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REVIEW ARTICLE

Microcephaly and Zika virus: a clinical and epidemiological analysis of the current outbreak in Brazil☆,☆☆

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Abstract
Objective: This study aimed to critically review the literature available regarding the Zika virus outbreak in Brazil and its possible association with microcephaly cases.
Sources: Experts from Instituto do Cérebro do Rio Grande do Sul performed a critical (nonsystematic) literature review regarding different aspects of the Zika virus outbreak in Brazil, such as transmission, epidemiology, diagnostic criteria, and its possible association with the increase of microcephaly reports. The PubMed search using the key word ''Zika virus'' in February 2016 yielded 151 articles. The manuscripts were reviewed, as well as all publications/guidelines from the Brazilian Ministry of Health, World Health Organization and Centers for Disease Control and Prevention (CDC – United States).

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☆☆ Study carried out at Instituto do Cérebro (InsCer) do Rio Grande do Sul and Faculdade de Medicina, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil.
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Summary of findings: Epidemiological data suggest a temporal association between the increased number of microcephaly notifications in Brazil and outbreak of Zika virus, primarily in the Brazil's Northeast. It has been previously documented that many different viruses might cause congenital acquired microcephaly. Still there is no consensus on the best curve to measure cephalic circumference, specifically in preterm neonates. Conflicting opinions regarding the diagnosis of microcephaly (below 2 or 3 standard deviations) that should be used for the notifications were also found in the literature.
Conclusion: The development of diagnostic techniques that confirm a cause–effect association and studies regarding the physiopathology of the central nervous system impairment should be prioritized. It is also necessary to strictly define the criteria for the diagnosis of microcephaly to identify cases that should undergo an etiological investigation.

PALAVRAS-CHAVE
Vírus Zika;
Microcefalia;
Gestação;
Desenvolvimento cortical;
Neuroimagem

Microcefalia e vírus Zika: um olhar clínico e epidemiológico do surto em vigência no Brasil

Resumo
Objetivos: O objetivo deste estudo foi realizar uma revisão crítica da literatura sobre o surto de vírus Zika no Brasil e sua possível associação com casos de microcefalia.
Fonte de dados: Especialistas em áreas afins do Instituto do Cérebro do Rio Grande do Sul realizaram uma revisão crítica (não sistemática) da literatura sobre o vírus Zika, suas formas de transmissão, a epidemia no Brasil, critérios diagnósticos e a possível associação com os casos crescentes de microcefalia. O uso da palavra chave ''*Zika virus*'' na base de dados do PubMed em fevereiro de 2016, retorna 151 publicações. Estes textos foram revisados assim como todas as publicações e recomendações do Ministério da Saúde, Organização Mundial da Saúde e Centro de Controle de Doenças (CDC – USA).
Síntese dos dados: Os dados epidemiológicos sugerem uma relação temporal entre aumento da notificação de casos de microcefalia e o surto de vírus Zika, principalmente no Nordeste do Brasil. Agentes virais comprovadamente podem ser causadores de microcefalia congênita adquirida. Não existe um consenso sobre a melhor curva de perímetro cefálico a ser utilizada, principalmente nos prematuros. Assim como também existem divergências sobre a definição de microcefalia (abaixo de 2 ou 3 desvios padrões) a ser padronizada nas notificações.
Conclusão: Deve-se priorizar o desenvolvimento de técnicas diagnósticas que confirmem uma relação causa–efeito e estudos sobre mecanismos da patogênese da infecção pelo Zika no sistema nervoso central. Também é necessário definir e universalizar os critérios diagnósticos para a identificação dos casos de microcefalia que devem ser submetidos à investigação etiológica.

Introduction

The World Health Organization (WHO) has issued a warning establishing an international state of emergency due to the microcephaly incidence increase in endemic areas with Zika virus (ZikaV) proliferation.[1]

The disease, which arrived in Brazil possibly in 2014, has spread in the Northeast region and is migrating to the Americas. It is believed that it will quickly continue spreading, as its main vector, the *Aedes aegypti* mosquito, is undergoing a period of wide dissemination due to the high summer temperatures in the southern hemisphere.[2–4]

A possible association between intrauterine infection by ZikaV and early microcephaly was initially proposed, based on the observation of physicians in Northeastern Brazil, who detected a sudden increase in the incidence of births of microcephalic children after identification of the virus entry in Brazil. However, this cause–effect association still needs to be proven.[5,6] The fact is that the ZikaV enters the central nervous system (CNS), breaking the protection of the blood–brain barrier, which has been previously demonstrated in animal experiments.[7,8]

The recent discovery of other forms of virus transmission, in addition to an infected insect bite, through sexual contact or secretions (saliva, urine), and the lack of vaccines or specific treatment has alarmed the population. Moreover, the lack of longer-duration biological markers that allow for diagnostic confirmation, geometrically increase the number of suspected cases and, consequently, the recording of false positive cases.[9–11]

Pediatricians are exposed to the demand for knowledge of this new disease, as they treat the neonate and