

Infant feeding in areas of Zika virus transmission

Summary of rapid advice guideline

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1. Introduction

1.1 Background

Zika virus is transmitted to humans through the bite of infected *Aedes* mosquitoes. Person-to-person transmission has also been reported from sexual contact,^{1,2} blood transfusion³ and perinatal transmission.⁴ Although the main mode of Zika virus transmission is through infected *Aedes* mosquitoes, current widespread transmission of the virus has raised questions as to whether transmission can also occur during breastfeeding, a practice that is essential to the survival and development of infants and young children.

A rapid advice guideline on infant feeding in areas of Zika virus transmission⁵ was developed following formal WHO procedures. This guideline replaces the interim guidance on breastfeeding in the context of the Zika virus published by WHO on 25 February 2016.⁶ This guideline now incorporates more evidence underpinning the recommendations. A summary of the information in the rapid advice guideline is reflected in this document.

1.2 Target audience

This document is intended to be used by governments including ministries of health, policy makers, and health-care workers to provide guidance on infant feeding in regions affected by transmission of Zika virus. It may also be used to inform communication to the general public.

2. Recommendation

2.1 Recommendation

Infants born to mothers with suspected, probable or confirmed Zika virus infection, or who reside in or have travelled to areas of ongoing Zika virus transmission, should be fed according to normal infant feeding guidelines. They should start breastfeeding within one hour of birth, be exclusively breastfed for six months and have timely introduction of adequate, safe and properly fed complementary foods, while continuing breastfeeding up to two years of age or beyond.

2.2 Rationale

Breastfeeding has significant benefits for mothers and children, in low-, middle-, and high-income countries. Children who are breastfed for longer periods have lower infectious morbidity and mortality, fewer dental malocclusions and higher intelligence than do those who

are breastfed for shorter periods, or not breastfed.

Breastfeeding also benefits mothers. It can prevent breast cancer and improve birth spacing, and may reduce a woman's risk of diabetes and ovarian cancer. Scaling-up breastfeeding can prevent an estimated 823 000 child deaths and 20 000 deaths from breast cancer every year.^{7, 8}

Zika virus ribonucleic acid (RNA) has been detected in breast milk from three mothers with confirmed Zika virus infection,^{9,10} and replicative virus was identified in cell culture.¹⁰ The breast milk samples where Zika virus RNA was found were collected at a time when the mothers were reverse transcription polymerase chain reaction (RT-PCR) positive for Zika virus in serum samples and had clinical disease.

Based on the documented presence of Zika virus RNA (detected by RT-PCR) and replicative Zika virus (detected in cell culture) in breast milk samples, breast milk may be considered as potentially infectious. However, there are currently no documented reports of Zika virus being transmitted to infants through breastfeeding.

The frequency of virus detection, virus kinetics and size of viral load of Zika virus in breast milk is unknown.

Although Zika virus is known to circulate in the blood before an infected person becomes symptomatic and the virus is detected, these parameters are not known in relation to the virus kinetics in breast milk.

No long-term complications have been documented for either of the two reported cases of neonates with confirmed Zika virus infection.⁹ However, in countries with ongoing transmission of Zika virus, there is scientific consensus that infection with Zika virus is a cause of Guillain–Barré syndrome, including among children who are less than 15 years of age.¹¹ No adverse neurologic outcomes or severe disease have been reported to date from infants and young children (0–23 months of age) with postnatally acquired Zika virus infection.¹¹ Any change to this situation should be carefully monitored.

Overall, the guideline development group felt that there was minor variability in the values and preferences around breastfeeding in the context of Zika virus. Mothers and caregivers, when reassured about breastfeeding in the context of Zika virus, support and place a high value on breastfeeding in most communities.

In light of the evidence available, the benefits of breastfeeding for the infant and mother outweigh any potential risk of Zika virus transmission through breast milk.

2.3 Remarks

These remarks are intended to present considerations for implementation of the recommendation, based on the discussion of the guideline development group.

The recommendation is consistent with the Global strategy for infant and young child feeding,¹² as endorsed by the Fifty-fifth World Health Assembly in resolution WHA54.2 in 2002, to promote optimal feeding for all infants and young children.

Mothers who decide to breastfeed should receive skilled support from health-care workers to initiate and sustain breastfeeding, whether they or their infants have suspected, probable or confirmed Zika virus infection.

Mothers and families of infants born with congenital anomalies (e.g. microcephaly), or those presenting with feeding difficulties, should be supported to breastfeed their infants. Skilled feeding support from health professionals, including breastfeeding support, should be provided.¹³

Families and communities are central in supporting optimal infant and young child feeding and improving infant health. Community cadres, when properly trained and supported, can serve as resources for counselling, practical support to mothers for breastfeeding and complementary feeding, solving problems, negotiating with caregivers and facilitating interactive peer sessions. Being aware of the complex set of values around breastfeeding better equips health workers to support pregnant and lactating women with their infant-feeding choices, even in the context of an outbreak.

Multidisciplinary teams may be necessary for infants who need specialist support in feeding, especially infants who have difficulty breastfeeding. This may be the case for infants born with congenital anomalies, including microcephaly, and long-term management may be necessary.

3. Summary of available evidence

3.1 Systematic review

A systematic review that followed the procedures of the Cochrane handbook for systematic reviews of interventions¹⁴ was done to determine the risk of transmission of Zika virus through breast milk or other breastfeeding-related bodily fluids (i.e. blood, sweat and saliva).¹⁵

The search included studies with any lactating adolescents or adult women with suspected, probable or confirmed Zika virus infection,¹⁶ or infants and young children receiving breast milk from women infected with Zika virus. Primary outcomes were infants or young children with suspected, probable or confirmed Zika virus infection who are currently consuming breast milk. Secondary outcomes included presence and viability of Zika virus in breast milk,

serum, sweat or saliva. The full search methodology and results are available in the published systematic review.¹⁵

A total of 472 records were identified though a database search after duplicates were excluded. Forty-two articles were assessed for eligibility of which 40 were excluded for reporting on non-Zika virus infections or ineligible populations. Although the search included studies with any women who were breastfeeding (either directly from the breast or expressing breast milk) regardless of the timing of the maternal infection (during pregnancy, at the time of delivery or postnatally), only three mother–infant pairs were found, all of which with suspected or confirmed infection during the perinatal period.¹⁵

Two studies were case-reports of three mother–infant pairs – two pairs from French Polynesia⁹ and one pair from New Caledonia.¹⁰ In the case-report from French Polynesia, two women delivered at 38 weeks of gestation with pruritic rash within two to three days of delivery. Both mothers and both neonates had Zika virus infection confirmed by RT-PCR on at least one serum sample. In one of the mothers (symptomatic with rash and mild fever on the third day after delivery), repeated serum RT-PCR tests were done and showed positive results for the first and fifth days after delivery, and negative results on the eighth, eleventh and thirteenth days after delivery. Her viraemia was thus documented by RT-PCR to span at least two days before the onset of symptom and up to four days after the onset of symptoms. Samples of breast milk gave positive RT-PCR results but no replicative Zika virus particles were detected in cell culture. The authors hypothesized that the infants were probably infected in utero or intrapartum because their sera were positive for the presence of Zika virus within one day of starting breastfeeding.⁹ No long-term complications were reported for either of the infants at two years of age (*personal communication, M Besnard, Centre Hospitalier de la Polynésie Française*).

In the mother–infant pair from New Caledonia, a febrile mother delivered a healthy infant after 37 weeks of gestation. Replicative Zika virus particles from breast milk were successfully inoculated into Vero cell culture. The infant's serum was negative for Zika virus by RT-PCR.¹⁰ No long-term complications were reported for the child at eight months of age (*personal communication, M Dupont-Rouyezrol, Institut Pasteur de Nouvelle-Calédonie*).

4. Guidance development

4.1 Acknowledgements

This guideline was coordinated by the Evidence and Programme Guidance Unit, Department of Nutrition for Health and Development, WHO Geneva. Dr Pura Rayco-Solon, Ms Zita Weise Prinzo and Dr Juan Pablo Peña-Rosas oversaw the preparation of this document. WHO acknowledges the technical contributions of the following

individuals from WHO (in alphabetical order): Dr Mercedes Bonet, Department of Reproductive Health and Research; Ms Elizabeth Centeno Tablante and Dr Maria Nieves Garia-Casal, Department of Nutrition for Health and Development; Dr Chessa Lutter, WHO Regional Office for the Americas; Dr Nigel Rollins, Department of Maternal, Newborn, Child and Adolescent Health; Dr Lisa Thomas, Enabling functions in support of the Polio, Emergencies and Country Collaboration cluster; Dr Constanza Vallenias, Department of Pandemic and Epidemic Diseases; and Mr Gerardo Zamora, Department of Nutrition for Health and Development.

4.2 Guideline development group

A guideline development group was formed and included experts with experience in the areas of infant feeding, nutrition surveillance, nutrition in emergencies, paediatrics and infectious diseases (virology and risk assessment). The group comprised of: Ms Maaïke Arts, United Nations Children's Fund, New York, United States of America; Dr Niklas Danielsson, European Centre for Disease Prevention and Control, Stockholm, Sweden; Dr Elsa Giugliani, Ministry of Health Brazil, Porto Alegre, Brazil; Dr Laurent Kaiser, Hôpitaux Universitaires Genève, Geneva, Switzerland; Dr Robert Lawrence, University of Florida, Gainesville, United States of America; Dr Ruowei Li, United States Centers for Disease Control and Prevention, Atlanta, United States of America; and Ms Marie McGrath, ENN, Oxford, United Kingdom.

4.3 Scope of the guideline, evidence appraisal and decision-making

A guideline development group meeting on microcephaly, Guillain-Barré syndrome, infant feeding and care of pregnant women in the context of Zika virus was held on 17–19 March 2016 in Geneva, Switzerland. During the meeting, the group discussed the balance of consequences of breastfeeding or consuming breast milk from a mother infected with Zika virus, and finalized the recommendation. Five experts served as technical peer-reviewers of the draft guideline.

The process followed the steps for guideline development as outlined in the WHO handbook for guideline development.¹⁷ The guideline development methodology is detailed in the full guideline.⁵

4.4 Management of competing interests

Declarations of interest were requested from all members of the evidence-synthesis teams, all members of the guideline development group, and all external persons invited to review the recommendation following the guideline development process, in compliance with the WHO conflict-of-interest policy. None of the members of the guideline group had any conflicts of interest to declare.

4.5 Plans for updating the guideline

This guideline was produced in response to a public health emergency and followed a rapid-advice framework. The WHO steering group will continue to follow the research development in the area of infant feeding, especially in the context of the Zika virus outbreak. The steering group will meet at or before six months from publication of the guideline, to review any new data and determine whether an update might be indicated. If the guideline merits an update, or if there are concerns about the validity of the guideline, the Department of Nutrition for Health and Development will coordinate the guideline update, following WHO rapid advice guideline development procedures.

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