

Review Article

Breastfeeding and Vertical Exposure to Zika Virus: A Literature Review

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Abstract

The Zika virus has been affecting a large part of the Brazilian population since 2014, and its pathology has raised questions on the transmission route, symptoms, prevention, and treatment, as well as on neurological changes, which were previously not associated with the disease. To clear doubts on the transmission of the virus during breastfeeding, this study aimed to review and analyze studies, published from January 2014 to April 2017, regarding the relationship between breastfeeding and Zika virus exposure and focusing on the importance of breastfeeding. A search was performed in main databases, resulting in 85 articles, of which 38 were selected based on search criteria. All articles reported on the presence of Zika virus RNA in human milk. Among them, 34.21% had no stance on breastfeeding, 28.94% supported it, 18.42% did not recommend it, while 18.42% explained the need for further studies on the subject. The World Health Organization recommends breastfeeding for all mothers infected with Zika virus because the benefits of breastfeeding outweigh the risks of disease transmission, and there is no scientifically proven case of transmission through this route.

ABBREVIATIONS

ZIKAV: Zika virus; PCR: polymerase chain reaction; WHO: World Health Organization

INTRODUCTION

In November 2014 and early 2015, the Zika virus (ZIKAV), a new virus transmitted by the *Aedes aegypti* mosquito, started to spread in Brazil. The manifestations were similar to those of dengue fever, with low fever, itching exanthema in the body, and conjunctivitis. Other symptoms included myalgia and mild joint pain [1,2]. A higher prevalence of microcephaly cases and central nervous system abnormalities was observed, associating cases of neurological changes with the virus [3,4].

ZIKAV originated from Asia and Africa and spread throughout French Polynesia in 2013, with some cases in Chile [5]. In May 2015, 1.5 million people were affected by ZIKAV in the northeastern region of Brazil. The virus spread throughout South America, Central America, and the Caribbean, alarming the Pan American Health Organization. More than 4,500 microcephaly cases were confirmed in February 2016, and a worldwide epidemic of ZIKAV was announced, with confirmed cases in Europe [6]. The idea of correlating ZIKAV with microcephaly

began as a result of a surge in the number of infected cases and newborns with reduced cephalic perimeter with no apparent cause, which initiated research and notification.

The viral transmission can either be vectored or non-vectored. The vectored route occurs through the bite of *Aedes aegypti* or other mosquitoes of the same species, which reproduce in clean standing water in unsealed water tanks, plant dishes, and tires, among other places [7]. The non-vectored form occurs without direct contact with the agent, such as sexual transmission through semen [7-9] and perinatal transmission, or transmission of the virus from the mother to the newborn during childbirth [4,10,11]. Blood transfusion is also a form of transmission [7,12]; asymptomatic blood donors with ZIKAV were detected, with 80% not showing clinical alterations [13]. Transplacental transmission can also occur through a pregnant woman affected by ZIKAV, transmitting the virus to the fetus through the placenta at any time during pregnancy [14].

Diagnosis is through polymerase chain reaction (PCR) and virus segregation in blood samples. The PCR technique allows to accurately identify the causative agent's DNA in the patient's blood samples. It operates by amplifying a specific fragment of the DNA molecule thousands of times in just a few hours [5,13].

The ZIKAV epidemic has raised questions about the transmission, prevention, and consequences of the disease, including some questions about breastfeeding and reproduction planning. Due to the extent and diversity of the cases, infected infants need to undergo an interdisciplinary follow-up by neurologists, pediatricians, speech therapists, physiotherapists, occupational therapists, psychologists, and social workers, to address different issues. Moreover, early evaluation and stimulation of neuropsychomotor function are essential to provide a better prognosis [5,15].

Considering the increased incidence of ZIKAV in Brazil and the association of swallowing disorders in newborns with congenital ZIKAV syndrome, a speech pathologist is necessary to evaluate the baby's feeding problems and stomatognathic functions, stimulate these functions, and design an appropriate intervention plan for each case, following the recommendation of the World Health Organization (WHO) [16], which is exclusive breastfeeding in the first 6 months of life for the overall development of the newborn and food security.

Considering the controversy surrounding the pathology of ZIKAV with unknown means of transmission, this literature review was conducted to build knowledge for action, allowing a stance on breastfeeding in ZIKAV cases and providing basis for both professional recommendations and performance of the mother regarding breastfeeding.

METHODOLOGY

This literature review aimed to group knowledge about breastfeeding and ZIKAV exposure in articles published between January 2014 and April 2017. The following combined keywords in English, Portuguese, and Spanish were used to identify articles on the topic in the Medline, SciELO, Bireme, Cochrane, and Embase databases: fonologia "Zika e amamentação", "Zika e aleitamento materno", "Zika e alimentação", "Zika and breastfeeding", "Zika and feeding", "Zika y lactancia materna", and "Zika y alimentacion".

We found 85 studies published in English and Portuguese in Medline, Bireme, and Embase, as shown in Figure 1. No studies were found in SciELO and Cochrane. Furthermore, no studies on ZIKAV related to speech therapy were found in any of these scientific databases. Among the 85 articles, the following were excluded: duplicate articles (13), nonscientific publications (9), articles not related to the subject (20), and unavailable articles (5). Thus, 47 articles were excluded, and the remaining 38 articles that addressed the subject of ZIKAV and breastfeeding were selected (Figure 1).

We established a guiding question, "What is the stance of the existing literature on breastfeeding in cases of ZIKAV exposure?" After article selection, we observed and analyzed the 38 articles, and classified the approach of each study based on the guiding question, as follows: has no stance on breastfeeding, is in favor, is against, and explains the need for further studies on the subject.

RESULTS

Among the analyzed studies are shown in Table 1, 34.21% [5,10,14,17-26] investigated the presence of ZIKAV RNA in breast milk but had no stance on breastfeeding or lactation.

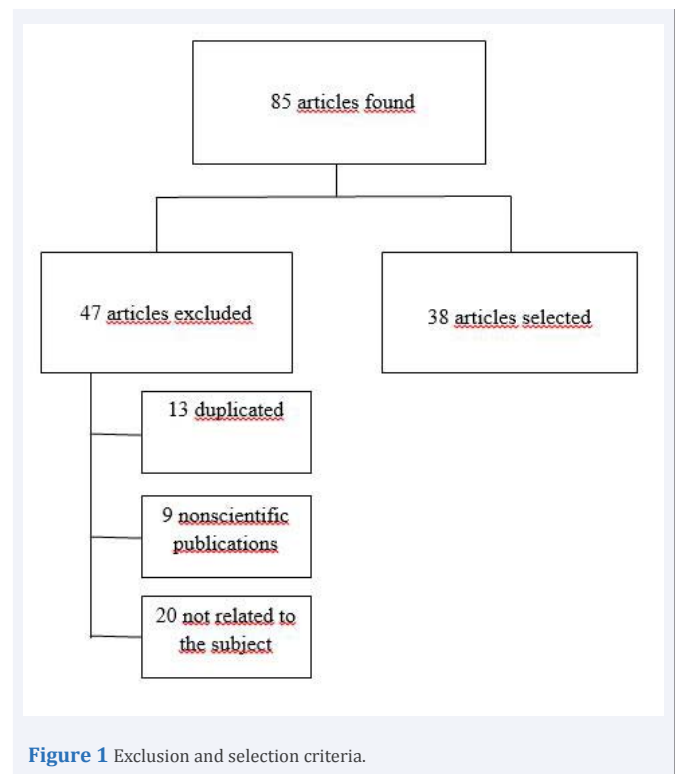


Figure 1 Exclusion and selection criteria.

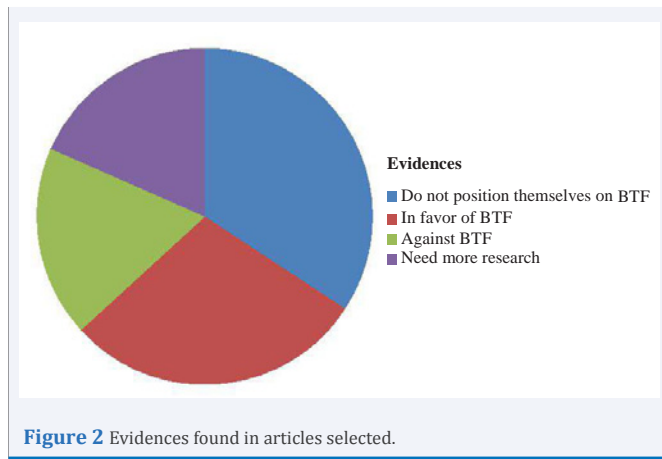
However, 28.94% [16,27-36] were in favor of breastfeeding and explained that despite the presence of ZIKAV in human milk, there is no scientific evidence of infants being infected through breastfeeding. Meanwhile, 18.42% [6,37-42] affirmed the possibility of contamination and were against breastfeeding, whereas 18.42% [43-49] explained the importance of further studies in this area (Figure 2).

DISCUSSION

In this literature review, a large proportion of the articles reported that breastfeeding is essential in all nations and should be treated as a public policy based on the benefits it brings in the short, medium, and long term, being advantageous to both the baby and the mother [16,27,36,50,51].

The WHO guidelines on breastfeeding reinforce that even in cases of suspected or confirmed ZIKAV infection, breastfeeding should be supported and encouraged. Exclusive breastfeeding is recommended from 1 hour after childbirth up to 6 months of age, to be continued with complementary foods up to 2 years of age or more [16,17,36]. Mothers and infants may need help in the breastfeeding process, and newborns with congenital ZIKAV syndrome may have swallowing disorders, requiring speech therapy to start and continue breastfeeding.

One study analyzed the milk of a mother with confirmed ZIKAV infection [18] and showed virus replication in breast milk. However, the newborn was not infected even though it was breastfed. Due to this study, some authors [6,37-42] supposed that breastfeeding may be a transmission vector, knowing that some diseases caused by flaviviruses of the same family with ZIKAV, such as dengue fever and other diseases, can be transmitted through breastfeeding [46]. However, until recently, there is no scientific evidence of this transmission route for ZIKAV.



This research shows that 28.94% of the studies analyzed [16,28-37] agreed with the recommendation of exclusive breastfeeding. Although ZIKAV RNA was detected in human milk, there was no virus replication in the culture, and the virus did not infect infants [9]. Nevertheless, this remains a controversial subject.

Breastfeeding helps in cognitive, affective, and social development, besides being a species-specific food, that is, “a living substance of great complexity, with specific composition for human species, containing fats, proteins, vitamins, water, sugar, enzymes, iron, antibodies and iron in exact proportions for the nutritional needs of the human baby” [52], which is easily digested and absorbed. Breastfeeding also contributes to the reduction of infant mortality and has prevented 823,000 deaths annually from children under 5 years of age by increasing their immunity and preventing diseases such as diarrhea and respiratory problems, otitis, and malocclusions [50,51]. Breastfeeding is also an economic policy that is sustainable, since it does not generate expenses or pollute the environment. It is renewable, natural, and free [50,51]. Current evidence suggests that the benefits of breastfeeding outweigh the risks of ZIKAV transmission through breast milk.

During breastfeeding, mothers and babies require assistance, as they commonly have difficulties establishing this practice [53]. Speech therapists have the competence to accompany the mother and baby in their feeding mishaps, evaluate their stomatognathic functions, encourage them, and tailor the intervention plan for each case [54]. Because of these findings, we searched the databases for any correlation between the work of speech therapists, breastfeeding, and ZIKAV infection; however, the search showed no studies focused on this correlation. Although this area is a “recent” subject, the search result encourages further research.

In Brazil, the region most affected by ZIKAV has been the southeast, followed by the northeast, midwest, south, and north [55]. The recommended/performed approaches throughout Brazil encourage breastfeeding, multidisciplinary follow-up, and early neuropsychomotor stimulation. The innovations in this pathology has promoted the search for new knowledge and approaches.

The institution of a ZIKAV epidemic protocol became a crucial

Table 1: Summary of the results of studies related to breastfeeding and Zika Virus.

Authors/ Year of Publication	Results
Chan JF, Choi GK, Yip CC, Cheng VC, Yuen KY ⁵ /2016	ZIKAV particles were detected in breast milk, but virus replication was not detected
Besnard M, Lastère S, Teissier A, Cao-Lormeau VM, Musso D ¹⁰ /2016	Collected breast milk from two infected and active mothers, and tested resulting in the presence of virus RNA. However, there was no replication of ZIKAV
Possas C ¹⁴ /2016	There is no research confirming the transmission of ZIKAV by breastfeeding
Russell K, Oliver SE, Lewis L, Barfield WD, Cragan J, Meaney-Delman D, et al. ¹⁷ /2016	Although the Zika virus has been found in breast milk, there are no cases associating breastfeeding with ZIKAV infection
Dupont-Rouzeyrol M, Biron A, O'Connor O, Hugon E, Descloux E ¹⁸ /2016	Tested samples of mother's milk from infected and active mother of ZIKAV and was found infectious particles of the virus. However the child was not infected.
Ghebreyesus A, Hungary MS ¹⁹ /2016	Detected ZIKAV in human milk, and consider a possible transmission vector. But there is no publication about infection per breastfeeding
Hennessey M, Fischer M, Staples JE ²⁰ /2016	Zika virus RNA was detected in breast milk, but there is no evidence of the relationship between infection and breastfeeding
Sampathkumar P, Sanchez LJ ²¹ /2016	The virus was detected in breast milk but was not associated with a form of transmission
Malone RW, Homan J, Callahan MV, Glasspool-Malone J, Damodaran L, Schneider Ade B, et al ²² /2016	Zika virus sequences were identified in breast milk by polymerase chain reaction (PCR), but reports did not indicate microcephaly as a complication
Boeuf P, Drummer HE, Richards JS, Scoullar MJL, Beeson JG ²³ /2016	Was detected RNA do ZIKAV, in breast milk,urine, saliva and semen.
Klase ZA, Khakhina S, Schneider Ade B, Callahan MV, Glasspool-Malone J, Malone R ²⁴ /2016	ZIKV RNA can be detected in breast milk, urine, semen, and sputum from infected individuals, replication-competent virions have been most readily cultured from semen samples.
Blázquez AB, Saiz JC ²⁵ /2016	For the nursing mothers, it is re commended that ZIKAV be detected in breast milk, even if there are no proven cases of transmission by this route.
Fleming-Dutra KE, Nelson JM, Fischer M, Staples JE, Karwowski MP, Mead P, et al ²⁶ /2016	Detected RNA of ZIKAV in breast milk, but wasn't proven replication or infection during breastfeeding.
Organização Mundial da Saúde ¹⁶ /2016	Breastfeeding on demand, and support to this process so many in cases of mothers infected with ZIKAV, as in cases of babies with congenital abnormalities
Drabkin A. ²⁷ /2016	There are no documents that correlate the transmission of ZIKAV to breastfeeding. Supports breastfeeding.
Maestre AM, Caplivski D, Fernandez-Sesma A ²⁸ /2016	Although ZIKAV has been found in breast milk, there is no evidence to support this relationship of transmission through breastfeeding. Breastfeeding is recommended.

Duff E ²⁹ /2016	There is no study that relates the transmission of Zika Virus to breastfeeding and because of its importance for the development of the baby, it is recommended to encourage this practice
Lockwood CJ ³⁰ /2016	The study says that breastfeeding is recommended because of the gains offered, although RNA of the virus has already been found in milk.
Falcao MB, Cimerman S, Luz KG, Chebabo A, Brigido HA, Lobo IM, et al ³¹ /2016	There is presence of ZIKAV RNA, however there is no case that confirms this form of transmission and the guidelines recommend breastfeeding
Lazear HM, Diamond MS ³² /2016	ZIKAV RNA was found in breast milk, and this route of transmission was documented in other flaviviruses. Nursing mothers can transmit the virus through this practice. But it is not yet known if it is infectious. Infected mothers are encouraged to breastfeed their children.
Pfaender S, Vielle NJ, Ebert N, Steinmann E, Alves MP, Thiel V ³³ /2017	WHO has published a guideline summarizing the current evidence regarding the risk of ZIKV transmission via breastfeeding in which mothers with suspected, probable or confirmed ZIKV infection are encouraged to breastfeed their children, as the beneficial effects of breastfeeding preponderate any potential risk of ZIKV transmission via breast milk. And The Zika virus becomes inactive in breast milk at a given time. And pasteurization helps prevent
Sharma A, Lal SK ³⁴ /2017	ZIKAV RNA was detected in human milk in the French Polynesia epidemic, and more recently the presence of infectious ZIKAV particles in the milk was found. However, there is no evidence of transmission of the virus through breastfeeding. For this reason WHO recommends breastfeeding, as the benefits outweigh the risks
Hajra A, Bandyopadhyay D, Hajra SK ³⁵ /2016	There is no restriction on breastfeeding to prevent transmission of the virus. Even though ZIKAV RNA was found isolated in human milk.
Organização Mundial da Saúde ³⁶ /2016	Recommendation for newborns of infected or suspected ZIKAV mothers to perform breastfeeding.
Wahid B, Ali A, Rafique S, Idrees M ⁶ /2016	It considers breastfeeding a possible route of transmission.
Jamali MSR, Bayrami S, Jamali MS, Golrokhi R, Golsoorat PF, Seyed AS ³⁷ /2016	It states that breastfeeding is also a way of acquiring the disease.
Patterson J, Sammon M, Garg M. ³⁸ /2016	Transmission through breastfeeding was published during the French Polynesia epidemic.
Mishra B, Behera B ³⁹ /2016	Breast milk has been reported as non vector transmission route during the outbreak in French Polynesia
Saiz JC, Vázquez-Calvo Á, Blázquez AB, Merino-Ramos T, Escribano-Romero E, Martín-Acebes MA ⁴⁰ /40 Ibrahim NK ⁴¹ /2016	High ZIKV RNA load was detected in breast milk samples from both mothers, the virus could not be multiplied in susceptible cell cultures. Transmission by breastfeeding must be considered. The transmission of ZIKAV can occur through breastfeeding

Passi D, Sharma S, Dutta SR, Ahmed M ⁴² /2017	Transmission through breastfeeding can not be excluded, although it is rare, ZIKV RNA has been reported in samples of breast Milk
Wooton AK ⁴³ /2016	Questions about the possibility of breast milk being a vector of transmission
Cavalcanti MG, Cabral-Castro MJ, Gonçalves JL, Santana LS, Pimenta ES, Peralta JM ⁴⁴ /2017	Transmission through breastfeeding is questionable since the presence of ZIKAV RNA in the isolation culture has been found and the results suggest that transmission through breastfeeding may be less efficient than other body fluids.
Plourde AR, Bloch EM ⁴⁵ /2016	The identification of the presence of ZIKAV RNA in various types of body fluids, like breast milk raises questions about transmission, but there are still no depth studies in these cases
Wang JN, Ling F ⁴⁶ /2016	Viral particles of ZIKAV were found in the breast milk, but virus replication was not detected, making this route uncertain but plausible. Other Flaviviruses like DENV and WNV have the transmission vector of breastfeeding. Further research is needed in this field.
German Advisory Committee Blood (Arbeitskreis Blut) ⁴⁷ /2016	The possibility of transmission via breastfeeding should be done further research
Waddell LA, Greig JD ⁴⁸ /2016	The identification of ZIKAVRNA in various types of body fluids raises questions about human vertical transmission via saliva, semen and human milk.
Marrs C, Olson G, Saade G, Hankins G, Wen T, Patel J, et al ⁴⁹ /2016	While there is no evidence of vertical transmission. CDC discusses the benefits of BTF outweigh the risk of transmission. Studies on the infectiousness of breast milk and sequela of neonatal infection are urgently needed.

step to foster research funding and enable clarification on the infection, forms of transmission, and whether breastfeeding is a possible transmission vector, providing information for the population of pregnant women and newborns with congenital ZIKAV syndrome.

FINAL CONSIDERATIONS

ZIKAV is detected in breast milk, but breast milk has not been considered a transmission vector due to the lack of virus replication studies that prove this relationship. The guidelines for mothers with suspected or confirmed ZIKAV infection and for newborns with congenital ZIKAV syndrome have been as follows: breastfeeding, early stimulation of neuropsychomotor development, and follow-up with a speech therapist and a multidisciplinary team [56].

Due to the lack of research addressing speech pathology in the follow-up of these cases, we suggest that research be conducted on this approach, building theoretical knowledge produced by clinical practice and considering the generation of microcephaly cases that may occur due to the ZIKAV epidemic in recent years.

Further studies are needed to clarify whether breastfeeding is a possible transmission vector. The virus' RNA has already been identified in breast milk, but there is no proven case of this route of infection. Moreover, we suggest long-term research to clarify

the dynamic process of breastfeeding and to better understand questions regarding the duration of RNA presence in human milk, viral load, and long-term follow-up for breastfed babies.

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