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Changes in zika virus syndrome seen by magnetic resonance imaging

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ABSTRACT

OBJECTIVE

To review, identify, and describe the imaging features of congenital zika virus syndrome.

METHODS

This is a review with emphasis on magnetic resonance (MRI) and its findings in the diagnosis of congenital zika virus syndrome. Articles, published in the last five years, were searched in PubMed databases. With the descriptors "Zika Virus Infection", "Zika Virus" and "Diagnostic imaging".

RESULTS

Twenty-four articles that approached MRI as a complementary tool to ultrasound findings were analyzed. In the fetal period, it is considered better to evaluate abnormalities such as: polymicrogyria, opercular dysplasia, lisencephaly-pachygyria and ventriculomegaly. In the postnatal period it presents high sensitivity and specificity, being the method of choice in the late suspicion of congenital syndrome of ZIKV, in the images it is possible to visualize craniofacial disproportion, microcephaly, cerebral atrophy and reduction of cerebral cortical thickness.

CONCLUSION

MRI shows as an important diagnostic method of morphological changes related to zika virus syndrome, contributing to the detailed study of congenital malformations, thus affecting maternal and child health and quality of life.

DESCRIPTORS

Zika Virus, Zika congenital syndrome, Diagnostic Imaging, Magnetic Resonance Imaging.

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INTRODUCTION

Zika Virus (ZIKV) is an RNA Flavivirus belonging to the Flaviviridae family, a group that also includes Dengue, West Nile and Yellow Fever viruses[1]. It was first isolated in 1947 in an infected rhesus monkey in the forest of Uganda, and in 1952 in humans[2,3].

The main means of ZIKV transmission is through the bite of the Aedes aegypti mosquito, present in predominantly tropical areas, such as the northern region of Brazil[4]. However, it is known that transmission can also occur via sexual contact, blood transfusion, organ transplantation, and vertically.

Phylogenetic analyses indicate that the epidemic was caused by an Asian genotype strain in the Americas at the end of 2013; however, it has generated worldwide interest since 2015 due to its association with outbreaks of congenital malformations, including severe neurological manifestations in the occurrence of intrauterine infection in pregnant women, which can lead to microcephaly, spontaneous abortions, growth restriction, stillbirths, fetal infection, oligohydramnios, premature rupture of membranes, and premature birth[5,6,7]. It has since been declared a global health emergency[3].

Pregnant women can contract the infection in any trimester, exposing the fetus to vertical infection[8]. Adverse outcomes may be related to the gestational age at which the infection occurred, indicating a higher risk between 14 and 17 weeks, with a higher incidence in symptomatic infections[9].

Clinical symptoms last an average of 5 to 7 days and occur in only 20% of mothers; among them are fever, maculopapular rash, arthralgia, and conjunctivitis. When dealing with newborns, five specific findings of the congenital syndrome are considered: severe microcephaly with partially collapsed skull; thin cerebral cortex with subcortical calcifications; macular scarring and focal retinal pigmentary spots; congenital contractures; and marked early hypertonia and symptoms of extrapyramidal involvement[10]. These findings can be seen on imaging examinations.

Ultrasonography is still the main test used for zika syndrome screening in fetuses, however when the results found are doubtful magnetic resonance imaging (MRI) is used to assist in diagnostic accuracy, because it is not influenced by oligodramnios, maternal body mass index, and the unfavorable positioning of the fetus[11,12]. However, MRI becomes the method of choice in cases where there is late suspicion of congenital ZIKV syndromes, usually after birth[13].

When compared to ultrasound alone, fetal MRI has increased diagnostic positive predictive value in brain abnormalities[12]. Its excellence in resolving soft tissues of the fetal brain makes the scan highly sensitive to developmental changes, allowing early detection of evolving anomalies[14,15]. However, one should be careful with this exam alone, since it has a lower negative predictive value than ultrasonography, and may be related to false-positive results[12].

This technique is extremely specialized because it does not use ionizing radiation and promotes greater tissue differentiation compared to ultrasound, allowing better description of the structures[12]. It is considered the gold standard for diagnosing fetal brain infections[16]. Therefore, imaging exams are extremely important when it comes to congenital diseases that affect the neurological system of the child; it is through them that one can make an early diagnosis and detail the proportion of damage related to infection; allowing to precisely address the demands of affected patients either with multidisciplinary care, interventionist or even conservative[17,18].

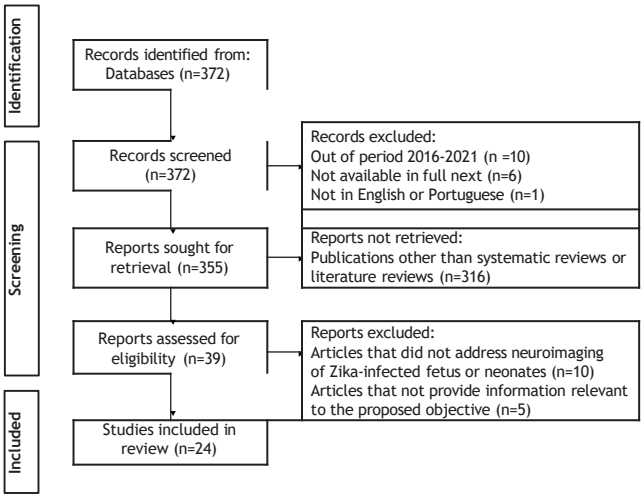
This paper describes the importance of MRI and its findings in the diagnosis of congenital syndrome of Zika virus.

METHODS

The study consisted of literature review with emphasis on magnetic resonance imaging and its findings in the diagnosis of congenital syndrome of zika virus. The search for scientific articles was performed in PubMed database. The descriptors used for the search were: "Zika Virus Infection", "Zika Virus" and "Diagnostic imaging" (((Zika Virus Infection) OR (Zika Virus)) AND (Diagnostic imaging)).

As inclusion criteria, literature reviews and systematic reviews were selected, which addressed neuroimaging (MRI and ultrasound) of fetuses or neonates obligatorily infected by ZIKV, being articles published in Portuguese and English languages and in the period between 2016 and 2021, available online in full text. Other types of studies were excluded from the search, such as those that did not address neuroimaging (ultrasound and magnetic resonance imaging) with direct relation to ZIKV infection in fetuses and neonates. The Flowchart describes the article selection, exclusion, and inclusion steps for this study.

Table 1. Flowchart of the literature search.



RESULTS AND DISCUSSION

Imaging studies are important in both early diagnosis and follow-up of congenital diseases. Ultrasonography is the exam routinely used by pregnant women to follow the development of the fetus. When there are suspected or confirmed cases of ZIKV, it is recommended to perform this exam to evaluate the fetal anatomy, growth and amount of amniotic fluid every four to six weeks. If fetal involvement is suspected, the frequency of the test is changed to every 15 days. If fetal malformations are found on obstetric ultrasound, MRI is recommended as a complementary tool, having validity both during pregnancy and in the neonatal period[9,16,19].

Studies show microcephaly as the main finding of the syndrome, but it is a nonspecific finding, and to differentiate it from other congenital infections there are characteristic findings: severe microcephaly with partially collapsed skull, calcifications in the cortical-subcortical junction, congenital contractures, marked early hypertonia and macular scarring and focal retinal pigmentary spots, all of which can be seen by MRI.

Fetal MRI is considered better at evaluating gyral cortical abnormalities, among them are: polymicrogyria, opercular dysplasia, and lisencephaly-pachygyria[20, 21]. When there is evidence of microcephaly and calcifications on fetal ultrasound, it is common to find on MRI some malformations such as ventriculomegaly due to white matter hypoplasia, cerebral atrophy and microphthalmia. When the evidence is in the white matter or cortices, abnormal myelination and laminar cortical

necrosis are observed on MRI T1- and T2-weighted images[11,20]. A very frequent finding is redundancy of the scalp skin in the occipital region of the fetus[11].

Melo and collaborators describe fetal deaths immediately after birth resulting from respiratory failure due to severe brainstem defects; a defect that can be evaluated by fetal MRI, giving the examination an important role in newborn survival[9].

When the reference becomes postnatal magnetic resonance imaging, its high sensitivity and specificity must be emphasized[16]. In these images it is possible to visualize numerous findings, among them the most common in almost all patients are: craniofacial disproportion, microcephaly, cerebral atrophy and reduced cerebral cortical thickness, enlarged subarachnoid spaces, lysencephaly, non-hypertensive ventriculomegaly secondary to cerebral atrophy, agenesis/hypoplasia of the corpus callosum, gross calcifications that are more commonly seen in the subcortical-cortical transition and in the basal ganglia[21].

Among all the more specific findings that can characterize patients with congenital ZIKV syndrome, intraparenchymal calcifications are the second most prevalent finding; when referring to the evaluation of this finding, one should be aware that MRI has a lower sensitivity when compared to ultrasonography[17, 22].

Like other imaging tests, MRI has advantages and disadvantages, among them: need for sedation, delay in performing it, high cost and low availability, especially in the Unified Health System (SUS)[9].

It must be emphasized that it is not only by means of imaging exams that the infection is diagnosed. The infected pregnant woman can undergo laboratory tests, such as molecular amplification (RT-PCR) in serum and urine samples; the most specific approach is during the acute phase of the disease. It is also possible to perform serological tests based on IgM detection by Enzyme Linked ImmunoSorbent Assay (ELISA), but they have limitations, including cross-reactivity with other Flaviviruses, which can generate false-positive results[23]. Diagnostic tests can be done at any time in suspected pregnant women; the biggest challenge is the laboratory confirmation of infection in the fetus during the gestational period. Attempted detection may be unsuccessful, as Zika virus RNA levels may be in a transient state, and detection is not possible[24]. Newborns with suspected congenital infection should have plasma and urine RT-PCR and plasma IgM serology by ELISA within the first 48 hours of birth[24].

CONCLUSION

Magnetic resonance imaging is an important diagnostic method for morphological alterations related to zika virus syndrome, contributing to the detailed study of congenital malformations, thus affecting maternal and child health and quality of life. The main MRI findings of the syndrome include intraparenchymal calcifications, alteration in the corpus callosum, and ventriculomegaly. Despite the recognized benefits of this method, it is not accessible to the population, and should be complementary to ultrasonography, with appropriate indications.

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