], without spatial analysis methods.

Ripley's K statistic[44] was used in two studies[12,22]. Bayes smoothing[46] was applied in two papers[40,41], while two papers[11,34] applied the Kulldorff analysis[47]. The Global K statistic[44] was applied in two studies[8,32]. In addition, two papers used only thematic maps such as the exploratory spatial analysis tool[25,36].

Standard deviational ellipse48 was applied in two papers[10,40]. The generalized additive model[49] was applied in two papers[19,29] as well as the Monte Carlo simulation[7,14]. The

Table 3 - List the software used each year.
***Tabela 3 -** Softwares utilizados por ano.*

Year	Software	Number of Studies
2001	GammaTM and Stat!TM	1
2003	Arcview	1
	Point Pattern Analysis (PPA)	1
2004	Geoconcept	1
2005	CrimeStat	1
	No information	1
2006	Arcview/ArcGIS	2
	No information	2
2007	Envi	1
2008	R	3
	ArcView/ArcGIS	3
	ArcInfo	1
	MapInfo	3
	Splus	1
	Point Pattern Analysis (PPA)	1
	GEODA	2
	No information	3
2009	Maxent Version 3.3.0 - beta	1
	Terraview	3
	R	1
	ArcView/ArcMap	3
	Splus	1
	Sigmastat 3.1	1
	No information	2
2010	GEODA1	1
	R	1
	TABWIN	1
	Arcview	1
	No Information	3
2011	SavGIS	1
	GEODA	1
	ArcGIS	1
	SatScan	1
	No information	1

Maxent algorithm[50] was applied in one paper[33]. Angular wavelet analysis[51] was applied in one study[39], the local K-function[44] was applied in a separate study[39] and in another study[38], cluster analysis was applied. In one paper[27], local K-means[44] was used.

The nearest neighbor statistic[51] was applied in one[21], Fourier harmonic analysis[52] was used in another[15] and, finally, inverse distance weighting[53] was applied in one study[28].

Spatial analysis of area data

LISA (Local indicators of spatial association)[54] was the method used most often in analyzing polygon data[22,23,26,30,37,40,41]. Another method commonly used was the Global Moran Index[18,21,30,40-42]. The Monte Carlo method was applied in one study[14], and the local Gi* statistic in another[17] (Table 1).

Software programs used for spatial analysis of dengue cases

Some articles did not report which software had been used to perform the spatial analysis of data. Further, in some cases, the method of spatial analysis was not referenced; instead, the focus was on the set of operations utilized. For example, it was clear in every article that different software had been used; in some cases, one software program was used to create the geographical coordinates (latitude and longitude), and another specifically to perform the spatial analysis.

The software programs used in the selected articles are given in Table 3. The most used were ArcGIS, GeoDa, TerraView and MapInfo. Several other software programs — for example, Satscan, Terrasee, Arc/Info, PPA, S-PLUS, and other customized ones — were used, but not as often.

Discussion

Despite place being a fundamental component of epidemiological investigations, the small number of papers found may indicate that the use of spatial analysis in studies of dengue is still uncommon. Among the possible reasons that may hinder the application of spatial analysis in the data analysis of dengue is the lack of health information systems that produce georeferenced entomological and epidemiological information, that is, the appropriate scales of analysis.

As from 2008, there was a significant increase in the number of articles that addressed the application of spatial analysis in studies of dengue. 72% of the published articles were found from that year on, perhaps due to the increased severity of the dengue epidemics the world observed during this period. The increase could also be a result of the need to develop new approaches to dengue fever research, to better understand the dynamics of the disease's transmission, and to formulate strategies to minimize its effects.

Among the works selected, there was a significant time interval between the occurrence of events (dengue cases), or even between the execution of serological and entomological surveys, and the publishing of the results of spatial analyses. This time lag might have been due to the natural flow of research, but it might also reflect the complexity and difficulties involved in conducting spatial analyses in countries where dengue is endemic.

The existence of such a long time interval between the collection of entomological and epidemiological information and the analysis and dissemination of results can lead to some bias against the early detection of epidemics and, therefore, to a reduction in the ability to identify the surveillance sites that require public health action.

Although most studies of dengue using spatial analysis were based on data from countries where the disease is endemic, the studies themselves were conducted elsewhere. The exception is Brazil, which has developed most of the spatial analyses, according to articles published in the countries themselves. Brazil and Thailand figured most among the countries studied — with 40% of the articles, followed by Peru and Vietnam.

The household has been the most commonly used spatial unit, followed by dengue cases and census tracts. This could be due to the actual characteristics of the entomological and epidemiological studies of dengue, which often focus on the areas surrounding the household because of the ecological characteristics associated with the spread of mosquitoes.

As can be observed in Table 1, twenty-one different methods of spatial analysis were found; however, only three of them were used frequently.

In analyzing the polygon data or areas, the most widely used indicator is LISA, and Moran's global statistic is the commonest way of measuring the degree of spatial autocorrelation in area data[52] — perhaps because of the ease of application and interpretation of results, greater availability of free GIS software, such as GeoDa, or the lack of health information on more greatly detailed scales.

For the analysis of point data, the methods most used have been the intensity estimator kernel. These methods are essentially graphics[55]. Perhaps for this reason, only four studies used just spatial analysis models in the methodology of the article, while the remainder applied various statistical methods in conjunction with the methods of spatial analysis. There were also cases in which the authors did not use any method of spatial analysis. In other words, the spatial analysis of the article was based only on distances calculated using the GIS environment. These distances were used as independent variables in the regression models.

The other eighteen methods of analysis were each used by only one or two articles, and always as a complement to traditional methods of statistical analysis.

Some of the methods might have been more used due to their greater popularization, because of ease of access, as generally they are implemented in commercial software of great diffusion capacity with easy-to-handle friendly interfaces, as also in those of the public domain, with a larger number of courses and tutorials which assist the user in their use. On the other hand, although some of the methods least used may be available, both in software of the public domain as also in commercial software, they have as yet been little disseminated and present little didactic material, often having relatively unfriendly interfaces which make their manipulation on the part of users who have little familiarity with special data, difficult. Although they are commercial software, ArcView/ArcGIS and MapInfo are among the software programs most used, probably because they present more friendly interfaces than do the free software programs and count on a wide range of programs for the dissemination of and training in their use. On the other hand, although they are free (software) programs, GEODA and Terraview are also frequently used, probably because they make the methods commonly used in spatial analyses in public health available free, together with didactic material, and are widely represented at technical and scientific events.

Despite these considerations, it is pertinent to point out that regardless of the degree of sophistication of the method used, the results shown in the papers pointed to the great utility of spatial analysis for the understanding the epidemiology of dengue fever on different continents and in different geographical areas. Furthermore, results have shown that the methods such as Kernel Estimation, LISA and Moran's, can quickly produce efficient information regarding the location of clusters of dengue cases and of hot spot areas of transmission. Such information can be a powerful tool for monitoring dengue transmission at the local level.

Finally, despite the development of the methods of spatial analysis applied in epidemiological studies, they are rarely used in studies of dengue. However, the identification of spatial patterns in most of the articles discussed above confirms the usefulness of the application of these techniques and the need for development and application of advanced spatial analysis beyond the limits of visualization.

Some spatial analysis methods should be used in conjunction with conventional methods as, for example, in the control diagrams currently used by public health programs to identify dengue risk. The use of these methods to advance scientific knowledge on the dynamics of dengue transmission and its spatial diffusion could certainly be incorporated into current surveillance strategies and may contribute to reducing social costs, by incorporating both the individual and contextual variables associated with dengue transmission.

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