

Factors associated with the occurrence of dengue epidemics in Brazil: a systematic review

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ABSTRACT

Objective. To identify and describe broadly the factors related to the occurrence of dengue epidemics in Brazil.

Methods. Systematic review of studies published in Medline, Lilacs, PubMed, Cochrane, BVS, Web of Science, Scopus, and thesis and dissertations databases using descriptors cataloged in DeCs and MeSH on dengue and factors associated with the occurrence of epidemics, published from 2008 to 2018.

Results. Thirty-five studies carried out in the country were selected. The epidemics recorded in Brazil were associated and/or correlated with multiple factors such as environment, socioeconomic conditions, climate, and aspects related to the vector, among others.

Conclusions. Dengue epidemics are complex and multifactorial. The continuity of the vector control actions was found to be relevant to the reduction of *Aedes aegypti* and for disease control. To contain the spread of the disease, effective measures are needed in all sectors, including health, education, economy, population, business, and government. Actions for the early detection of cases of the disease can prevent new outbreaks of epidemics.

Keywords

Dengue; risk factors; epidemics; Brazil.

Since the report of the first dengue epidemic in Brazil (1), the country has been presenting successive epidemics and uninterrupted expansion of the disease (2). As of 2008, a concomitant circulation of the four serotypes of the dengue virus (DENV) was observed in the five Brazilian regions, due to the reintroduction of DENV-4 after almost 30 years without being identified (3). Additionally, the vectors *Aedes aegypti* (4,5), the main transmitter in urban areas, and *Ae. albopictus* are present in suburban and peri-urban areas of the country (3,4).

An important public health problem, dengue creates a social and economic burden for endemic countries (6). Brazil was responsible for 65% of the dengue cases reported in the Americas between 2014 and 2019 (5). In addition, a 266.1% increase in

the rate of disability-adjusted life years per 100 000 inhabitants was observed between 2000 and 2015 (7).

Several factors have been related to the spread of the disease and the vector in the country, such as population growth, migration, air travel, inadequate urbanization, malfunctioning health systems, population density, and socioeconomic inequalities, among others (8). In addition to the increasing number of cases of the disease, the increase in reports of severe forms in the last decades may be related to the concomitant circulation of different serotypes of the virus, as well as the virulence of the circulating strains (9).

Considering the current scenario of dengue in Brazil, we aimed to identify and describe broadly the factors related to the

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occurrence of dengue epidemics in Brazil in order to contribute to the better understanding of the dynamics of the epidemics in different scenarios.

METHODS

A systematic review was carried out on the determinants for the occurrence of epidemics and/or outbreaks of dengue in Brazil from 2008 to 2018.

Study design

The research was carried out in different electronic scientific databases, using descriptors related to the factors associated with dengue in Brazil. The studies were identified and included in the first semester of 2018.

This study was registered in the International Prospective Register of Systematic Reviews (PROSPERO, 2018) under the registration number CRD42018095019 and followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA, 2015).

Eligibility criteria

Studies that measured the association and/or correlation of specific factors with dengue epidemics and/or outbreaks, published in Brazil between 2008 and 2018, in English, Portuguese or Spanish were included in the systematic review. The searches were conducted in March 2018.

Studies carried out within the Brazilian territory, as well as epidemiological studies that describe the association between the occurrence epidemic and/or dengue outbreak and social, economic and environmental variables were included. Case series studies, studies restricted to the description of cases or variables and studies with bias or inconsistencies were excluded.

Databases

The bibliographic search was carried out in the following electronic databases: Medline, Lilacs, PubMed, Cochrane, VHL, Web of Science, Scopus and Library of Theses and Dissertations from Coordination for the Improvement of Higher Education Personnel-CAPES/Brazil.

Search strategy

The searches were conducted using the descriptors cataloged in the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH), in Portuguese, English, and Spanish, found in the title or in the study abstracts. The boolean operators "AND" and "OR" were used for a more specific search in the titles.

The following search terms were used in the databases: Group 1: Dengue/Dengue Virus/*Aedes*; Group 2: Disease Outbreaks/Epidemics; and Group 3: Epidemiology. To characterize the demographic, environmental, and socioeconomic variables, the following groups of descriptors were used: (1) risk factors; (2) life style; (3) urban; (4) social and economic conditions, and (5) cultural characteristics. The bibliographic search was assisted by a professional librarian at the Universidade Federal de Minas Gerais, tested and reproduced by two researchers.

RESULTS

Analysis of studies

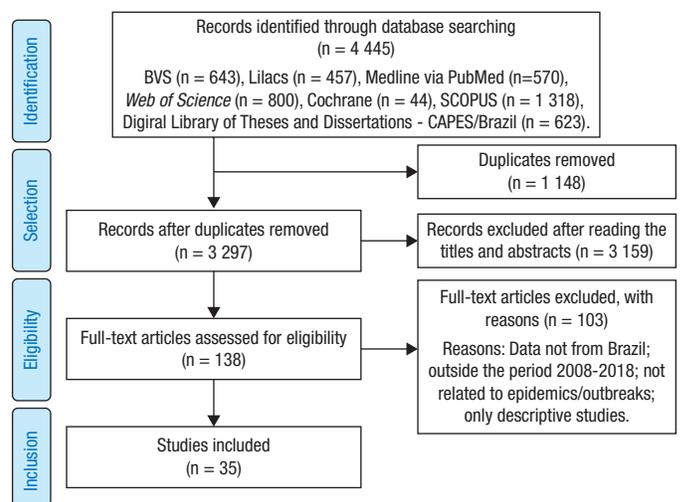
Initially, 4 445 studies were systematically selected in the bibliographic search. Of these, 1 148 were excluded due to duplication and after reading the titles/abstracts (3 159). Then, 103 studies were excluded after reading the full text, remaining 35 included studies (Figure 1). Two independent reviewers examined the titles and abstracts of all manuscripts that met the inclusion criteria. The selected titles were read in full and additional studies were excluded. When the two reviewers did not agree to the exclusion of a study, a third reviewer was asked to read the title and help with the decision. Manuscripts that did not answer the text question, which were not related to the study question (dengue epidemic) and other languages (except English and Spanish and Portuguese) were excluded.

Thirty-five studies complied with the eligibility criteria and were included in the systematic review. Most of them were conducted in the Southeast region of Brazil (N = 22), followed by the Northeast (N = 6), North (N = 3), Central-West (N = 1), and South (N = 2). In addition, one study was carried out in the whole country (N = 1) (Table 1 and Figure 2). Six studies were published in 2010, six in 2015, five in 2017, three in 2008, three in 2011, and four in 2014. The years 2009, 2012, 2013, and 2016 had two publications each. Meteorological and climatic variables were described as related to the dengue epidemic 17 times, followed by the variables related to the vector (12 times), and the socioeconomic and variable related to environmental factor environmental factors (eight times each). Also, we found other associations between dengue and other factors in four studies (Figure 3).

Variables related to the vector

The incidence of dengue was associated or correlated with the amount of eggs collected in ovitraps (10,11) and the entomological indices: Building Infestation Index (IIP) (10-12), Breteau Index (IB) (13-15), Container Index (IR) (16,17), Larvae Index (IL) (17), Pupae per property (PP) (17), and Pupae per hectare (PH) (17).

FIGURE 1. Flowchart of the selection of studies on the factors associated with the occurrence of dengue epidemics in Brazil



Source: Prepared by authors

TABLE 1. Chronological categorization of the studies on the factors associated with the occurrence of dengue epidemics in Brazil published between 2008 and 2018, according to the geographic area and type of factor

Authors	Year	Region	Related factors				
			Vectors	Climatic	Socioeconomics	Environmental	Others
Zeidler et al.	2008	North					
Teixeira & Medronho	2008	Southeast					
Castro et al.	2008	North					
Monteiro et al.	2009	Northeast					
Teixeira	2009	Southeast					
Melo et al.	2010	Northeast					
Scandar et al.	2010	Southeast					
Duque et al.	2010	South					
Barbosa	2010	Southeast					
Cardoso	2010	Southeast					
Souza et al.	2010	Central-West					
Gomes	2011	Northeast					
Malavasi	2011	Southeast					
Teixeira e Cruz	2011	Southeast					
Nhantumbo et al.	2012	Southeast					
Oliveira	2012	Southeast					
Costa, et al.	2013	South					
Varejão	2013	Southeast					
Baía	2014	North					
Farinelli	2014	Southeast					
Johansen	2014	Southeast					
Mondini & Chiaravalloti-Neto	2014	Southeast					
Martins et al.	2015	Northeast					
Silva	2015	Southeast					
Chiaravalloti-Neto et al	2015	Southeast					
Vargas et al.	2015	Southeast					
Araújo et al	2015	Southeast					
Barbosa, Silva	2015	Northeast					
Rodrigues et al.	2016	Brazil					
Pinto	2016	Southeast					
Arantes e Pereira	2017	Southeast					
Correa Filho	2017	Northeast					
Carneiro et al.	2017	Southeast					
Vicente et al	2017	Southeast					
Ferreira	2017	Southeast					

Source: Prepared by authors

Two studies evaluated the number of eggs found in strata and the incidence of dengue and showed correlation to the findings of eggs in the neighborhoods (10) and evaluated districts (11). The number of eggs deposited by *Ae. aegypti* in ovitraps negatively correlated with the incidence rate of dengue cases in a state in the North region of Brazil (10). In the Southeast, a greater risk of dengue incidence was found in locations that had more than 20 eggs per strata analyzed (16).

A negative and weak association (6,14) and a positive and weak correlation (10) among the incidence of dengue and IB for *Ae. aegypti*, and positive and weak association for *Ae. albopictus* (8,18) were found in three studies. The IIP has been positively

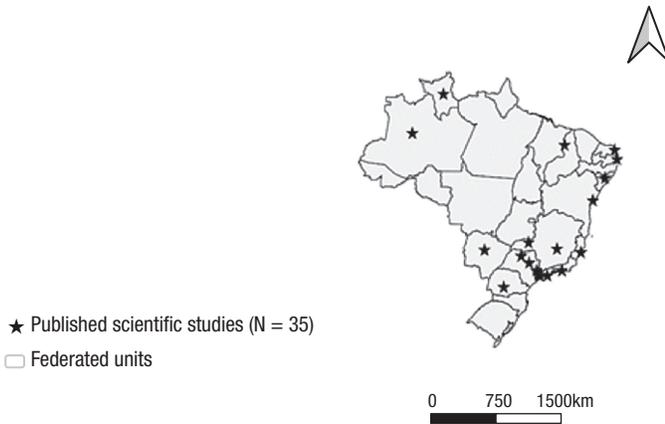
correlated with the incidence of dengue in several studies (6,11,12,14,18,19). There was also a positive and significant correlation between the incidence of dengue and IL grouped by month and considering two months of lag in two epidemic years studied (17). The IR was another indicator that showed a significant positive correlation with the incidence of dengue (16).

One of the selected studies also used the indicators from the World Health Organization (WHO) *Força Motriz-Pressão-Estado-Exposição-Efeito/Ação* (FPPEEA) adapted for the analysis of the occurrence of dengue and showed a positive correlation between the Rapid Index Survey for *Ae. aegypti* (LIRAA) with the average number of dengue cases (13).

Climatic or meteorological variables

More than half of the studies showed an association or positive correlation between climatic and/or meteorological variables and the dengue incidence. Precipitation (6,10,12,14,18,20-24),

FIGURE 2. Distribution of the studies published between 2008 and 2018 on factors associated with the occurrence of dengue epidemics in Brazil, according to the geographical area of study



Source: Prepared by authors

was the predominant factor, followed by temperature (12,16,20,24-28), relative air humidity (24,29), wind direction and speed (24), and average sunspots per month (16).

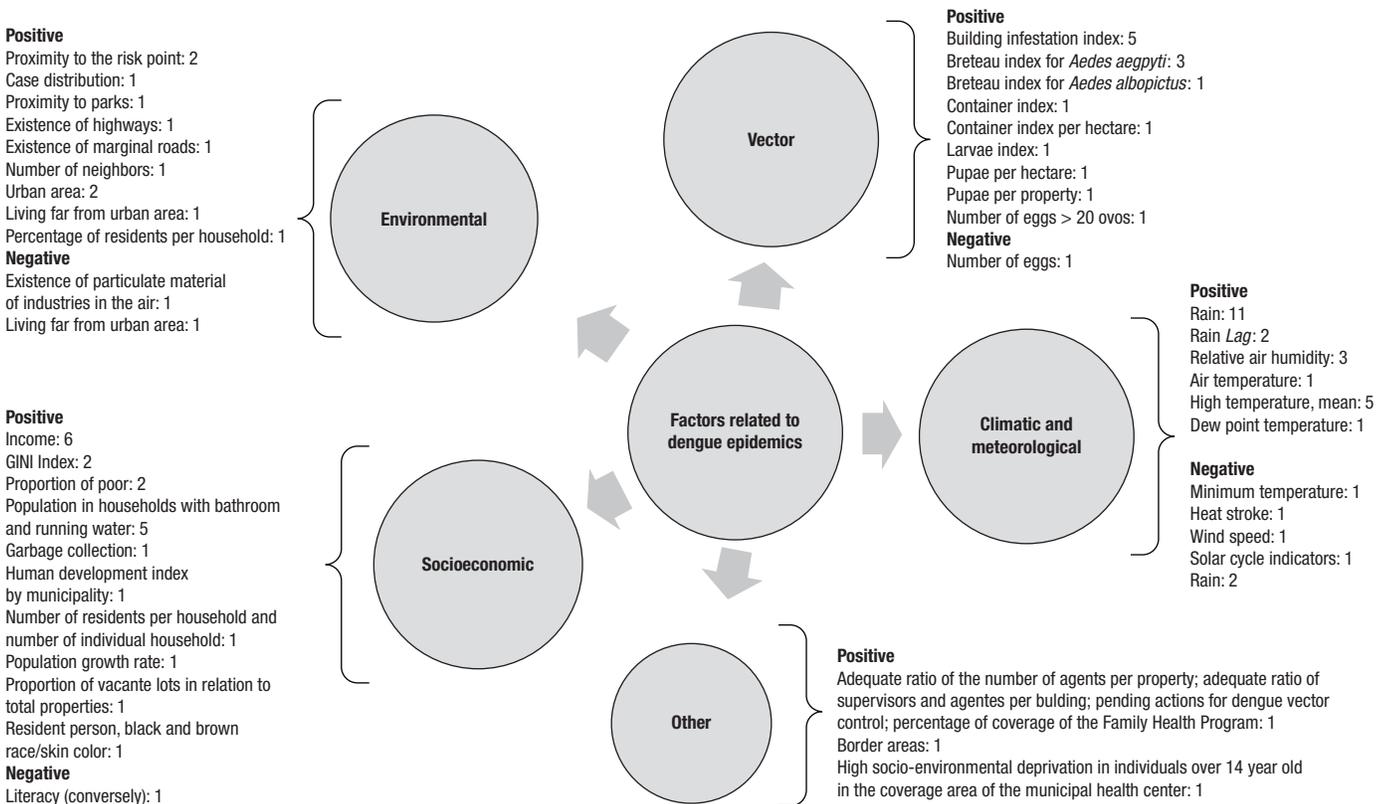
There was a strong positive correlation between precipitation and the number of dengue cases (12), the incidence rates (15,23), and dengue epidemics (18,20,21). Rainfall accounted for only 13.2% of the variation in dengue incidence rates in one study (22).

In a GLM model, a direct association was observed between the incidence of dengue and rainfall and the time lag of a month of rainfall. CAR spatial model for each month, revealed that the incidence of dengue was directly associated with the rainfall in January, March, May, and June, and with the time-lag of rainfall in July (5).

The variables temperature (25); mean temperature without lag and with a lag of one, two, or three months (16); high temperature (26); maximum temperature (27); monthly average and monthly minimum temperature measured at 9 am, 3 pm, and 9 pm (16); sea surface temperature (34); minimum temperature (20); air temperature (24); and land surface temperature above 32 °C (28) were correlated and positively associated with the number of dengue cases in different regions of the country. In one study, the minimum temperature showed a weak and negative correlation with the notifications of the disease (27).

The variables dew-point temperature (27); wind direction (24); solar cycles (30); and wind flow (20) were also positively

FIGURE 3. Positive and negative correlations/association to the occurrence of dengue epidemics verified in the studies published on the factors associated with the occurrence of dengue epidemics in Brazil between 2008 and 2018



Note: The numbers for each factor correspond to the number of studies that presented the positive or negative correlations described. More detailed information is available from the authors upon request.
Source: Prepared by authors

correlated with the incidence of dengue in epidemic years. In addition, the humid climate without a dry season and with a rainy season in the summer; the humid climate without a dry season and with a rainy season in the summer and dry winter; the hot summer with no dry season; and the mild summer with no dry season showed an association with the occurrence of dengue in a study conducted in Brazil (30). The variable relative humidity correlated with dengue epidemics in three studies (20,24,29).

Socioeconomic factors

Many factors were considered including population density and income (31), population growth rate (22), proportion of people living in poverty (21), a lower per capita income (21), a lower proportion of the population in households with bathrooms and running water (21), Gini index (6,30), population with access to piped water, proportion of permanent private households with garbage collection (32), number of literate people responsible for the household (33), human development index (34), gross domestic product (30), and proportion of vacant lots on the total number of properties (22).

Several authors pointed out the small proportion of properties with running water (32), the smaller proportion of the population in households with bathrooms with running water (21), the proportion of permanent private households with garbage collection (35,36), the residents in permanent private households with a general water distribution system (37), and the permanent private households with garbage collection by cleaning service, and water supply from the general network as variables associated or correlated with the incidence of dengue (37).

Income was identified as a predictor of the incidence of dengue when assessed by the Gini index (6,30). In studies conducted in different Brazilian regions that evaluated the variables related to lower per capita income (21,31), income (27), monthly income of 1 to 2 wages (27,37), residents with 3 to 5 minimum wages (27), and proportion of individual houses (27), individuals were most affected by the dengue epidemic.

The literacy rate was also associated or correlated with the incidence of dengue. The analyzed variables were literate people aged five years or older (37), literate responsible (21), illiterate chief (37), and illiterate people (37). In another study, the variable literate person responsible for the household showed a negative association with the incidence of dengue (35).

In one study, poverty was positively associated with the incidence of dengue (21). There was also a positive and significant correlation between the Municipal Human Development Index and the number of dengue cases (21). Only one study identified a correlation between the variable black and brown color/race and the incidence of dengue (37).

Variables related to environmental factors

The environmental variables strategic point; proximity to parks and urban areas (24), existence of highways and marginal roads (38), presence of type A2 (13) deposits, and presence of particulate material (PM10) released by industries (29) were evaluated.

In two studies, houses close to risk points or strategic points showed an important role in the dispersion of the vector mosquito, thus influencing the speed of the spreading of the transmission right after it is installed (39,40). The variables proximity to parks and urban areas (20), shorter distance between urban centers and municipalities (26), existence of highways, and existence of marginal roads in the districts (38) showed a significant association or correlation with the dengue epidemics.

Other factors

The organization of surveillance and health care services was also identified as predictor of dengue epidemics in the country. The period of diagnosis and the registers of the disease were variables associated with the incidence of dengue (25). In addition, the adequate ratio of the number of agents and field supervisors who did not reach the stipulated target of visits was associated with the dengue epidemic in one study (21). The percentage of coverage of the teams of the Family Health Program (Programa de Saúde da Família) showed a negative correlation with the dengue epidemic in another study (15). Intervention indicators such as pending actions in dengue vector control programs were also positively associated with dengue transmission in 10 to 24.9% (15). There was also a positive correlation between dengue epidemics and the ratio between the distance from the first detected dengue case and the number of neighbors (39) and the variables areas of boundary and borders with Brazil in two Brazilian states (Maranhão and São Paulo) and one country (Paraguay) (41).

DISCUSSION

We analyzed publications available in different scientific electronic databases for the years 2008 to 2018. Among the factors related to dengue epidemics, the climatic or meteorological factors stood out in 17 studies. In addition, related variables socioeconomic, environmental, and other factors also stood out. To the best of our knowledge, this is the first study to present a broad description of the factors involved in dengue epidemics in Brazil.

Indicators such as IIP, IB, and ITR were addressed by several authors (6,11,12,15,32,42), who mostly found them related with dengue epidemics. Few studies showed a positive but weak correlation between larval indicators and the incidence of dengue (6,14,16). Other studies presented a strong positive correlation (13,17), suggesting that these larval indicators have the potential to describe the behavior of dengue in the years studied.

Studies that assess the pupal stage are more likely to be accurate in understanding the biology of *Ae. aegypti* when compared to studies with larvae. The duration of a pupa is about 2 days depending on the temperature (3), so these studies are more difficult to be performed. Therefore, studies with pupae can provide more adequate responses for the control of the vector and the reduction of arboviruses.

The mortality rate of pupae is almost zero. Pupae become adult individuals, unlike the larvae, which are influenced by the temperature of the environment, the volume of water, the amount of food present in the container and, therefore, have a higher mortality rate (4,43). Corroborating this finding, a study carried out

in 2014 in São José do Rio Preto (Sao Paulo), showed that pupal indicators were positively associated with the incidence of dengue (42). Prioritizing the finding of immature forms of the vector at strategic points or points of risk has been a constant target in the plans proposed to intensify vector control in interepidemic periods (44). Two studies have evaluated these points and showed that they influence the speed of spreading of dengue (39,40).

Rain was positively associated or correlated with dengue epidemics in different regions of the country (6,10,12,14,18,21,23). Temperature, another factor that influences various stages of *Ae. aegypti* development, has been correlated or associated with dengue epidemics in several studies (12,16,20,24-26,28). At temperatures favorable to their life cycle, insects not only complete their development but do so more quickly, which can increase the vector's competence for arboviruses (45,46). The present systematic review also showed three studies (20,24,29) in which the relative humidity of the air was correlated or associated with the oviposition behavior of the mosquito populations studied, which consequently correlated to dengue epidemics in these regions.

Variables related to economic social factors played an important role in the dengue epidemics in the state of Amazonas (44), in the municipalities of Salvador (Bahia) (36), Natal (Rio Grande do Norte) (22), Várzea Paulista (Sao Paulo) (33), Caraguatuba (Sao Paulo) (41), São José do Rio Preto (Sao Paulo) (47), Osasco (Sao Paulo) (37), Araraquara (Sao Paulo) (35), Rio de Janeiro (Rio de Janeiro) (14), Itaboraí (Rio de Janeiro) (32), Vitória (Espírito Santo) (48), and in Brazil as a whole (36). It was observed that in all regions of Brazil, the socioeconomic factor was determining for the dengue epidemic. Some structural problems of the current health system continue to be positively associated with dengue epidemics, such as the number of field agents per property and the ratio of endemic agent supervisors to buildings, which is lower than initially proposed for the coverage of certain areas (21).

The association between the occurrence of dengue and the proportion of containers to store water at ground level was shown in one study (13). A similar result was seen in another study carried out in 2015 (after the 2014 water crisis) in the Southeast region, which showed a correlation between the same group of containers with the incidence of dengue (49). The population's behavior of retaining water in storage containers allows the development of immature forms of the *Ae. aegypti*, which were verified in several states in the Southeast and Northeast regions of the country (36).

The vectors *Ae. aegypti* and *Ae. albopictus* are commonly found inside homes and in properties close to homes, such as vacant lots and backyards (3). Studies in the Southeast region have shown that the proximity to parks, urban areas, and the number of neighbors, in addition to the proportion of the human population, are directly associated with the incidence of dengue (14,20,26). Nevertheless, the authors of a study carried out in 2017, in the Greater ABC Paulista, argue that the presence of pollution from factories in industrial areas negatively correlates with the increase in the number of dengue cases (29).

Another reported difficulty is the number of pending actions in the vector control of dengue, as a high proportion of properties are closed or deny access to the endemic agents (15). In addition, it was found that the low coverage of the Family Health Program (15) and the insufficient coverage of the Municipal Health Center for individuals (50) were also considered risks for dengue epidemics.

Although we followed the recommendations of PRISMA, there is a possibility of publication bias, which may hinder generalizations of the results in the present study. Also, most of the studies were ecological type, so it is important to consider the possibility of ecological bias. The ecological studies presented different methodologies and analytical approaches, so this can be a problem for external validity and generalization. The quality assessment wasn't possible due to the lack of a specific and robust tool to evaluate ecological studies.

We hope that the information reported here can guide the understanding of the installation of epidemics in the country given the different problems related to the environment, infrastructure, meteorological and climatic characteristics, and the great Brazilian territorial extension. Another relevant aspect verified in the studies included in the present systematic review is the recommendation for the continuity of effective actions to control the vector in non-epidemic periods to avoid a subsequent epidemic. Studies that continuously investigate the factors associated with dengue epidemics should be encouraged. The endemic-epidemic character of the disease in Brazil, associated with the circulation of other arboviruses transmitted by *Ae. aegypti*, reinforce the need for comprehensive studies in different areas of knowledge for the improvement and the development of new strategies and/or tools for its control and prevention.

In conclusion, factors associated with dengue epidemics go beyond the health sector and reveal inequalities on social determinants of affected populations. The vector's ability to adapt to human-inhabited environments, the organization of geographic spaces in urban centers, people's cultural habits, the socioeconomic level of the population, changes in the population's behavior, social inequalities, social determinants of health, and the country's climate, among others, are factors that favor the risk of dengue epidemics. In the studies analyzed here there was an association between the variables "air pollution produced by the factory" and "wind speed" as an inhibitor of mosquito proliferation in some regions, which can reduce the occurrence of epidemics. Therefore, the development of a vaccine, the fight against the vector, the provision of adequate water, education actions targeting the population, the structuring of services to prevent and combat the vector, as well as measures for the early detection of cases are important in the control of the disease in Brazil.

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Authors' contributions. SCS, JMTB and DSB: conception and design of the study, data analysis. SCS, JMTB and DSB, MC and AEE: data interpretation and critical review of the manuscript. All authors revised and approved the final submitted version.

Conflicts of interest. None declared.

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Factores asociados a la aparición de epidemias de dengue en Brasil: revisión sistemática

RESUMEN

Objetivo. Determinar y describir de manera amplia los factores relacionados con la aparición de epidemias de dengue en Brasil.

Métodos. Se llevó a cabo una revisión sistemática de los estudios publicados en MEDLINE, LILACS, PubMed, Cochrane, BVS, Web of Science, Scopus y en bases de datos de tesis y trabajos de final de grado con los descriptores catalogados en DeCS y MeSH sobre dengue y factores asociados con la aparición de epidemias publicados entre 2008 y 2018.

Resultados. Se seleccionaron 35 estudios llevados a cabo en Brasil. Las epidemias registradas en el país se asociaron o se relacionaron con diversos factores, como el medioambiente, las condiciones socioeconómicas, el clima y aspectos relacionados con el vector, entre otros.

Conclusiones. Las epidemias de dengue son complejas y multifactoriales. Se constató que la continuidad de las medidas de control de vectores es pertinente para la reducción de *Aedes aegypti*, así como para el control de la enfermedad. Para contener la propagación de la enfermedad son necesarias medidas eficaces en todos los sectores, como la salud, la educación, la economía, la población, las empresas y el gobierno. Las medidas de detección temprana de casos de la enfermedad pueden prevenir nuevos brotes de epidemias.

Palabras clave

Dengue; factores de riesgo; epidemias; Brasil.

Fatores associados à ocorrência de epidemias de dengue no Brasil: uma revisão sistemática

RESUMO

Objetivo. Identificar e descrever, de forma geral, os fatores relacionados à ocorrência de epidemias de dengue no Brasil.

Métodos. Revisão sistemática de estudos publicados entre 2008 e 2018 nas bases de dados MEDLINE, LILACS, PubMed, Cochrane, BVS, Web of Science e Scopus e em bancos de teses e dissertações, com o uso de descritores de dengue e de fatores associados à ocorrência de epidemias catalogados no portal DeCS/MeSH.

Resultados. Trinta e cinco estudos realizados no Brasil foram selecionados. As epidemias registradas no país foram associadas e/ou correlacionadas a vários fatores como meio ambiente, condições socioeconômicas e climáticas, e aspectos relacionados ao vetor, entre outros.

Conclusões. As epidemias de dengue são complexas e multifatoriais. Observou-se que ações contínuas de controle vetorial são essenciais para a redução da população de *Aedes aegypti* e o controle da doença. Para conter a propagação da dengue são necessárias medidas multissetoriais eficazes, abrangendo saúde, educação, economia, população, negócios e governo. As ações visando à detecção precoce de casos da doença contribuem para prevenir novos surtos epidêmicos.

Palavras-chave Dengue; fatores de risco; epidemias; Brasil.
