

Microcephaly outbreak in Brazil*

DOI: 10.5935/1415-2762.20150061

In November 2015 the Brazilian Ministry of Health declared a public health emergency after 268 cases of microcephaly were reported in the state of Pernambuco. That figure is much higher than the average nine cases registered per year between 2010 and 2014. The sharp increase in the number of cases suggests that thousands of children might be affected by the condition. According to the latest Epidemiological Report on Microcephaly, until 19 December 2015, 2,782 suspected cases of microcephaly related to infection by ZIKA virus were identified in 618 municipalities of 20 states and 40 suspected deaths had been reported. Pernambuco, Sergipe, Paraíba, Maranhão and Piauí are amongst the states in which such increase has been reported (from 11.8 to 27.4 times the average from 2000 to 2014). In Minas Gerais, 55 suspected cases are currently being investigated.

A varied number of factors are associated with the infection: mother's nutritional deficiencies and drug abuse during pregnancy as well as other infections such as rubella, toxoplasmosis and cytomegalovirus, among others, also during pregnancy. A number of abnormalities and/or metabolic, genetic syndromes, as well as environmental stressors and unidentified causes could affect brain development and be associated with the disease.

Although not conclusive, studies suggest that the main suspected cause of the outbreak is maternal infection by ZIKA virus transmitted by the *Aedes aegypti* mosquito. The ZIKA virus (ZIKAV) is an RNA virus member of the Flaviviridae family of the Flavivirus genus. Two strains of the virus, one African and one Asian, are known and described to date. Its main mode of transmission is by vectors but the literature describes others, such as occupational transmission in research laboratories, perinatal, sexual, and during blood transfusion. Laboratory confirmed cases were reported in 18 Brazilian states the highest incidence being in the North East region.

Fever caused by the ZIKA virus is, in most cases, self-limiting lasting 3 to 7 days, usually without serious complications and there are no report of deaths. Hospitalization rate is low. According to the literature, over 80% of those infected by the disease do not develop clinical manifestations. Its symptoms are maculopapular pruritic rash, intermittent fever, no purulent conjunctival hyperaemia and no rash, arthralgia, myalgia, headache and less often, oedema, sore throat, cough, vomiting and hematospermia. There is a possible correlation between ZIKAV infection and the occurrence of Guillain-Barré syndrome in areas where dengue virus is also transmitted.

The Ministry of Health announced the positive results by testing the amniotic fluid of two women who had contact with the ZIKAV and whose babies were diagnosed with microcephaly in ultrasound examinations. Tests performed by the Flavivirus Laboratory of the Oswaldo Cruz Foundation (FIOCRUZ) show that the virus is able to cross the placenta and reach the amniotic fluid. Its presence in the amniotic fluid was ascertained by samples collected amongst pregnant women and subjected to PCR (Polymerase Chain Reaction). A partial sequencing of the virus genome allowed the researchers to identify it as an Asian strain of the ZIKAV.

A complicating factor is that, unlike dengue, for example, there is no serological test commercially available to diagnose the disease.

Abnormal laboratory findings associated with the infection during the course of the disease include leukopenia, thrombocytopenia and slight elevation of serum lactate dehydrogenase, gamma-glutamyl transferase and inflammatory activity markers (C - reactive protein, fibrinogen, and ferritin). Specific laboratory tests are based on the detection of viral RNA from clinical specimens. Viremic period was not established yet, but it is believed to be short, which would allow, in theory, direct detection until 4-7 days after the onset of symptoms. Consequently, materials to be examined should be collected until the 4th day from the onset of the disease. Nucleic acids of the virus have been detected in humans between 1 and 11 days after onset of symptoms and virus was isolated in non-human primate up to 9 days after experimental inoculation.

Regardless of the cause, an increase in the number of microcephaly cases calls for the attention of paediatricians given the consequences for children and their families. Its sequelae have yet not been fully described but most affected children would present hearing and/or vision impairment, different levels of neurological and motor deficits and cerebral palsy.

Given this extremely serious scenario we are currently supervising and organizing a task force of volunteer health professionals in order to combat the epidemic. In the state of Minas Gerais, the Paediatrics Society works in partnership with the Belo Horizonte local authority, Minas Gerais State government, the Ministry of Health and the Federal University of Minas Gerais. Specialists in the field are evaluating suitable treatments for the affected babies. The evaluation of a child with microcephaly includes the analysis of the infant and its family full medical history, pregnancy history, physical examination, serological tests of mother and baby, imaging tests (brain computed tomography and/or magnetic resonance imaging and transfontanellar ultrasound). The best method and the opportune developmental stage in which to use such tests are controversial. An interdisciplinary approach and referral to specialists in Infectious Diseases, Genetics, Neurology and Paediatric Ophthalmology, among other professionals, may be required for diagnosis and follow-up.

The Ministry of Health advises that all cases of microcephaly should be immediately reported via an online form. Moreover, pregnant women should undergo antenatal consultations and carry out all tests recommended by their physician; they should abstain from alcohol or any other drugs, avoid self-medication and direct contact with people with fever or infections. Some measures should be taken in order to reduce the exposure to disease-transmitting mosquitoes: elimination of breeding sites, protection against mosquito bites, such as keeping doors and windows closed or screened, wearing trousers and long-sleeved shirts and use insect repellents allowed for pregnant women.

It is worrying that for at least two decades the same strategies have been implemented against dengue fever epidemics with no success. Therefore, new approaches should be used to combat the *Aedes aegypti*, the main transmitter of the epidemics that plague the country. The widespread use of chemical agents in order to destroy the vectors is Brazil's main weapon against the epidemics. The downside of such approach is that several of these products are toxic to humans and the mosquitoes may develop resistance to them.

An alternative to reduce mosquito population is through biological control. It consists in launching the vectors' natural predators or competitors in their midst. This technology is still being researched. Another method is environmental control which means sanitation, i.e. to create adverse conditions for the development of vectors. Besides its long-term effect, such measure improves the population health and well-being, as well as contributes to economic activities. According to recent IBGE data, approximately 44% of the population live in areas with no sanitation, which is a basic human right.

The country is facing a serious economic crisis. Nevertheless it has to ensure the availability of resources to address such serious challenge or risk a humanitarian disaster of alarming proportions and the threat of a future generation of children with severe sequelae.

**Originally published as:*

– *Brief Communication in the supplemental edition 25/S6 of the Revista Médica de Minas Gerais /Sociedade Mineira de Pediatria, as reference below:*

RP kings. Increased cases of microcephaly in Brazil. Rev Med Minas Gerais. 2015 Jul/ Dec: 25 (Suppl.6): S88-S91.

– *Editorial in the Revista Médica de Minas Gerais, volume 25, number 4, Oct/Dec. 2015 as reference below:*

RP kings. The microcephaly outbreak in Brazil. Rev Med Minas Gerais. 2015 Oct / ten: 25 (4): 463-5.

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