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Neuroepidemiological and social risks in neonates related to Zika Virus

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ABSTRACT

Zika Virus (ZIKV), a Flavivirus transmitted by Aedes aegypti, has emerged as a serious global health problem following the Zika fever epidemic in Brazil in 2015. Infection in pregnant women can lead to Congenital Zika Virus Syndrome (CZS), characterized by microcephaly and other severe neurological malformations in neonates. Primary prevention is crucial, given the association between ZIKV and serious neurological complications, requiring ongoing support for those affected.

Keywords: Zika Virus, Microcephaly, Pregnant women.

INTRODUCTION

Zika virus (ZIKV) is a virus of the genus Flavivirus that takes its name from being first isolated in 1947 from the blood of a rye sentinel monkey in the Zika forest, Uganda. With *Aedes aegypti* as a vector, it causes Zika fever, which presents symptoms like other arboviruses, such as Dengue or Chikungunya. The symptomatology of Zika fever can last up to a week, including fever, myalgia, arthralgia, arthritis, rash, headache, conjunctivitis, and edema (Sales *et al*., 2024).

In May 2015, the World Health Organization reported the first local transmission of ZIKV in Brazil. In November 2015, Brazil's Ministry of Health declared a public health emergency due to the increase in the number of births of children diagnosed with microcephaly in Pernambuco during that period, possibly linked to the Zika fever outbreak. In 2016, causality between the infection of pregnant

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women by the virus and microcephaly in children was confirmed (Rodrigues *et al*., 2024). Thus, the relationship between the infection of pregnant women by ZIKV and the reduction of the head circumference of newborns came to be called Congenital Zika Virus Syndrome (CZS), presenting with clinical and physical alterations that included neurological, ocular, and auditory disorders, craniofacial disproportion, malformations in joints and limbs, in addition to microcephaly in neonates (França *et al*., 2018).

Microcephaly is a pathology that causes structural and functional alteration of the neurological system, and is defined by head circumference less than two standard deviations for sex and gestational age. Resulting in neuropsychomotor delay in various degrees of impairment, presenting deficits in intellectual and speech development, in addition to delay or failure to achieve child development milestones, such as sitting, crawling, and walking, resulting in a low quality of life and life expectancy (Costa *et al*., 2022).

Microcephaly and other serious congenital brain diseases usually occur when the mother is infected with ZIKV in the first 12 weeks of pregnancy. It is believed that during this period the virus is able to cross the placental barrier, reaching the brain of the fetus, evidencing the tropism of ZIKV by these cells, culminating in an inflammatory process that damages the vascularization of the fetus, reducing its ability to develop (Silva *et al*., 2021).

Regions located in tropical areas, as is the case of numerous cities in Brazil, are considered areas of predominance of *Aedes aegypti*, the main vector of ZIKV, which shares the same environment as well as the same time of activity with the human species, providing a scenario of perpetuation of the mosquito species and many losses to our society. Therefore, the best way to avoid new infections is to use primary prevention, especially for pregnant women (Silva *et al*., 2021). However, the challenge regarding Zika virus infection lies not only in the control of the disease, but also in the possible sequelae of congenital infection and neurological complications (Sales *et al*., 2024). Therefore, for children born with microcephaly, the Unified Health System (SUS) offers support for their development, and these patients should be included in the early stimulation program from birth to 3 years of age, a time when the brain evolves the most, aiming to reach the maximum potential of the child, both physical and neurological. cognitive and social (Silva *et al*., 2021).

Thus, the evident relationship between ZIKV infection in pregnant women, as well as the occurrence of microcephaly and other congenital malformations, demonstrate the seriousness of the disease - especially in Brazil, which stands out for the dissemination of the vector of this virus. Therefore, the effective response to the Zika virus and its consequences should focus not only on the prevention of infection, but also on the continuous and adequate support of pregnant women, as well as affected neonates.

OBJECTIVE

The present literature research aimed to investigate the association between Zika Virus infection and neurological aspects, with a focus on congenital disorders. The study sought to understand the relationship between Zika virus and congenital neurological disorders, to understand the factors that influence viral infection in pregnant women, and to recognize prophylactic measures to prevent Zika virus transmission in pregnant women.

METHODOLOGY

This is an analytical literature review, developed from scientific articles consulted with the help of the main electronic databases, such as SciELO, PubMed, Google Scholar and others, published between 2015 and 2024 and which presented the theme of the Zika virus and their related risks in neonates, using the descriptors "zika", "zika virus" and "microcephaly" together with the Boolean operator "*and*". In addition to these, for the composition, data were obtained from research reference sources, such as the Ministry of Health. The alternative hypothesis that guided the study was based on the question: Are there significant neuroepidemiological and social risks from maternal contagion by the Zika virus in neonates? The debate about the initial question took place in collective meetings among the researchers participating in the present work, through discussions and exchanges consistent with the methodology of the Arco de Maguerez, developed by Charles Maguerez. From this, the articles within the proposed period, which dealt with the theme and were presented in the Portuguese language, were selected. In addition, in order to achieve the proposed objectives, in addition to the scientific basis, a technical visit was carried out, supported by medical experience, in a maternal and child reference hospital in the state of Maranhão. The preparation of an informative folder for the composition of the social intervention, together with the pregnant women, about the theme was carried out through the Canva platform, in addition to the figure for the composition of the present work.

DEVELOPMENT

The most severe manifestation caused by ZIKV described in the literature is microcephaly, resulting from congenital infection (Ribeiro *et al*., 2017). Within the standards established by the World Health Organization (WHO), microcephaly is defined as the size of the skull measured with a measurement of less than two standard deviations, being diagnosed through techniques and equipment, according to the standard mean for sex and gestational age. In addition, the standard measure that is less than less standard deviations is established as severe microcephaly (Ministry of Health, 2019).

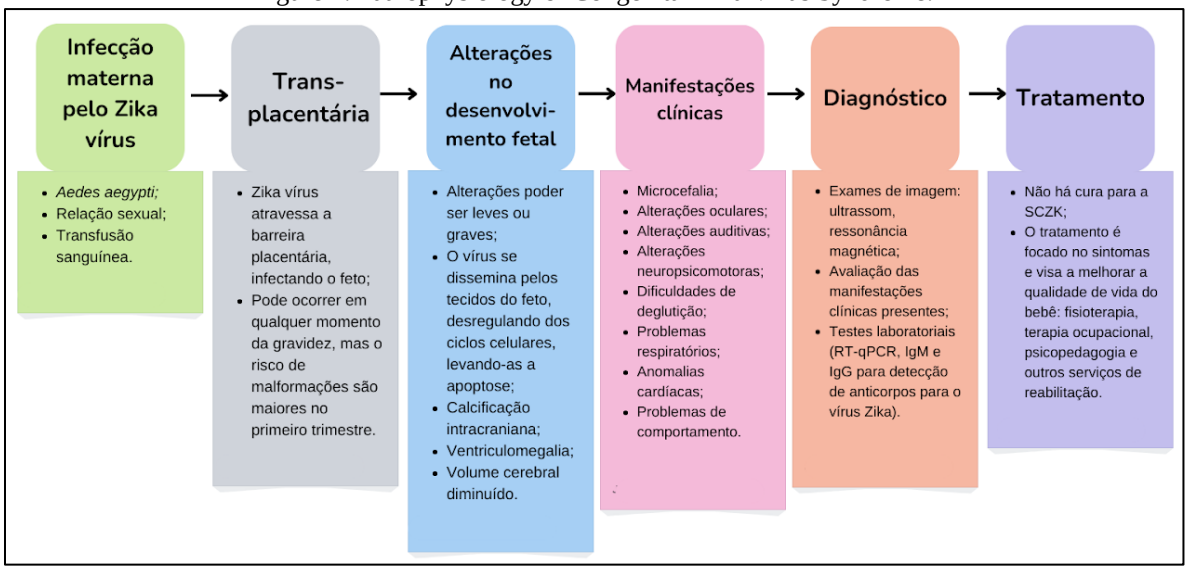
According to a study conducted by Brasil *et al*. (2016), it was found that Zika virus infection during the gestational period has deleterious effects on the fetus and can lead to fetal death, growth

restriction and a spectrum of central nervous system abnormalities, which is an expectation of poor prognosis. In this sense, microcephaly was the most apparent sign in children affected by ZIKV and may be associated with other alterations that may even appear in the second and third trimesters of pregnancy (Souza *et al*., 2018).

According to Amorim *et al*. (2020), of the cases of infection caused by the Zika Virus, in 80% of them the infection is asymptomatic. Another important characteristic of this virus is its ability to spread through different body tissues, embryonic cells and its ability to cause the dysregulation of cell cycles, leading the cells to undergo apoptosis. These mechanisms of dissemination in various tissues, the ability to dysregulate cell cycles and induce cell apoptosis are the key to understanding the relationship between Zika virus infection and microcephaly.

In addition, the Osvaldo Cruz Foundation (Fiocruz) detected ZIKV in the amniotic fluid of pregnant women, whose prenatal ultrasound showed a microcephalic fetus. It is thus evident that the virus can cross the placental barrier and reach the fetal tissues. Thus, intrauterine transmission is also feasible (Nunes *et al*., 2016).

Figure 2: Pathophysiology of Congenital Zika Virus Syndrome.



Source: Authorial

Among the 10,200 live births with suspected congenital Zika virus syndrome (CZS) in 2015 and 2016, 2,018 cases were confirmed. The prevalence coefficient of CZS was 3.8 per ten thousand live births in 2015 and 3.1 per ten thousand live births in 2016, with the highest prevalence in the Northeast region in both years (12.6 in 2015 and 7.1 in 2016) (França *et al*., 2018). In addition, data from the Ministry of Health from November 2015 to July 2018 recorded 16,348 suspected cases of Zika infection, with 19.7% of them confirmed, and the majority (59.3%) concentrated in the Northeast region. It was observed that

the affected mothers were usually single, over 30 years old, with low education, self-declared black, low-income, and living in peripheral areas with little public policy coverage (Freitas *et al*., 2019).

From 2015 to 2020, there were 69 abortions confirmed with CZS, and of the live neonates confirmed with the syndrome, 14.4% (493) died, with an average age of 1.4 months. The case fatality rate among the cases of Zika-related congenital microcephaly was 10% (Donateli, 2023 *apud* Brasil, 2021). There was a significant relationship between CZS and adverse outcomes, such as prematurity (14.7%) and low birth weight (31.2%), especially in the Northeast region. These outcomes reinforce the connection between nutritional and health conditions with social, environmental, and economic factors (Donateli, 2023 *apud* Carvalho, 2013; Costa *et al*., 2018).

From this perspective, poverty is a social determinant that is related to the Zika epidemic. The disease had a higher incidence in the Northeast of Brazil, where climatic conditions favor the spread of the mosquito vector and socioeconomic vulnerability is prevalent. In addition, a large part of the population of this region lives in precarious conditions, with limited access to basic health, sanitation and education services. In this sense, Freitas *et al*. (2022) It highlights that the predominance of dwellings with characteristics favorable to the proliferation of the mosquito, such as lack of basic sanitation, accumulation of water in inadequately stored containers, and precarious urban infrastructure, is also a contributing factor to the accelerated spread of the disease. In addition, the prevalence of microcephaly is higher among non-white people, reflecting their lower opportunities for social advancement, income, and education compared to whites.

Together, Sá *et al*. (2017) highlight the fatigue and difficulty of mothers in reconciling domestic chores with the care of the child, husband and other children. In this context, the father figure is extremely important, considering the burden faced by mothers. The way parents react to their child's disability significantly influences the child's development, as highlighted by Prado (2013). Thus, these findings highlight the importance of public policy planning, aiming at comprehensive surveillance of the demands of children and families impacted by CZS (Donateli, 2023).

The literature review gathered broad and diversified knowledge about the neuroepidemiological and social risks in neonates related to Zika virus infection during pregnancy, as well as the diagnosis and its implications for the child and family members.

In addition, the help of Dr. Marizélia Rodrigues Costa Ribeiro, a physician with extensive experience in the maternal-infant area, was extremely enriching to the work, who clarified and presented, with a wealth of details, replicates about the questions that significantly guided the entire research process. Below, we present the main questions addressed by our interviewee and their respective answers, related to the neuroepidemiological risks associated with the Zika virus.

When does the mother usually receive the diagnosis? Is it more common for the family to receive the diagnosis prenatally or only after delivery?
"With ultrasound, it's more common to have this diagnosis that you didn't have in the past. At the beginning of the microcephaly outbreak, it was a very difficult time for the mothers. Some children are born without a pediatrician in the delivery room, which makes diagnosis difficult. If the child didn't have something that drew a lot of attention, many of them went unnoticed. Many of them did not have their head circumference measured, sometimes they did not even have their weight measured. So a lot of moms didn't get the news until later. Another problem was that we didn't have access to exams [...] Of the 79 children who came to us, 30 were not born with microcephaly, but almost all of them presented later. The ultrasounds did not show any alterations that were not striking[...] ***Professor Zeni Lamy did qualitative research on the delivery of the news to the family. The mothers spoke of omission, doubt in relation to the diagnosis, and when the news was given, it was done in a very traumatizing way, leading to depressive feelings of fear and guilt.*** *The mothers didn't know how to deal with the news, so they began to organize themselves in groups and get information through the media. The professionals were not prepared to communicate in a way that was technical but also humanized. Every mother expects her child to be born normal, but they had a child in their arms with signs of disability.*

Does this neonate with microcephaly survive? How long?
"The babies were born well. Good vitality assessment (8, 9 and 10). They were not born with a low weight or length. I don't have the mortality of these children, but the seizure was what complicated it the most. I have news of 5 or 6 children who, at the time we were doing the research, until 2019, that they had died from pneumonia."

What accompaniments are offered by the Government for mothers living in the interior of the state?
"All these more serious children who were diagnosed at this first moment are followed up at the maternal and child center, at APAE, in offices. From 2015 to 2016 we had a big spike of 134 children referred. What draws the most attention, which may be difficult, was very easy before: they called, made an appointment and left with the appointment scheduled. Now it is necessary to enter this PROCON application, which is a difficulty for mothers who often do not have a high level of education. These mothers had ophthalmological, nutritional, occupational therapy, speech therapy, neuropediatrician, psychiatrist, orthopedics, care for children born with cleft lip and palate. In the beginning, it was organized in such a way that everyone had access. They did CT scans. Children who had bulky ventriculomegaly, who needed to have valves placed, also had access. In this initial period, even children who were in the countryside, when they were totally Zika cases, had access to services. It was a leap forward to organize a service for children with disabilities. In relation to transportation, the right to travel to the capital was granted, the benefit so that mothers could also support themselves. Mothers have their professional lives interrupted and the question arises: "these children dying, will this mother lose this benefit?" I've seen moms complaining about it a lot. Today there is a proposal for compensation to be paid in a single installment and without income tax for mothers who had SCZK or Guillain-Barré due to Zika. But there is a problem, it would only cover children who were already receiving the government benefit. The Continuous Payment Benefit (BPC). Those who did not have the BPC would not receive it. It was also possible for these mothers to have the right to a quota of diapers, some medications. But I also see mothers who need to buy anticonvulsants and other medications that are expensive. They were given wheelchairs, but the children are growing up and the chair can no longer support them."

What measures should be taken by pregnant women to avoid Zika virus infection?
"Wear long clothes, repellents that can be used on pregnant women, which should also be ironed on clothes, use of mosquito nets, screens, use air conditioning to be able to close the room. Avoid circulating at the earliest time, from 7 am to 10 am; and at the end of the day, from 3:30 p.m. to 7 p.m., which is the time when Aedes aegypti is most active. You must always be careful not to facilitate the formation of breeding sites. So is the danger of sexual transmission. Prenatal care should be done in order to obtain the diagnosis, in case of alterations, to investigate them. Prevent and be aware of symptoms. Zika is not over."

Thus, therefore, the interview conducted with the physician Dr. Marizélia Rodrigues Costa Ribeiro

showed the importance of understanding how mothers are affected, in addition to understanding the development and inclusion of neonates with microcephaly. Their meticulous analyses highlighted the complexity of these topics, underscoring the continued need for vigilance and research to mitigate the devastating impacts of this condition.

Taking into account the objectives of the present study associated with neuroepidemiological and social risks in neonates related to Zika virus, the team sought to recognize prophylactic measures of Zika virus infection in pregnant women, performing an intervention aimed at pregnant women at the Maternal-Infant University Hospital, in São Luís/MA. To this end, the group met and, through a conversation directly with the pregnant women, it was explained in a detailed and clearly understood way what the Zika virus would be, its importance and relationship with microcephaly, what symptoms can arise in the face of infection, the importance of adopting prevention measures and care for neonates in the face of Congenital Zika Virus Syndrome. In addition, to support the conversation, an informative folder was prepared as a means of helping pregnant women during the conversation.

FINAL THOUGHTS

In summary, the relationship between the Zika virus and the risks of microcephaly in neonates presents a combination of social, clinical and epidemiological aspects. The spread of the virus has been facilitated by factors such as urbanization, inequalities in access to healthcare, and environmental changes. In the clinical aspect, the virus causes neurological damage, especially in fetuses that are already developing.

Epidemiologically, the spread of the virus was rapid, triggering numerous cases in the most economically vulnerable population. Thus, when talking about such an important subject, it is necessary to highlight the importance of health and prevention as a way to combat proliferation and protect society, especially the most defenseless part.

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