



RESEARCH ARTICLE

ZIKA VIRUS, FROM DISCOVERY TO THE PRESENT DAYS: BIBLIOMETRIC REVIEW STUDY

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ABSTRACT

Facing the crescent transmission of Zika virus in Brazil and elsewhere, the objective of this study was to analyze the number and features of publications since the discovery of the virus until May 2016. A bibliometric and integrative review of literature using the single descriptor "Virus Zika" to reach researches around the world. Were found 428 papers and 321 analyzed in this study, of which 59.8% were indexed in PubMed database. The increasing number of publications of different aspect of the virus and epidemics is remarkable and show the rapid answer from research institutes, universities and groups, financial agencies to face this emergent public health threat.

INTRODUCTION

The Zika virus was identified in monkeys of the species *Rhesus* in 1947 in the Zika forest in Uganda, Africa, during a research on sylvatic yellow fever⁽¹⁾. It is an arbovirus of the genus *Flavivirus* and family *Flaviviridae* that contains single-stranded RNA and is transmitted by *Aedes* mosquitoes¹⁻⁸. Between 1964 and 1970, about 171 arbovirus of 15 different types were isolated in humans in Nigeria, including Zika virus⁹. By the end of the last century, the virus was known a zoonotic pathogen with sporadic cases in humans in African countries and later in Southeast Asia^{8,10}. In Africa, the virus had remained in sylvatic cycle, infecting monkeys and *Aedes* mosquitoes. The spread of the disease in Asia evolved for transmission in humans by *Aedes aegypti* mosquitoes and then to the Pacific Islands and South America^{2, 9, 11-15}. After an outbreak of a disease characterized by rash, conjunctivitis, fever, arthritis and arthralgia in Yap Islands, Federated States of Micronesia, between April and May 2007, the disease was clinically distinct from dengue, identifying similar reports in prior outbreaks³⁻⁵. Until this epidemic in Micronesia, there were 14 reported cases of the disease in humans by Zika

virus in the literature, and there was no report of transmission outside Africa or Asia^{5, 16}. The biggest outbreak in humans was observed in French Polynesia, between 2013 and 2014, after the disease had spread to other Pacific islands where the *Aedes* sp is present¹⁷. In the Americas, autochthonous cases related to the Asian strain of the Zika virus were associated with tourists who came to Brazil for the soccer World Cup in 2014, constituting a possible gateway to the virus circulation in the country and an epidemiological alert to America⁷. Finally a complete genomic analysis of the virus in the Americas found that the disease arrived in Brazil between the months of May to December 2013, during the Confederations Cup¹⁸. Originating from French Polynesia, this virus found in Brazil favorable environmental (climatic, urban) and sociodemographic conditions, and the presence of a massive amount of vectors, which increased its circulation¹⁸. Suspected cases were reported in the cities of Natal, Rio Grande do Norte, and Recife, Pernambuco, and other smaller towns⁷. The first reported outbreak in Brazil and the Americas took place between April and May 2015, in Camacari, Bahia⁶ and the autochthonous transmission of Zika virus was confirmed in the Northeast region of the country by the Ministry of Health in the same period¹⁰. With the increase of transmission Zika virus and suspected association with cases of microcephaly in northeastern Brazil, was noticed the increase in scientific

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publications about the disease and its complications. The aim of this study was to analyze features of the publications since the discovery of the virus until May 2016. Examining the scientific agenda on emerging circulation of Zika virus in a quantitative perspective allows us to observe the trend of the publications, to analyze the characteristics of the studies and to place the research on the topic in the scientific literature.

MATERIALS AND METHODS

It was performed a bibliometric and integrative literature review guided in the terminologies registered in Descriptors of Health Science (DeCS) by the Virtual Health Library, developed from the Medical Subject Headings (MeSH) of the US National Library of Medicine, which allows the use of common terminology in Portuguese, English and Spanish languages. This study only used the expression Zika virus (which has synonymous: Zika fever virus, Zikavirus, ZIKV) as descriptor for searching published articles. The analyzed databases were LILACS (Latin American and Caribbean Health Sciences), SciELO (Scientific Electronic Library Online), BVS (Biblioteca Virtual emSaúde), MEDLINE (Medical Literature Analysis and Retrieval System Online) and PubMed (National Library of Medicine – NLM® - of the United States). Based on this, the relevant references for the survey of results against the proposed objective were selected. The selection of publications was based on the following inclusion criteria: the article should be indexed in the consulted databases, have been published between January 1947 and May 2016 in any language, be related to the theme "Zika virus" and be of public domain for consultation.

A total of 428 studies were found. Among these, 25 were found in LILACS database, 28 in SciELO, 3 in the BVS, 116 in MEDLINE and 256 in PubMed.

The flowchart of the selection of the articles that composed the bibliometric revision is in Figure 1.

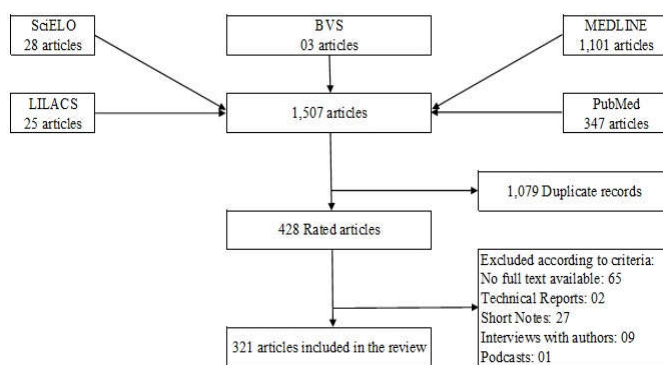


Figure 1. Flowchart of the selection of the studies that compose the bibliometric review

After reading the material, authors carried out a review for identification of the proposed subject in the articles, since the discovery of the virus until the current epidemics. For data collection, it was used a form applied to all selected articles from the final sample. The information was grouped according to authors, publication source, year of publication, language (considering the first language of publication in magazines), thematic area, country of origin, objectives, applied methodology, results and conclusions. Authors selected 321 publications for this study, discarding the works indexed in

more than one database, the technical reports, the short notes, the interviews with authors and the podcasts.

RESULTS AND DISCUSSION

Most of the studies were indexed in the PubMed database (59.8%), although most of the articles indexed in MEDLINE were also present in PubMed, which has greater efficiency and uniqueness in most publications on the topic "Zika virus." Table 1 shows a quantitative analysis of publications selected for the study according to the journal. It was found that 9.3% (n = 30) of articles have been published in the Emerging Infectious Diseases Journal, 8.4% (n = 27) in The Lancet, 8.4% (n = 27) in the Morbidity and Mortality Weekly Report and 5.9% (n = 19) in the PLOS Neglected Tropical Diseases, from a total of 114 journals.

Table 1. Number of publications per periodic, from 1947 to May 2016

Name of the Journal	No. of Publications	
	n	%
Emerging Infectious Diseases Journal	30	9.3
Morbidity and Mortality Weekly Report	27	8.4
The Lancet	27	8.4
PLOS Neglected Tropical Diseases	19	5.9
The New England Journal of Medicine	10	3.1
BMJ	8	2.5
Eurosurveillance	8	2.5
Nature	7	2.2
Science	7	2.2
Bulletin of the World Health Organization	5	1.6
Genome Announcements	5	1.6
International Journal of Infectious Diseases	5	1.6
Journal of the Formosan Medical Association	5	1.6
The American Journal of Tropical Medicine and Hygiene	5	1.6
The Lancet Global Health	5	1.6
Asian Pacific Journal of Tropical Medicine	4	1.2
PLOS Currents	4	1.2
The Journal of Infection in Developing Countries	4	1.2
The Journal of the American Medical Association - JAMA	4	1.2
Blood Transfusion	3	0.9
Cadernos de Saúde Pública	3	0.9
Emerging Microbes & Infections - Nature	3	0.9
F1000 Research	3	0.9
Jornal de Pediatria (Rio de Janeiro)	3	0.9
Journal of Clinical Virology	3	0.9
PLOS One	3	0.9
Revista da Associação Médica Brasileira	3	0.9
Transactions of the Royal Society of Tropical Medicine and Hygiene	3	0.9
Acta Médica Portuguesa	2	0.6
Arquivos Brasileiros de Oftalmologia	2	0.6
BMC Medicine	2	0.6
Brazilian Oral Research	2	0.6
Bulletin de la Société de Pathologie Exotique et de ses Filiales	2	0.6
Cell Reports	2	0.6
Frontiers in Microbiology	2	0.6
Journal of Global Infectious Diseases	2	0.6
Journal of the Chinese Medical Association	2	0.6
Medicine (Baltimore)	2	0.6
Memórias do Instituto Oswaldo Cruz	2	0.6
New Microbes and New Infections	2	0.6
Revista da Sociedade Brasileira de Medicina Tropical	2	0.6
Revista do Instituto de Medicina Tropical de São Paulo	2	0.6
The Brazilian Journal of Infectious Diseases	2	0.6
The New Microbiologica	2	0.6
The Weekly Epidemiological Record	2	0.6
Ultrasound in Obstetrics & Gynecology	2	0.6
Virology Journal	2	0.6
AIDS Reviews	1	0.3
American Journal of Perinatology	1	0.3
American Journal of Public Health	1	0.3

Annals of Clinical Microbiology and Antimicrobials	1	0.3
Annals of Tropical Medicine and Parasitology	1	0.3
Archives of Disease in Childhood	1	0.3
Archives of Virology	1	0.3
Arquivos de Neuro-Psiquiatria	1	0.3
Archivos Venezolanos de Puericultura y Pediatría	1	0.3
BMC Genomics	1	0.3
BMC Infectious Diseases	1	0.3
Boletín de Malariología y Salud Ambiental	1	0.3
Brasil - Ministério da Saúde	1	0.3
Brazilian Journal of Medical and Biological Research	1	0.3
British Journal of Hospital Medicine	1	0.3
British Journal of Nursing	1	0.3
Canadian Medical Association Journal	1	0.3
Cell & Bioscience	1	0.3
Cell Host & Microbe	1	0.3
Cleveland Clinic Journal of Medicine	1	0.3
Clinical Microbiology and Infection	1	0.3
Dongwuxue Yanjiu Journal	1	0.3
EBioMedicine	1	0.3
Elife	1	0.3
EMBO Molecular Medicine	1	0.3
Epidemics	1	0.3
Epidemiologia e Serviços de Saúde	1	0.3
Epidemiology and Health	1	0.3
Global Health Action	1	0.3
ID Cases	1	0.3
Infectious Diseases of Poverty	1	0.3
International Maritime Health	1	0.3
JMIR Public Health and Surveillance	1	0.3
Journal of Korean Medical Science	1	0.3
Journal of Medical Virology	1	0.3
Journal of Virology	1	0.3
Medical Microbiology and Immunology	1	0.3
Medical Surveillance Monthly Report	1	0.3
Medicina (Buenos Aires)	1	0.3
Médecine et Maladies Infectieuses	1	0.3
Molecular Cytogenetics	1	0.3
Netherlands Journal of Medicine	1	0.3
Nigerian Postgraduate Medical Journal	1	0.3
North American Journal of Medical Sciences	1	0.3
Oman Medical Journal	1	0.3
Pediatric Neurology Briefs	1	0.3
PeerJ	1	0.3
Pharmacy & Therapeutics	1	0.3
Revista Brasileira de Ginecologia e Obstetrícia	1	0.3
Revista Brasileira de Hematologia e Hemoterapia	1	0.3
Revista Brasileira de Medicina do Trabalho	1	0.3
Revista Chilena de Infectología	1	0.3
Revista Chilena de Pediatría	1	0.3
Revista Colombiana de Anestesiología	1	0.3
Revista de Neutología	1	0.3
Revista de Investigación Clínica	1	0.3
Revista MVZ Córdoba	1	0.3
Revista Salud Bosque	1	0.3
Scientific American	1	0.3
South African Medical Journal	1	0.3
Swiss Medical Weekly	1	0.3
The Anatolian Journal of Cardiology	1	0.3
The Journal of Hygiene	1	0.3
Transfusion	1	0.3
Tropical and Geographical Medicine	1	0.3
Vector-Borne and Zoonotic Diseases	1	0.3
Zhonghua Wei Zhong Bing Ji Jiu Yi Xue	1	0.3
Total	321	100

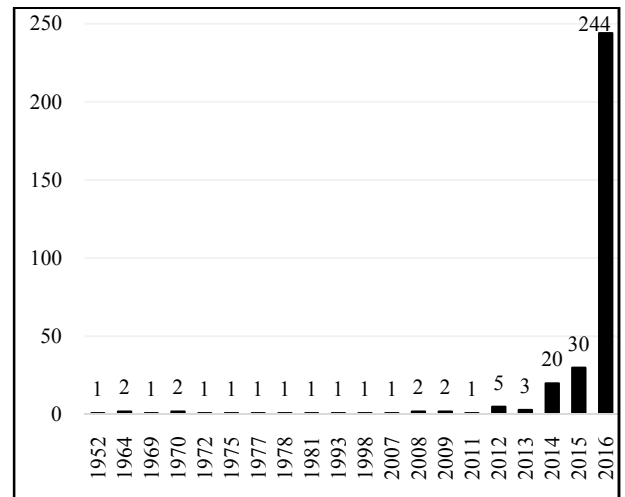


Figure 2. Historical series of publications about Zika virus, from 1947 to May 2016

By checking the different types of publication, it was found that 87.7% (n = 100) of the journals are registered in the Thematic Area of Medical Sciences and regarding the subject of each journal, 27.2% (n = 31) are about Medicine, 10.5% (n = 12) are about communicable diseases and 8.8% (n = 10) are about tropical medicine, as shown in Table 2. According to the catalog of books, journals and audiovisual material of the National Library of Medicine US (NLM Catalog) and to the Scientific Journals Portal on Health Sciences of the Brazilian Virtual Health Library.

Table 2. Number of publications about Zika virus by thematic area and subject, from 1947 to May 2016

Type of Publication	No. of Publications	
	n	%
Thematic area		
Medical Sciences	100	87.7
Biological Sciences	11	9.6
Sciences	3	2.6
Total	114	100.0
Subject		
Medicine	31	27.2
Communicable Diseases	12	10.5
Tropical Medicine	10	8.8
Public Health	8	7.0
Microbiology	7	6.1
Epidemiology	5	4.4
Pediatrics	5	4.4
Virology	5	4.4
Sciences	3	2.6
Genetics	3	2.6
Molecular Biology	2	1.8
Gynecology and Obstetrics	2	1.8
Hematology	2	1.8
Veterinary Medicine	2	1.8
Neurology and Psychiatry	2	1.8
Anesthesiology	1	0.9
Cell Biology	1	0.9
Biomedicine	1	0.9
Cardiology	1	0.9
Critical care	1	0.9
Vector diseases	1	0.9
Nursing	1	0.9
Pharmacy	1	0.9
Infectology	1	0.9
Occupational Medicine	1	0.9
Dentistry	1	0.9
Ophthalmology	1	0.9
Perinatology	1	0.9
Government Protocol	1	0.9
HIV/AIDS	1	0.9
Total	114	100

Regarding the language of publication, 97.2% of the selected publications were written in English, 1.6% in Spanish and 1.2% in Portuguese, which shows that the majority are published in English to increase the potential for dissemination of the publication. Some published works were available in more than one language, but English has always been the first choice of presentation of articles in journals. When analyzing the publications over this period, it was found that 244 (76%) of the works were published in 2016, as shown in Figure 2. It is clear that the epidemic of Zika virus since 2015 has resulted in increased research and consequently number of publications.

As regards the place of publication, the United States stood out with 129 articles (39.3%), followed by England, with 85 (26.4%), and Brazil, with 29 (9%), as described in Table 3. It is noteworthy the position of Brazil among the countries that most develop researches on this emerging national public health problem. This can be explained by the rapid dissemination of virus in the country and the increase in cases of microcephaly. In Brazil was observed a rapid response of research financing agencies, as well as institutes and universities in the form of allocation of resources, public notices and mobilization of research groups. As the main scientific language in health area is English, the great demand of the papers published in that language is evident, so that communication among researchers worldwide is facilitated. The types of conducted studies identified were: 145 (45.2%) editorials^{6-8,10,17,19-158}, 52 (16.2%) laboratory studies (basic research^{1,3,4,11,18,159-205}, 36 (11.2%) cross-sectional studies^{5,9,12-16,206-234}, 30 (9.3%) are case reports^{2,235-263}, 25 (7.8%) literature reviews²⁶⁴⁻²⁸⁸, 12 (3.7%) ecological studies²⁸⁹⁻³⁰⁰, 10 (3.1%) descriptive reports³⁰¹⁻³¹⁰, 7 (2.2%) cohort studies³¹¹⁻³¹⁷, 2 (0.6%) case-control studies^{318,319}, 1 (0.3%) an intervention study³²⁰ e 1 (0.3%) a government protocol³²¹. There are several gaps in knowledge of the Zika virus, including its molecular structure, the origin of the virus, and the role of hosts and vectors involved in the transmission cycle²⁸⁶.

Table 3. Number of publications about Zika virus by Country, from 1947 to May 2016

Country	No. of Publications	
	n	%
United States	126	39.3
England	85	26.5
Brazil	29	9.0
China	13	4.0
France	11	3.4
Netherlands	8	2.5
Italy	8	2.5
Switzerland	8	2.5
Canada	7	2.2
Colombia	3	0.9
India	3	0.9
Chile	2	0.6
South Korea	2	0.6
Portugal	2	0.6
Venezuela	2	0.6
South Africa	1	0.3
Germany	1	0.3
Argentina	1	0.3
Austria	1	0.3
Spain	1	0.3
Mexico	1	0.3
Nigeria	1	0.3
Oman	1	0.3
Pakistan	1	0.3
Poland	1	0.3
Sweden	1	0.3
Turkey	1	0.3
Total	321	100

In the first decades, there had been little research on the disease, the vectors, the transmission, complications related to human health and its spread. Only after 2007, with an increase in reported cases in humans, research has increased significantly, so the interest of scholars started to face towards epidemiological and clinical aspects in order to understand the impact on human populations. The World Health Organization and governments are clearly concerned with the susceptible population to clinical complications, particularly related to pregnant women and newborns, neurological conditions, as well as to the potential genetic evolution of this RNA virus,

that might compromise possible control strategies²¹⁶. Also, a major gap is the lack of knowledge about the animal reservoirs and viral expansion hosts, including domestic animals and the natural vectors of Zika virus, as well as the transmission capacity by vectors of the genre *Aedes*, *Anopheles* and others^{279, 285}. Investigations on the dynamics of transmission and geographical spread of the virus are highly relevant^{178, 298}. The increase in publications on the Zika virus in its various aspects has been remarkable, and the open access of journals and scientific publications in recent years has shown the rapid response of the scientific community to an emerging public health problem.

Conclusion

Based on scientific articles and surveyed literature, it can be stated that the increase in the number of publications occurred in face of the high number of cases since 2015, and mainly due to notification of cases of microcephaly, suspected of being associated with the infection, since the beginning. Together with the large number of basic research on the structure and interactions of Zika virus, epidemiological studies can help to elucidate the long-term consequences of the infection and identify other risk factors, with the potential for intervention. The dynamic of the epidemic and its pandemic character in various social contexts around the world still require mapping and research. Moreover, the understanding of additional risk factors associated with complications of the disease, the synthesis of a vaccine and of drugs to treat the infection and its complications are still major challenges for science and public health worldwide. The information shared in research networks in a collaborative and solidary way can potentiate efforts to combat the epidemic and the improvement of control and prevention measures.

Conflict of interest

The authors declare that there is no conflict of interest.

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