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EDITORIAL / *EDITORIAL*

Zika virus: challenges of public health in Brazil

Zika vírus: desafios da saúde pública no Brasil

Comissão de Epidemiologia da Abrasco*

In October 2014, an outbreak of a febrile rash illness of unknown etiology was identified in Rio Grande do Norte, Northeastern Brazil, whose clinical symptoms were mild fever or no fever, maculopapular rash, itching, arthralgia, and limb edema, lasting for 4 – 7 days[1]. In the following months, similar cases have been identified in other states in the Northeast, and then in other regions of the country. In early May 2015, Zika virus (ZIKV), an arbovirus that, until then, had circulated neither in Brazil nor in continental America, was confirmed through RT-PCR tests in 16 of 46 samples from Bahia and Rio Grande do Norte[2]. In a short period, the ZIKV infection was confirmed in different Brazilian states, spreading to several countries in Latin America and the Caribbean, as well as cases were reported in the United States and Europe.

In November 2015, the Ministry of Health declared emergency in Public Health and, in February 2016, the World Health Organization identified the emergency situation as of international importance, facilitating research initiatives and disease control in the country.

The circulation of ZIKV occurred simultaneously to dengue epidemics (DENV) of major proportions in dense regions chronically infested by *Aedes aegypti*, and simultaneously to the circulation of another emerging arbovirus, chikungunya (CHIKV)[3,4]. These three arboviruses (DENV, CHIKV, and ZIKV) have the mosquito *A. aegypti* as their main vector.

The co-circulation of DENV, CHIKV, and ZIKV in Brazil complicates the clinical management of patients; has implications on the transmission in the elderly, pregnant women, and young children; and still has limited laboratory support.

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The impact of viral co-circulation is still little known. As in the case of reinfection by different serotypes of DENV, the interaction of arboviruses (dengue serotypes 1-4, CHIKV, and ZIKV) could theoretically result in more intense viremia or other immunological changes[5] that could trigger autoimmune diseases, such as Guillain–Barré syndrome.

The association of microcephaly cases with the infection of pregnant women by ZIKV was recently presented through virological and pathological fetal images and analyses[6], and confirmed by Brazilian studies through virus identification and sequencing in amniotic fluid from two women who had the infection during pregnancy and fetuses with microcephaly[7,8]. Although microcephaly is linked to many environmental and genetic exposures, drug use during pregnancy, infections such as rubella, toxoplasmosis, and cytomegalovirus, among others, the association with ZIKV infection follows the increase of cases of microcephaly and other neurological malformations in Brazil since 2015[9].

Until March 12, 2016, the Emergency Operations Center in Public Health on Microcephaly of the Brazilian Ministry of Health (MOH) announced the confirmation of 863 cases of microcephaly and/or alteration of the central nervous system (CNS), which suggest congenital infection, still based on the previous criteria for head circumference of 32 cm for newborns with 37 or more weeks of gestation[10]. On March 10, the cutoff point was reduced to 31.9 cm for boys and 31.5 cm for girls. The investigation of 6,680 cases of microcephaly already ruled out 1,349 of them, with 97 cases of microcephaly and other neurological disorders confirmed by specific laboratory criteria for ZIKV (PCR technique and serology)[10].

Other hypotheses, never confirmed, have been suggested to explain the increase in microcephaly cases, including the assumption that this and other malformations are associated with the use of the larvicide pyriproxyfen. In addition to evidence from recent studies that connect the neurological disorders in infants to previous infection of pregnant women by ZIKV, it is worth noting that in the epidemic in French Polynesia, in 2013–2014, in which this larvicide was not used, microcephaly cases were found in a retrospective study[11], and that in the city of Recife, one of the areas most affected by the ZIKV epidemic and with the highest number of microcephaly cases[9], the referred larvicide was also not used.

The transmission of ZIKV in Brazil raises many concerns: the social and ecological context in the Americas, particularly in Brazil, promotes the spread of arboviruses and the occurrence of severe cases associated with viral co-circulation; the current strategy in handling the vector in most areas has proven ineffective; climate and environmental conditions are appropriate for the activity and reproduction of the vector; cities crowded with intense flow of travelers makes Brazil not only vulnerable to large outbreaks but also a dispersal point of cases for the rest of the world.

Despite the economic and political difficulties faced by the country, research groups and institutions are working hard in facing this huge challenge to global public health. Several studies have been suggested and are underway to answer basic questions about this emerging disease, but little is known. A scientific agenda was proposed in a joint venture between the Ministry of Science and Technology and the Oswaldo Cruz Foundation, advising six broad research areas, from the production of knowledge on the infection, disease and outcomes, development of diagnostic tests, clinical management protocols and development of vaccines, to interventions on the health-care system[12]. Among the many questions that remain unanswered, it is worth highlighting a few: what is the real dimension of the ZIKV epidemic in Brazil? What is the percentage of affected pregnant women and, among them, what is the proportion of infants with neurological changes? What are the immunological characteristics of pregnant women that facilitate infection of the fetus? What genetic profile of the fetus, or type of immune response, acts in triggering more severe neurological impairment? How do the temporal and spatial dynamics of the distribution of ZIKV-infected vectors behave and how does it relate to asymptomatic and symptomatic cases? How does the interaction between *A. aegypti* and ZIKV occur? Are there other vectors with potential for transmission? What are the clinical implications of the co-circulation of ZIKV and other flaviviruses?

These are just some of the many questions to be answered. The apparent rapid expansion of the ZIKV transmission area in Brazil must now be seen as an emerging public health challenge, not only for the country but also for all America. Several epidemiological studies are being conducted or are in the planning stages in the country, with the aim of knowing the disease from a clinical, epidemiological, and laboratorial point of view. Animal models have been suggested to investigate how the virus affects the nervous tissue; other research groups seek biochemical pathways and proteins in the central nervous system that are targets of congenital infection and potential therapeutic loci.

There are efforts underway for the synthesizing of a protective and immunotherapeutic vaccine, in addition to conducting sensitive and specific serological reactions, with little cross-reactivity to other flaviviruses.

PERSPECTIVES

Faced with the challenge of handling a still unknown disease and with few diagnostic tools available, many actions have been proposed, including: strengthening the Unified Health System (SUS) and the complex epidemiological surveillance system to detect suspected cases; strengthening the support and assistance network to affected patients; organizing a network of laboratories with well-defined criteria for the investigation of suspected cases using PCR reaction until serological tests are available; investing heavily in vector control, training of health professionals and in community participation to fight off the epidemic; using known larvicides and insecticides with technical rigor, as well as alternative substances previously assessed by the National Health Surveillance Agency (ANVISA) which showed proven efficacy, as well as using biological control methods that do not harm the environment; improving the health information systems of the Informatics Department of the Unified Health System (DATASUS) and the Mortality Information System (SIM), the Live Births Information System (SINASC), the Information System for Notifiable Diseases (SINAN), and the Hospital Information System (SIH) to continue providing reference information to guide specific epidemiological investigations.

In the research area, research efforts should be coordinated with the integration of groups to streamline and increase the response speed on various aspects of the disease in the country. Therefore, it is suggested that research protocols in place are disseminated to facilitate the comparison of results; simplifying the exchange of biological materials and partial research results; and proposing and conducting multicentric studies. Strengthening the Department of Science and Technology (DECIT) to formulate, implement, and prioritize the research agenda that is of national interest.

The Brazilian Collective Health Association (Abrasco) can promote the integration of efforts, stimulating, mediating, and assisting in the formation of research networks that act in solidarity, increasing investment and streamlining endeavors and competencies. It can and should, being a scientific association with great respectability in the country, contribute to the dialogue between academia, particularly the groups involved with the research, the population, and the government, disseminating the results of studies, informing policies and stimulating their immediate application.

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REFERENCES

1. Zanluca C, Mel VCAD, Mosimann AP, Santos GIVD, Santos CNDD, Lu K. First report of autochthonous transmission of Zika virus in Brazil. Mem Inst Oswaldo Cruz 2015; 110(4): 569-72.
2. Campos GS, Bandeira AC, Sardi SI. Zika virus outbreak, Bahia, Brazil. Emerg Infect Dis 2015; 21(10): 1885-6.
3. Roth A, Mercier A, Lepers C, Hoy D, Duituturaga S, Benyon E, et al. Concurrent outbreaks of dengue, chikungunya and Zika virus infections – an unprecedented epidemic wave of mosquito-borne viruses in the Pacific 2012-2014. Euro Surveill 2014; 19(41): 2-9.
4. Ioos S, Mallet HP, Leparc Goffart I, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. Med Mal Infect 2014; 44(7): 302-7.
5. Coffey LL, Forrester N, Tsetsarkin K, Vasilakis N, Weaver SC. Factors shaping the adaptive landscape for arboviruses: implications for the emergence of disease. Future Microbiol 2013; 8(2): 155-76.
6. Mlakar J, Korva M, Tul N, Popovic M, Poljšak-Prijatelj M, Mraz J et al. Zika virus associated with microcephaly. N Engl J Med 2016; 374(10): 951-8.
7. Calvet G, Aguiar RS, Melo AS, Sampaio SA, de Filippis I, Fabri A, et al. Detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil: a case study. Lancet Infect Dis, 2016. Disponível em: http://dx.doi.org/10.1016/S1473-3099(16)00095-5 (Acessado em 21 de março de 2016).
8. Brasil P, Pereira JP Jr, Raja Gabaglia C, Damasceno L, Wakimoto M, Ribeiro et al. Zika virus infection in pregnant women in Rio de Janeiro - Preliminary Report. N Engl J Med 2016; Mar 4. [Epub ahead of print].
9. Teixeira MG, Conceição N, Costa M, Oliveira WK, Nunes ML, Rodrigues LC. The Epidemic of Zika Virus – Related Microcephaly in Brazil: Detection, Control, Etiology, and Future Scenarios. Am J Public Health 2016; 106(4): 601-605.
10. Brasil. Ministério da Saúde. Monitoramento dos casos de microcefalia no Brasil. Inf Epidemiol SUS 2016; 17. Disponível em: http://portalsaude.saude.gov.br/images/pdf/2016/marco/16/COES-Microcefalias---Informe-Epidemiol--gico-17--SE-10-2016--16mar2016--13h.pdf (Acessado em 21 de março de 2016).
11. Cauchemez S, Besnard M, Bompard P, Dub T, Guillemette-Artur P, Eyrolle-Guignot D, et al. Association between Zika virus and microcephaly in French Polynesia, 2013-15: a retrospective study. Lancet 2016, Mar 15.
12. Barreto ML, Barral-Neto M, Stabeli R, Almeida-Filho N, Vasconcelos PF, Teixeira M, Buss P, Gadelha P. Zika virus and microcephaly in Brazil: a scientific agenda. Lancet 2016; 387(10022): 919-21. Disponível em: www.thelancet.com (Acessado em 23 de fevereiro de 2016).