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POINT OF VIEW

Zika virus : A threat potential and unexpected health and development of children

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In November 2015, the Brazilian Ministry of Health announced a surprising increase in the records of newborn children with microcephaly in the country[1]. Parallel to this fact, at the beginning of that year there was an increased incidence of clinical manifestations related to Zika virus in the Northeast Region, where the highest concentration of primary microcephaly cases had initially been observed in the states of Bahia, Pernambuco, and Rio Grande do Norte[1].

In the second half of 2015, there were many reports of pregnant women who later that year gave birth to microcephalic infants, in some cases associated with severe malformations of cortical brain development and arthrogryposis[2]. At some time during pregnancy, especially during the first months, these pregnant women presented with the clinical manifestations of Zika virus infection, such as fever, dry conjunctivitis, arthralgias, asthenia, and often a maculopapular, pruritic, and diffuse rash[1,3]. In addition, cases of GuillainBarré syndrome, many of which have atypical forms of presentation, have been reported in individuals who contracted the Zika virus infection[4].

From these observations, the scientific community has tried to establish a cause-effect relationship between maternal Zika virus infection and the congenital neurological syndrome related to it[5].

Zika virus was originally discovered in 1947 in the Zika valley, Uganda[3]. It is an arthropod-borne virus (arbovirus), mainly transmitted by the bite of the *Aedes* spp., which belongs to the genus Flavivirus, as is the case of the dengue, yellow fever, and West Nile viruses. Together with Pestivirus and Hepacivirus, they comprise the *Flaviviridae* family[3].

A correlation appears to exist between microcephaly and Zika virus infection, particularly during the first half of pregnancy[6]. However, it remains unclear why only about 9%-11% of all reported and proven primary microcephaly cases have been laboratory-linked to the virus. According to the latest epidemiological bulletin of the Ministry of Health, from the beginning of the investigation until March 19, 6,671 suspected cases of microcephaly were reported, of which 907 were confirmed, 1,471 were discarded, and 122 had a positive laboratory result for Zika virus[7].

It is likely that there are other factors causing this exponential increase in cases of microcephaly in the country. Other congenital infections, such as TORCH infections, may also be involved. Another possible explanation for this may be related to the measurement and control of compulsory registration of children born with head circumference (HC) below 31.9 cm for male newborns and 31.5 cm for females (following the guidelines of the World Health Organization). Furthermore, the two changes in HC cutoff level made by the Ministry of Health since last year and epigenetic mechanisms may have contributed to the increase in the number of microcephaly cases to be investigated[8,9].

Regarding microcephaly and Zika virus, it is important to emphasize what is already common knowledge in pediatric practice: microcephaly, whether or not associated with other malformations of the central nervous system, is not a developmental disorder or a neurological disease *per se*[10]. Regardless of its etiology, microcephaly is a clinical and neurological sign, which indicates that those newborns need to be investigated with complementary neuroimaging, neurophysiological, and genetic exams and have their neuropsychomotor development regularly monitored from the time of diagnosis.

While monitoring the development of these infants, as delays, deviations, and disorders of developmental milestones are observed, pediatricians will have a key role in guiding parents

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and family regarding their child's difficulties, referring them to a development specialist or pediatric neurologist for a more comprehensive assessment.

In all cases of development delay, the earlier the diagnosis, the better the response to stimuli. These stimuli must happen in all dimensions, with healthcare professionals working in multidisciplinary teams in early child development stimulation centers, which would include the parents, family, and daycare staff.

The SBP has played a key role in helping the Ministry of Health and the population, in the formulation of measures that impact vector proliferation control; providing guidance to parents and caregivers about insect bite prevention through barrier products (repellents and screens); formulation of technical-scientific guidelines[9] related to early and accurate diagnosis of developmental disorders that are common but not mandatory results of microcephaly; and regarding the recommendations on the multidisciplinary treatment options to provide the best possible guidance to parents and their families.

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