Review Article

Zika virus infection during pregnancy and microcephaly in newborns: an integrative literature review

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ABSTRACT

Fever from the Zika virus is poorly known, with only 18% of human infections having clinical manifestations. In recent months, the number of cases of neonatal microcephaly, possibly related to the Zika virus, grew significantly in Brazil, emerging as a global health problem. The aim of this study was to seek evidences in the literature to gather and synthesize the knowledge produced on the relationship between the infection from the Zika virus during pregnancy and the neonatal consequences through an integrative literature review. The search for references was carried out in the databases of BVS, PubMed, CINAHL, Web of Science, in government sites (Ministry of Health and FIOCRUZ), and the World Health Organization, identifying four articles and four protocols that complied with the criteria established. The articles had a low level of evidence, but helped determine evidence of transplacental transmission of the Zika virus; however, there is still no evidence that the Zika virus triggers microcephaly.

Descriptors: Zika Virus Infection; Microcephaly; Pregnancy; Infant, Newborn; Community Health Nursing.

INTRODUCTION

The first case of the Zika virus was identified in humans in 1952[1] and described up until the year 2007 as causing sporadic infections in humans in Africa and Asia. In 2007, an outbreak was reported in the Federated States of Micronesia, corresponding to the first diagnostic of the Zika virus beyond Africa and Asia.

Since then, the infection has spread to other Pacific islands, subsequently reaching Brazil and Colombia[2].

Brazil was the first country to identify a possible relationship between the Zika virus infection during pregnancy and the occurrence of microcephaly in newborns (NB). After setting up a national task force, from the first 35 cases of NB with microcephaly reported in eight states (August to October, 2015), it was found that all the mothers lived in or had visited areas infected by the virus during pregnancy. Furthermore, 25 (71%) of the NB had severe microcephaly (head circumference more than three standard deviations below the mean for age and sex), 17 (49%) had a neurological abnormality, and all 27 NB who underwent neuroimaging tests showed abnormalities. These cases did not show any correlation with positive serological tests for other infectious processes (syphilis, toxoplasmosis, rubella, cytomegalovirus, and herpes simplex), nor in a changed family genetic profile[3].

In 2015, the Centers for Disease Control and Prevention (CDC) tested samples from Brazilian pregnant women who showed symptoms of infection from the Zika virus, of which two pregnancies ended in miscarriage and two NB with microcephaly died shortly after birth. The four cases obtained a positive result for infection from the Zika virus, indicating that the fetuses and NB were infected during pregnancy. The tests identified the presence of the virus in brain samples of the NB and genetic sequencing analysis showed that there is a similarity with the virus circulating in Brazil[3].

Since October 2015, the number of cases of neonatal microcephaly possibly related to the Zika virus significantly increased in Brazil, including cases detected in approximately 724 municipalities in the country[4].

In Brazil, from October 2015 to January 2016, approximately 4,783 cases of microcephaly were reported and 76.7% (3,670/4,783) of these cases are still under investigation. Of all the cases, 66.4% (3,174/4,783) were reported in the year 2015 and 33.4% (1,599/4,783) in the first 15 days of January 2016. Of the cases reported, 23.2% (1,113/4,783) have already been investigated and classified, and of these, 36.3% (404/1,113) were confirmed as microcephaly and/or alteration of the central nervous system (CNS) suggestive of a congenital infection by a clinical-radiological or clinical-laboratory criterion[5].

The Zika virus is an arbovirus of the genus Flavivirus, isolated in 1947 in the Zika forest in Uganda. Its main vector in Brazil is the mosquito *Aedes aegypti*. The occurrence of occupational transmission in a research laboratory, perinatal and sexual, has been described in scientific literature[6].

According to the World Health Organization (WHO), a born-alive infant is considered to have microcephaly when the head circumference is less than two or more standard deviations from the reference for the sex, age, or gestational period[7]. Currently, the Ministry of Health (MH) considers microcephaly in children with a head circumference equal to or less than 32 cm[4].

Microcephaly is associated with neurological disorders[8] in approximately 90% of cases. The cases analyzed to this date by computed tomography and transfontanellar ultrasound show changes similar to calcifications around the brain, especially in the periventricular, parenchymal, and thalamus regions, and in the basal ganglia[3]. These changes may have a significant impact on the development of these NB.

Considering the alarming increase of microcephaly cases reported daily in the country, it is important

to deepen our knowledge of the Zika virus during pregnancy and its possible neonatal consequences so that we can outline actions to prevent infection, monitor the prenatal care of infected pregnant women, as well as provide adequate care to promote the health of both mothers and NB with microcephaly.

Therefore, this study has the following objectives: seek evidence available in the literature in order to identify, gather, and synthesize the knowledge produced about the relationship between the Zika virus infection during pregnancy and microcephaly; and summarize the main recommendations of the protocols of official agencies for preventing and managing the Zika virus infection during pregnancy.

METHODS

For this study, the integrative review method was used, which has the specific aim to summarize the data present in the empirical and theoretical literature to broaden the understanding of a particular phenomenon.

Thus, the following stages were followed: defining the research subject and question; establishing criteria for the inclusion and exclusion of studies and literature search; categorization of the studies; evaluation of the studies included in the review; interpretation and discussion of the results; and synthesis of the knowledge[9-10].

The main question of the review was: What is the scientific evidence available in the literature on the relationship between the Zika virus infection during pregnancy and microcephaly in NB?

Data were collected in the following electronic databases: VHL (Virtual Health Library) PubMed (Medical Publications), CINAHL (Cumulative Index to Nursing & Allied Health Literature), Web of Science, along with government websites (Ministry of Health and FIOCRUZ) and the World Health Organization. The search in electronic sources was conducted from January 15 to February 11, 2016 through advanced searches in the databases using Zika and Virus as controlled descriptors with the interposition of the Boolean operator AND. Inclusion criteria were articles available in full online regardless of the methodological approach, with the exception of review articles and editorials published in Portuguese and English with abstracts indexed in the databases listed above with data related to the infection from the Zika virus during pregnancy and microcephaly. There was no restriction as to the period of publication of scientific papers.

After defining the guiding question and locating and selecting the articles, 421 potentially eligible publications were identified to be included in this review. Once duplicate articles were removed (n=218), the abstracts of 203 records were analyzed to make sure they would meet the eligibility criteria and would answer the question that guides this review. After reading the abstracts, 181 articles were excluded, and a full reading was done of 22 articles. In total, four articles and four protocols met the inclusion criteria and answered the review question, which were included in the synthesis and analysis of the data as detailed in Figure 1.

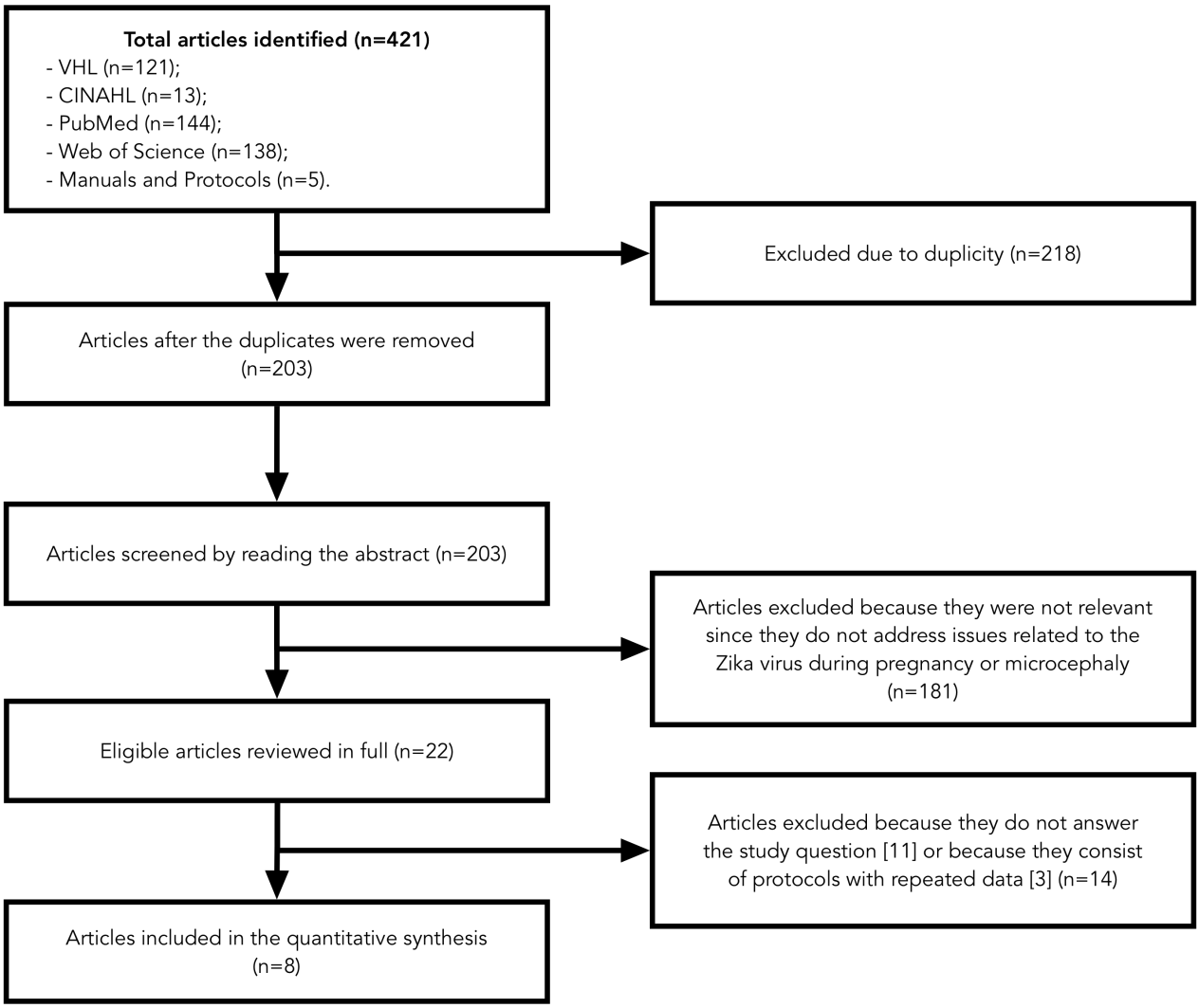

Figure 1: Flowchart of the selection of publications.

RESULTS

From all articles found (n=421), four protocols and four articles met the eligibility criteria and answered the question that guides this review, and were thus selected. After the analytical reading of the articles and protocols selected, data systematization was carried out according to tables 1 and 2.

The level of evidence of the articles was classified from I to V through a model developed by Drummond and Silva[11] in 1998, where the closer to V the lower the level.

Table 1: Description of the studies selected for review according to author, article title, journal, and year of publication.

Author, Title, Journal	Country and year	Method	Abstract	Level of evidence
Besnard M, Lastere S, Teissier A, Cao-Lormeau V, Musso D[12] Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014 Euro Surveill	Sweden, 2014	Case study	Report of two cases of suspected Zika identified in NB and their mothers in French Polynesia through the polymerase chain reaction (PCR). In one case, the researchers identified an RNA load of the Zika virus in her breast milk, but virus replication was not identified, thus there is no evidence of Zika transmission through breast milk. It was concluded that, due to the serious neonatal diseases reported caused by arboviruses such as Chikungunya and Dengue, a strict perinatal monitoring of the infections from the Zika viruses be carried out and that the data about the impact of the infection from Zika on the NB are still limited.	V
Melo AS, Malinger G, Ximenes R, Szejnfeld PO, Sampaio AS, Bispo de Filippis AM[13] Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg? Ultrasound Obstet Gynecol	England, 2016	Case study	The presence of cerebral calcifications was identified by fetal ultrasonography in two cases diagnosed with fetal microcephaly in Paraíba, Brazil. The pregnant women had symptoms of Zika during pregnancy, but their blood tests were negative for the disease. Amniocentesis was done and a subsequent quantitative real-time PCR, which came positive for the Zika virus in both NB, so they likely represent the first intrauterine diagnoses of the virus' transmission. The genotype of the Zika virus found in both cases are of Asian origin.	V
Ventura CV, Maia M, Bravo-Filho v, Góis AL, Belfort Jr R[14] Zika virus in Brazil and macular atrophy in a child with microcephaly The Lancet	England, 2016	Case study	Ocular examinations were performed on three children with microcephaly who were born in Brazil in the period of the Zika virus outbreak, and well-defined macular neuroretinal atrophy was identified in one of them. The three children had macular stain of crude pigment and loss of foveal reflex, fundus changes in the macular region, and brain calcifications detected by computed tomography. Although the infection was not confirmed by PCR, the cases fulfilled the criteria of vertical infection by the Zika virus.	V
Ventura CV, Maia M, Ventura BV, Van Der Linden V, Araújo EB, Ramos RC, Rocha MAW, Carvalho MDCG, Belfort Jr R, Ventura LO[15] Ophthalmological findings in infants with microcephaly and presumable intra-uterus Zika virus infection Arq. Bras. Oftalmol.	Brazil, 2016	Case study	Ocular examinations were performed on 10 infants diagnosed with microcephaly whose clinical diagnosis proved vertical infection by Zika virus. The serology of all the infants was negative for toxoplasmosis, rubella, cytomegalovirus, syphilis, and human immunodeficiency virus (HIV). Seven mothers reported symptoms (malaise, arthralgia, and rash) during pregnancy, six of them in the first trimester. All infants had normal anterior ocular segment and normal eye axial length; however, four had myopia with hyperopia being the most common in this period, nine infants showed optic nerve hypoplasia and pallor. More studies should be conducted to understand the meaning of these changes to the eye by the Zika virus.	V

Table 2: Recommendations for preventing and controlling infection by the Zika virus in pregnant women.

Protocols	Institution, year	Summary of key recommendations
Protocol of surveillance and response to the occurrence of microcephaly, version 1.3[4]	Department of Health Surveillance. Division of Communicable Disease Surveillance, 2016	- Avoid times and places with the presence of mosquitoes.
		- Use clothing to protect exposed parts of the body.
		- Use repellents and carefully check their labels for guidance.
		- Especially during dusk and dawn, remain in locations where there are barriers to the entrance of insects such as protection screens, mosquito nets, air conditioning, or others available.
		- Keep your vaccination schedule up-to-date and pay attention as to the nature and quality of what you eat (water, food, medicine) or have contact with and the potential of these products affecting the baby's development.
		- Communicate to health professionals any change in your health status, especially during the 4th month of pregnancy, or about the persistence of a pre-existing disease at that stage.
		- Integrated management of vectors (elimination of breeding sites, urban sanitation campaigns, blocking of cases, space fogging in high incidence areas).
Health care protocol and response to the occurrence of microcephaly related to infection by the Zika virus, version 1[16]	Health Care Department, 2015	- Avoid times and places with the presence of mosquitoes.
		- Use clothing continuously that protects exposed parts of the body such as arms and legs.
		- Practice vector control (eliminate in the house possible mosquito breeding areas), cleaning the land, proper disposal of trash and materials and proper use of water.
		- Check with your healthcare professional about using repellents and check the label for the concentration of repellent and frequency of use for pregnant women. Only use products regulated by ANVISA.
		- Stay in locations with barriers to the entrance of insects (e.g. protection screens, mosquito nets, or other barriers available).
		- Carry out all the prenatal tests recommended by the Ministry of Health.
		- Follow the vaccine schedule recommended by the Ministry of Health.
		- Seek health services in the case of infections, skin rash, exanthema, or fever.
		- Investigate and give orientation about medicines used, exposure to toxic substances, and the use of tobacco, alcohol, and other drugs during pregnancy.
		- Follow the supplementation of folic acid and ferrous sulphate as recommended.
		- Participate in educational practices, especially those promoting breast feeding, normal delivery, and healthy life habits; care for the newborn; the risks of smoking, using alcohol and other drugs; and the use of medication during pregnancy.

Protocols	Institution, year	Summary of key recommendations
Petersen EE, Staples JE, Meaney-Delman D, Fischer M, Ellington SR,	Centers for Disease Control and Prevention (CDC), 2016	Interim guidelines for health professionals in the United States who provide care for pregnant women during the Zika virus outbreak.
Callaghan, WM, Jamieson DJ[17]		- Pregnant women should consider delaying travel to areas with the transmission of the Zika virus in progress and, if they do travel, to be strongly advised to take measures to prevent mosquito bites.
Interim Guidelines for Pregnant Women During a Zika Virus Outbreak - United States, 2016		- Guidelines on how to carry out the screening, testing, and management of women who return pregnant.
		- Pregnant women diagnosed with a Zika virus infection should receive support treatment with referral to specialized services.
Staples JE, Dziuban EJ, Fischer M, Cragan JD, Rasmussen SA, Cannon MJ, *et al.* [18]	Centers for Disease Control and Prevention (CDC), 2016	Interim guidelines for US health care providers who provide care for the NB of mothers who traveled or resided in an area that has the presence of the Zika virus during their gestation period:
		- Identify children whose mothers were potentially infected with the Zika virus (women traveling or living in an area with transmission of the Zika virus during pregnancy; or infants of mothers with positive or inconclusive results for infection by the Zika virus) and review fetal ultrasounds and maternal tests for infection by the Zika virus.
		- Monitoring of NB with microcephaly or intracranial calcifications or laboratory evidence of a possible congenital infection from the Zika virus in order to evaluate possible long-term consequences and notification of the case to the State, territory, or local health department.
Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection - United States, 2016.		- The monitoring of the child should include cranial ultrasound to assess the subclinical findings, unless the results of prenatal ultrasound from the third quarter did not show brain abnormalities, eye examination, and a repeat audience screen described above for infants.
		- Monitoring the development and screening during the first year of life is recommended for all children with congenital infection from the Zika virus.
		- Mosquito bite prevention for pregnant women and with childbearing potential: use air conditioning or window and door screens when indoors, wear long-sleeved clothes and pants, wear clothing and equipment treated with permethrin, and use insect repellents.

DISCUSSION

Evidence of perinatal transmission of the Zika virus in cases of microcephaly

The French Polynesia has experienced since October 2013 the largest outbreak of infection from the Zika virus. The estimate is that since early February 2014, 11% of the population has been affected (about 28,000 infections) with possible perinatal transmission in two cases, whether via the placenta during childbirth, breastfeeding, or by direct contact between mother and NB[12,19-20]. However, the number of infections in NB has been probably underestimated for the lack of diagnosis and monitoring.

In Brazil, the first two cases of microcephaly in NB related to Zika virus have been described. In the state of Paraiba, two pregnant women who presented symptoms related to infection by the Zika virus had fetal diagnosis of microcephaly by ultrasound. The amniotic fluid of the pregnant women was analyzed and both were found to contain genetic material (RNA) of the Zika virus by the RT-PCR (Reverse Transcription - Polymerase Chain Reaction) technique in real time in both cases analyzed[12]. The cases showed similarities with other intrauterine infections, but with more serious and larger brain injuries, which are characteristics that resembled the reports from the CDC in 2002 with the infection from the West Nile virus, an arbovirus just like Zika, thus suggesting an infection by the Zika virus[13].

According to the epidemiological report No. 11 of the Ministry of Health[5] with data updated to January 30, 2016, 17 cases of microcephaly were confirmed by clinical criteria. The Zika virus was identified from samples from two cases of miscarriages, two NB residing in the state of Rio Grande do Sul, one NB in Ceará, and the others (12/17) born in Pernambuco. Only the case of Pernambuco was identified by serology, but the others were by PCR.

Another recently identified fact strengthens the virus' transmission capacity during pregnancy. A patient with clinical symptoms indicative of the Zika virus infection in early pregnancy experienced abortion in the eighth week and had placental samples analyzed by RT-PCR techniques, which suggest infection of placental cell by the Zika virus and placental transmission. RT-PCR exams were also performed to rule out dengue infection, which were negative[21].

Furthermore, ocular abnormalities were found in two studies in NB with microcephaly. One study evaluated 10 infants with microcephaly whose diagnosis was made by evaluating the head circumference associated with negative serology for rubella, toxoplasmosis, syphilis, HIV, and cytomegalovirus in infants and seven mothers of these reported symptoms of infection by the Zika virus, six of which in the first quarter. Some changes were observed in these NB such as optic nerve hypoplasia, myopia, and hyperopia[15]. In another study, three children with microcephaly were evaluated and fundus changes were identified in the macular region, but in these cases the infection from the Zika virus was not confirmed by PCR, but the cases matched the criteria of vertical infection from the Zika virus since other congenital infections were excluded by serology, and one of the mothers reported having a skin rash and arthralgia in the first gestational trimester, which are common symptoms for the Zika virus infection[14].

Other forms of transmission of the Zika virus than the transplacental route should be a concern for pregnant women. The Laboratory of Flavivirus Molecular Biology of the Oswaldo Cruz Institute analyzed saliva and urine samples from two patients collected during the presentation of symptoms compatible with the Zika virus. The presence of genetic material from the Zika virus was confirmed by RT-PCR in real time; however, these findings do not prove the possibility of infection from other people systemically through these fluids[22]. In Texas, a case of infection by the Zika virus was confirmed in a non-traveler, raising strong suspicions of sexual transmission[23] since the Zika virus has been isolated in semen from a patient in Tahiti[6].

Only 18% of human infections with the Zika virus result in clinical manifestations. Among them, the most common are maculopapular rash, low fever, arthralgia, myalgia, and headache while conjunctival hyperemia not purulent and without pruritus, edema, sore throat, coughing, vomiting, and hematospermia were reported less frequently. The symptoms subside after three to seven days[16].

During pregnancy, the presence of a rash infection does not necessarily indicate the occurrence of fetal microcephaly. However, this signal has been reported frequently in the gestational history of some women who have had NB with this malformation. So it is important to consider this in the investigation of possible etiological hypotheses for this change[24].

In order to qualify the surveillance of microcephaly related to infection by the Zika virus, WHO with the support from other agencies defined the criteria for identifying cases. States and municipalities should carry out the investigation of the following cases: "1. Pregnant woman with possible infection from the Zika virus; 2. Fetus with changes in the CNS possibly related to infection from the Zika virus; 3. Spontaneous miscarriage due to possible association with infection from the Zika virus; 4. Stillbirth due to possible infection from the Zika virus; 5. Live newborn with microcephaly possibly associated with infection from the Zika virus" (pg.22)[4].

The monitoring of pregnant women who had rash illness and confirmation of infection from the Zika virus will make it possible to better understand the possible fetal and neonatal outcomes.

Recommendations for prevention and control of Zika virus infection in pregnant women

According to protocols published by the Ministry of Health in recent months, the conduct of health professionals should begin with reproductive planning. Couples or women who wish to become pregnant should be advised by health professionals on how to prevent infection from the Zika virus, as well as the consequences of this infection during pregnancy, especially in the first gestational trimester[16]. The CDC recommends that women who want to become pregnant and pregnant women should consider the possibility of postponing trips to countries with a Zika virus outbreak, but if these women do travel to these areas, it is recommended that they receive guidelines from health professionals on measures for preventing mosquito bites and to follow them carefully[25].

Furthermore, health professionals should be ready to offer contraceptive methods, identify pregnant women early on through an active search, offer access to quick pregnancy tests and early prenatal care in a

timely manner, carry out health education activities with a focus on preconception counseling, along with giving orientation and providing information to women and couples who wish to get pregnant on the situation of microcephaly related to Zika[16].

It is recommended that all pregnant women be identified early on in the territory covered by health teams with ready prenatal care in order to intervene in a timely manner during pregnancy either with preventive or therapeutic measures[16].

Pregnant women can be infected in any trimester[26]. The incidence of infection in pregnant women by the Zika virus is still unknown, and data on the infected pregnant women are limited meaning that there is no evidence that this group is more susceptible to this infection or that the severity is greater during this period[17].

During prenatal care, it is important to guide pregnant women and their family members about mobilization and combating the vector (eliminating possible mosquito breeding areas), how to remain attentive to the cleanliness of their neighborhood, daily check of household containers with standing water, installing protection screens on doors and windows[16], and avoiding times and places with the presence of the mosquito. A study done by the Federal University of Minas Gerais found that bites from the *Aedes aegypti* mosquito usually happen between 7:30 and 10 am and between 3:30 and 7 pm[27], but that the mosquito could still bite at other times.

The dispersability capacity of the *Aedes aegypti* mosquito by flight is small, rarely exceeding 100 meters. However, it has been confirmed that a female can fly up to three kilometers away for laying her eggs when there is no appropriate recipients in the surrounding area[27].

Other protection and prevention measures during pregnancy include avoiding contact with people with fever, rashes, or infections, use of mosquito nets, continual use of clothing to protect arms and legs (exposed areas of the body), keep rooms closed with the air conditioner on, and use insect repellents[28].

Data from studies in humans and animals as to using repellents made from n-diethyl-meta-toluamide (DEET) show that there is no danger to the health of the NB nor toxicity by breastfeeding[16-17]. Therefore, repellents should be applied to the skin in areas exposed and on the clothes and reapplied according to the indication of use of each manufacturer or in the case of contact with water or excessive sweating[16]. DEET at a concentration from 6.65% to 20% protects in average from 110 to 230 minutes, respectively[29]. DEET-based repellents should contain a minimum concentration of 20%, but there are products below this concentration available in the market, which calls for caution when purchasing to make sure to get the appropriate repellent[30-31].

According to the compendia of international cosmetic ingredients, other repelling substances are recognized as safe for use, such as Icaridin or Picaridin; EBAAP or IR3535, and essential oils such as citronella, although safety studies for pregnant women have not yet been done on them[16]. CDC recommends using clothing and equipment with a permethrin base[17,31].

The possibility of transmission happening sexually or by other body fluids (e.g. saliva and urine),

although not proven, suggest that pregnant women should use condoms with every sexual relationship and avoid sharing cups and cutlery[22].

If during prenatal care the pregnant woman is diagnosed with a rash, regardless of the gestational age, the case must be notified and she should continue under the monitoring of health care services that she was receiving, unless changes arise that modify the classification of obstetrical risk[16,24].

It is important to emphasize that the early identification of a cranial circumference lower than expected for the gestational age during prenatal care can provide greater success in probing actions of epidemiological suspicions related to microcephaly, as well as better prepare and guide adequately the family for the birth of a NB with malformations[16].

Therefore, local health services are instructed by the MH to immediately notify the platform of the Center for Strategic Information for Health Surveillance (Cievs) of all the cases of fetuses showing signs suggestive of intrauterine infection from the Zika virus. The MH protocol defines that the reports should meet the fetal diagnostic criteria through ultrasound or other imaging method available, which identifies head circumference with two standard deviations below the mean for gestational age and sex[16].

The protocol also recommends that all suspected cases of microcephaly related to the Zika virus be registered using the form Public Health Events Report (RESP-Microcephalia). This form is available online for both public and private services. Therefore, it is important to emphasize that early detection, proper notification, and adequate records are essential to begin the process of research, confirming or dismissing cases of microcephaly related to Zika, and to contribute to the description of this new disease and to better health care[16].

The test recommended in Brazil for Zika virus confirmation is the reverse transcription - polymerase chain reaction (RT-PCR), which is a test available in some reference laboratories in the Unified Health System (SUS) and in the private network. Reference laboratories and research centers are working to develop platforms that can perform specific serologic tests because up until now there are no serological tests available for detecting specific antibodies for the Zika virus[16].

Health teams must be prepared to receive pregnant women with a suspected case of microcephaly with all their anxieties, fears, and doubts through attentive and qualified listening, without making judgments, nor with prejudice, allowing mothers to express themselves freely[16].

Once the Zika virus infection or microcephaly is confirmed or suspected, the care at labor and birth should not be modified[15]. Though WHO defends the right of pregnant women to have access to safe abortion practices in the case of suspected or confirmed microcephaly[32], this fact opens a broad discussion on the legalization of abortion in some countries where this practice is prohibited.

The woman should have her rights safeguarded: have a companion of their choice, should not remain fasting, choose the most comfortable position for birth, and she should not be subjected to routine or unnecessary interventions. Infection from the Zika virus or the presence of microcephaly is not indicative of a cesarean section.

The MH protocol continues to recommend collecting blood samples from the umbilical cord, cerebrospinal fluid (CSF), and urine of NB at birth to carry out specific serology for arboviruses and other research protocol diseases (TORSCH - toxoplasmosis, rubella, cytomegalovirus, herpes virus, and syphilis)[16].

At birth the NB must be given care in accordance with the routines recommended by the Mo and in the case of needing to follow neonatal resuscitation, follow the care proposed by Ordinance SAS/MS No. 371 of May 7, 2014 and Technical Note No. 16 of June 16, 2014[16,33]. Therefore, the NB shall be guaranteed the right of early skin-to-skin contact, clamping of the umbilical cord at the appropriate time, breastfeeding in the first hour of life, and be subjected to routine procedures only after these initial procedures[16].

The Fernandes Figueira National Institute for the Health of Women, Children, and Adolescents of the Oswaldo Cruz Foundation and the Brazilian Network of Human Milk Banks issued a statement that there is not enough scientific evidence to change the current breastfeeding practices considering infection from the Zika virus[34], so breastfeeding should be maintained even in suspected or confirmed cases.

Follow-up of women after birth and of their NB with microcephaly by a specialized multidisciplinary team is essential to ensure acceptance, support, and information to the family and to offer early stimulation for NB in order to reduce possible delays in development and socialization. The MH issued a protocol with guidelines for such follow-up and announced the training of professionals and expansion of specialized services; however, the guarantee of access and the quality of this follow-up for all NB with microcephaly and the family members will certainly be a major challenge for Brazil and other countries affected[8].

CONCLUSION

The data analyzed on the development and dissemination of the Zika virus, its relation to pregnancy and perinatal consequences made it possible to establish that there is evidence of transplacental transmission of the Zika virus. However, there is still no scientific explanation showing that the Zika virus triggers microcephaly since studies show only an association between them.

To date, microcephaly is the only perinatal complication associated with the Zika virus, along with possible eye disorders such as optic nerve hypoplasia, myopia and hyperopia, and fundus changes.

It is important to point out that this review included only case reports because it is a new disease, so studies for higher levels of evidence are needed. The production of these studies is dependent on the incidence of cases and on the diagnostic capacity to confirm the causal relationship between the infection of pregnant women by the Zika virus and microcephaly and other possible perinatal consequences still unknown. It is hoped that the efforts of the world scientific community in researching these evidences will contribute to the eradication of this disease.

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