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CONGENITAL ZIKA VIRUS INFECTION AND CONGENITAL NEUROLOGICAL ABNORMALITIES IN NEWBORN INFANTS: A LITERATURE REVIEW

Elizandra Franciele Fernandes da Silva
Universidade do Oeste Paulista (UNOESTE)
Jaú - SP
https://orcid.org/0000-0003-1214-5496

Sofia Cisneiros Alves de Oliveira
Universidade Federal de Sergipe Campus Lagarto (UFS)
Lagarto - SE
https://orcid.org/0000-0003-3689-7238

Amanda Brigone Pecchio
Universidade de Taubaté (UNITAU)
Taubaté - SP
https://orcid.org/0000-0003-4069-7968

Joana Bader Sadala Brandão
Universidade Nilton Lins (UNL)
Manaus - AM
https://orcid.org/0000-0002-0868-7770

Daniéli Vitória Da Silva Grando
ATITUS Educação (ATITUS)
Passo Fundo- RS
https://orcid.org/0000-0002-8851-2283

Olívia Brito Braga
Faculdade São Leopoldo Mandic (SLM)
Campinas - SP
https://orcid.org/0000-0002-0531-3925

Thalita Martins Moreira de Oliveira
Universidade de Vassouras (UV)
Vassouras - RJ
https://orcid.org/0000-0003-3446-9774

Eduarda Almeida Dutra da Conceição
Universidade Evangélica de Goiás (UniEVANGÉLICA)
Anápolis - GO
https://orcid.orq/0000-0002-3705-6337

Carolina De Carvalho Lima Batista
Centro Universitário UniDomPedro (UNIDOM)
Salvador- BA
https://orcid.org/0000-0001-7789-0679

Tamara Araujo Pereira Campos
Faculdade da Saúde e Ecologia Humana (FASEH)
Vespasiano/MG
https://orcid.org/0000-0002-2498-6770

Nicole Beria Callegari
Universidade Positivo (UP)
Curitiba- PR
https://orcid.org/0000-0003-4702-0175

Neidejany de Assunção do Sacramento
Universidad Nacional de Rosario (UNR)
Rosario - Argentina
https://orcid.org/0000-0001-7050-6697

Abstract: Introduction: The Zika virus has the ability to tropism in neuronal cells of fetuses, congenitally causing neurological disorders. **Objective:** To discuss the relationship between congenital Zika virus infection and the onset of congenital neurological abnormalities in newborns, including their neurological manifestations, and their impact on quality of life. **Methods**: Bibliographic review developed from October to November 2022, with searches in the PubMed and LILACS databases, 15 articles being selected after applying inclusion criteria. **Discussion:** Infections in the first trimester of pregnancy are those that result in serious malformations, which reinforces the importance of adequate prenatal care. The diagnosis of infection during the gestational period consists of serological and ultrasonographic examinations. The main manifestation observed intrauterine and after birth was microcephaly, which is characterized by the interruption of brain growth, with little cortical differentiation. However, changes in sensory organs can also occur. **Final considerations:** The studies demonstrate advances in the screening of such changes through possible radiological and laboratory changes during prenatal care, and also through postnatal neuroimaging tests.
Keywords: Zika virus; Newborns, Congenital Neurological Abnormalities; Microcephaly.

INTRODUCTION

The zika virus (ZIKV), of the Flaviviridae family, is an arbovirus whose main vector is an arthropod of the genus Aedes. One of its most alarming manifestations comes from its ability to attack neuronal cells and cause permanent neurological damage (HU et al., 2017). Thus, it became a public health problem in Brazil, mainly in the Northeast region, when, in mid-October 2015, there was a substantial increase in the number of cases of microcephaly in newborns associated with ZIKV infection

during pregnancy (ESCOSTEGUY C. C. et al., 2020).

Clinically, the Congenital Zika Virus Infection Syndrome (CZS) manifests itself as a result of an infectious process and affects, above all, the central nervous system (CNS), resulting in severe structural and functional neurological impairment of newborns (NB). Based on this, microcephaly stands out, in which the SCZ leads to a malformation that results in the reduction of the newborn's head circumference. Added to this, it is clear that this is not the only existing alteration in the development of such cases, since they may also present impairment in psychomotor development in the first months of life, congenital contractures, including increased muscle tone and cervical hypotonia, and abnormalities eyepieces (SAAD T. et al., 2018).

Structural and functional changes at the CNS level occur mainly due to maturation damage in specific brain regions. Such an infection leads to substantial damage to the fetal brain with considerable loss in fetal neuronal progenitor cells, especially in the temporal cortex, dentate gyrus and hippocampus. However, there is still no clear knowledge of the pattern of such injuries, especially when it comes to mild involvement in patients (DA SILVA PONE M.V. et al., 2020).

Since the report of the first cases of congenital Zika virus infection in 2015, there are still several questions related to its pathophysiology, effective measures for the prevention and clinical management of such conditions, since the long-term neurological impacts are not yet fully elucidated (DA SILVA PONE M.V. et al., 2020). In this context, the objective of the present study is to discuss the relationship between congenital ZIKV infection and the appearance of congenital neurological abnormalities in the NB, including its neurological manifestations and its impact on the quality of life of affected patients.

METHODOLOGY

The present bibliographic review study was developed from October to November 2022. The formulation of its guiding question was in accordance with the criteria of the PVO strategy, an acronym that represents: population or research problem, variables and outcome, which gave This gave rise to the question: "What is the relationship between congenital Zika virus infection and the appearance of congenital neurological abnormalities in newborns and their impact on quality of life?". In this sense, according to the parameters mentioned above, the population of this research refers to patients who suffered congenital infection by the Zika Virus, analyzing the relationship of such infection and the appearance of congenital abnormalities in newborns and which are the impacts linked to the quality of life of these patients.

The searches were carried out through searches in the PubMed Central (PMC) and Latin American and Caribbean Literature in Health Sciences (LILACS) databases. The following descriptors were used in combination with the Boolean term "AND": Zika Virus Infection, Newborn, Congenital Abnormalities and Nervous System Malformations. The inclusion criteria were: articles in English, Spanish and Portuguese; published in the period from 2017 to 2022 and that addressed the themes proposed for this research, systematic review, cohort and case-control studies, available in full. Exclusion criteria were duplicate studies in both databases, available in abstract form and that did not directly address the studied proposal.

After associating the descriptors used in the searched databases, a total of 408 articles

were found. Of which, 381 articles belonged to the PubMed database and 27 articles to LILACS. After applying the inclusion and exclusion criteria, 13 articles were selected from the PubMed database and 2 articles from LILACS, using a total of 15 studies to compose the collection.

REVISION

The mechanism of transplacental ZIKV infection is not yet fully elucidated, as is the relationship between long-term viremia and the development of SCZ (FREITAS D.A. et al., 2020). It is known that maternal infection can occur through mosquito bites and through sex, causing placental damage such as placental insufficiency that can lead to fetal death and spontaneous abortions, especially in the first and second trimester of pregnancy (PLATT D.J.; MINER J.J, 2017).

The main manifestation of SCZ observed was the development of microcephaly, characterized by the interruption of brain growth, with little cortical differentiation, few gyri and informally named as ''drawer" format, with collapse of the cranial vault, sutures are inverted and the bones predominantly in the occipital region. Consequently, there is a compromise in the neurological development of the newborn, with the possibility of impairment in behavior, cognition and social interaction (CAMPOS D.M.O. et al. 2021).

Infections in the first trimester of pregnancy are those that usually result in more severe malformations (SAAD T. et al., 2018). The study by Mulkey S.B. et al. (2019), showed that at 20 weeks of gestation, it was possible to identify a drop in the fetal head circumference percentile on ultrasound. Thus, radiology can serve as an ally in the early diagnosis of microcephaly. It must also be stated that there is the possibility of developing microcephaly both right after birth and in the postnatal period, and after birth it presented a worse prognosis. (CAMPOS D.M.O. et al. 2021).

According to sarno M. et al. (2017), cell cultures demonstrated that ZIKV has a preference and also causes apoptosis of neural progenitor cells, although it also replicates in smaller quantities in mature neurons. Progenitor cell apoptosis contributes to the development of microcephaly and other neurodevelopmental outcomes, but they detected normal development of the brain parenchyma up to 24 weeks. From that moment on, a slow growth in head circumference, asymmetry between abdominal circumference and head, excess skin in the nuchal and frontal folds, in addition to posterior fossa lesions with cerebellar hypoplasia (Dandy-Walker type lesions) were observed. Taken together, placental infection was one of the factors that contributed to intrauterine growth restriction(SARNO M. et al., 2017).

In addition to microcephaly, the development of epileptic seizures has been noted, which initially have such a subtle presentation that they are often not identified as such, but which later evolve into complex, generalized or focal seizures, even reaching drug-resistant manifestations (SAAD T. et al., 2018). Guillain-Barré Syndrome is also among the severe neurological disorders caused by ZIKV infection. This polyneuropathy manifests itself with the progressive involvement of muscle weakness and areflexia, with possible respiratory and motor aggravations and even death (CAMPOS D.M.O. et al. 2021).

Sensory and neurodevelopmental changes are also associated with congenital ZIKV infection. Among such manifestations are damage to the back of the eye, including macular scars and focal retinal pigment spots, hypertonia soon after birth and arthrogryposis (HCINI N. et al., 2021). The retinal pigment epithelium is highly permissive and susceptible to death induced

by ZIKV and through disruption of the blood-retinal barrier, ocular involvement may be the result of different mechanisms: damage to the retinal pigment epithelium and axonal transport (WOOD A.M.; HUGHES B.L., 2018). Developmental delay in the first days of life, manifested through hyperexcitability and increased muscle tone, as well as osteoarticular malformations, for example arthrogryposis, are also frequent findings in severe cases and may be related to poor intrauterine movement in some patients (ESCOSTEGUY C. C. et al., 2020).

According to Verjàn-Carrillo, E.J. et al. (2021), there is an increased risk of sensory hearing loss (SNHL) in babies exposed to the Zika virus in utero, confirmed in about 1 in 10 babies analyzed. This risk is increased by 14 times when associated with the presence of microcephaly. Findings that make the in-depth study of neurodevelopmental and sensory changes essential. Ophthalmological abnormalities are described in children with or without microcephaly and can affect the pale optic disc, chorioretinal atrophy and colobomas (ESCOSTEGUY C. C. et al., 2020).

The diagnosis of ZIKV infection is widely discussed and includes important exams during the gestational period. Among such exams are serological exams, ultrasonography, amniocentesis and even fetal neurodevelopment monitoring protocols. Laboratory tests indicated for the diagnosis of maternal infection include the polymerase chain reaction via reverse transcriptase (RT-PCR), in addition to the IgG and IgM avidity test (ESCOSTEGUY C.C. et al., 2020). Amniocentesis is the most used intrauterine method for diagnosis, however, in those without fetal ultrasound findings, but it must not be performed before 21 weeks of gestation (WOOD A.M.; HUGHES BL., 2018).

While in imaging exams, the most characteristic findings of the syndrome are microcephaly, with a head circumference 3 or more standard deviations below the mean for gestational age (WOOD A.M.; HUGHES B.L., 2018). Also, the presence of cerebral calcifications, ventriculomegaly and cerebral atrophy are pointed out as important indicators of the presence of the infection (ESCOSTEGUY C. C. et al., 2020. Patients with a positive maternal or fetal diagnosis must be carefully monitored because, although they are often In asymptomatic cases and without prenatal ultrasound findings, the possibility of developing congenital Zika syndrome must not be excluded (WOOD A.M.; HUGHES B.L., 2018).

Postnatal evaluations are extremely important in the follow-up of newborns with congenital Zika virus infection. Thus, it is essential that there is access to information about maternal exposure to Zika virus infection during pregnancy so that they can receive the recommended postnatal evaluations (MULKEY S. B. et al., 2019). Postnatal imaging can detect changes not observed in fetal imaging, requiring follow-up to assess neurological development through early neuroimaging findings (DA SILVA PONE M. V. et al., 2018).

The SCZ outcomes are of many uncertainties involved whose impact is still unknown on child development until adulthood, requiring health care to maintain their quality of life. Sensory, postural and tonus changes, especially in ankle dorsiflexion, leg positioning and asymmetries, have an impact on locomotion and spatial capacity (DE SOUZA T. G. et al., 2022). Gastroenterological evaluation in patients with significant gastroesophageal reflux disease in order to improve irritability, crying and sleep, which also brings well-being (SAAD T. et al., 2018). Regarding Guillain Barré Syndrome associated with Zika virus, it was found that quality of life reflects the clinical course of

the disease, with lower quality of life at the beginning of the disease (MIRANDA R. N. et al., 2020). necessary for neuropsychomotor development, pharmacological and surgical interventions to provide the best recovery and rehabilitation (SAAD T. et al., 2018).

FINAL CONSIDERATIONS

Congenital ZIKV infection is related to congenital neurological abnormalities, leading to severe functional and structural damage to affected patients. The studies demonstrate advances in the screening of such changes through possible radiological and laboratory changes during prenatal care, and also through postnatal neuroimaging tests. There is a need for studies that follow the evolution of such patients affected in the postnatal period, especially after the application of tools for neurocognitive and motor stimulation according to the individuality of each case and severity of manifestations. possible approaches to minimize impacts on the quality of life of children affected by the condition.

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