Lack of Transmission of Zika Virus Infection to Breastfed Infant

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ABSTRACT: Zika virus (ZIKV) continues to affect certain parts of the World. Here we report a case that supports breastfeeding regardless of mother ZIKV status by providing clinical and virological studies.

KEYWORDS: Zika virus, breastfeeding, transmission

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Zika virus (ZIKV) belongs to the family of *Flaviviridae* closely related to dengue fever and other related viruses that use arthropods as vectors. It was first described in 1947 from rhesus monkey and later in 1952 when it was first identified in human. Both occurred in Uganda where it received its name.[1]

The first reported outbreak was 60 years later, but it was only known to cause mild illness.[2] It was only later, in the second outbreak in French Polynesia in 2013 where the association with Guillain-Barré Syndrome (GBS) was made, and in Brazil in 2015 where increased congenital development disorders in babies were observed.[3] The World Health Organization (WHO) reported the association between ZIKV with GBS and congenital disorder of the central nervous system in February 2015.

The recent WHO guideline recommends breastfeeding regardless of ZIKV status of the mother; however, exact risk of transmission of ZIKV from mother to new born is unknown.[4] This report demonstrates that ZIKV infection in lactating mother did not transmit infection to infant despite the presence of ZIKV RNA in milk.

A 38-year-old post-partum mother in area with known ZIKV infestation in Bangkok, Thailand had an uncomplicated natural birth of her child in February 2017 with no growth defect. Since birth, the child was exclusively breast-fed and the mother remained well until December 8, 2017 when she developed fever. Her husband was diagnosed with ZIKV a week before her becoming ill. Initially, she suffered a low-grade fever and fatigue, followed by morbilliform itchy red rash, bilateral orbital pain, and submandibular lymphadenopathy on the following day. Bilateral conjunctivitis and polyarthralgia were evident before presenting to Chulalongkorn University Hospital on December 12. All symptoms were resolved by December 20 (12 days). The baby was fed breast milk until December 12 when the mother tested positive for ZIKV, after which the mother decided to stop breastfeeding (Figure 1).

The mother's expressed breast milk was routinely stored at −20°C. Thence, a total of 22 consecutive milk specimens were collected from December 1 until her illness was resolved. The mother's serum and urine and her baby's urine were also collected at short intervals from December 12, 2017 until January 5, 2018. Both urine and serum samples were examined for ZIKV RNA using real-time polymerase chain reaction (RT-PCR) (RealStar Zika Virus RT-PCR Kit; Altona, Germany), and serum for IgG and IgM by enzyme-linked immunosorbent assay (ELISA) method (EUROIMMUN, Germany) at the WHO Collaboration Centre for Research and Training on Viral Zoonoses, Chulalongkorn University. Her baby's urine was also sent for RT-PCR (Figure 2).

ZIKV RNA was detected in the breast milk as early as 3 days before her symptoms started (December 5) and remained detectable in the breast milk for 11 days (December 15) (cycle threshold [Ct], with level of detection between 29.27 and 38.08). ZIKV RNA was still detected in the mother's urine until December 26 but not in blood. Urine collected on January 5, 2018 was negative for ZIKV RNA.

The baby was carefully monitored despite remaining healthy. No fever or rash was observed. The child's urine

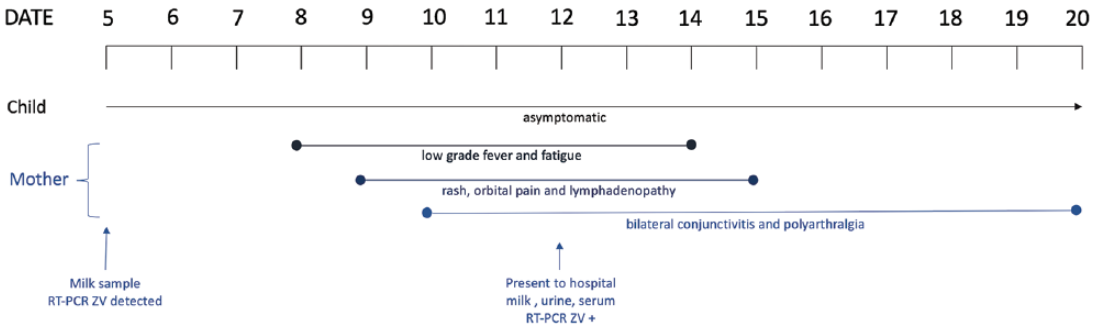

Figure 1. Timeline of symptoms and progression for mother and child; breastfeeding stopped on day 12 (December 12, 2017).
RT-PCR, real-time polymerase chain reaction.

Samples / Date	Milk	Urine	Blood	Urine (Child)
1/12/17	NEG	-	-	-
2/12/17	NEG	-	-	-
3/12/17	NEG	-	-	-
4/12/17	NEG	-	-	-
5/12/17	POS	-	-	-
6/12/17	POS	-	-	-
7/12/17	POS	-	-	-
8/12/17	POS	-	-	-
9/12/17	POS	-	-	-
10/12/17	POS	-	-	-
11/12/17	POS	-	-	-
12/12/17 (feed stopped)	POS	POS	POS IgG (+) IgM (+)	NEG
13/12/17	POS	-	-	-
14/12/17	POS	-	-	-
15/12/17	POS	POS	-	NEG
16/12/17	NEG	-	-	-
17/12/17	NEG	-	-	-
18/12/17	NEG	-	-	-
19/12/17	NEG	NEG	-	NEG
20/12/17	NEG	-	-	NEG
21/12/17	NEG	-	-	-
22/12/17	NEG	POS	-	NEG
26/12/17	-	POS	POS IgG (+) IgM (-)	NEG
5/01/18	-	NEG	-	NEG

Figure 2. RT-PCR results for mother and child; dates correlate with Figure 1.
RT-PCR, real-time polymerase chain reaction.

samples were negative for ZIKV RT-PCR (collected 7 times between December 12, 2017 and January 5, 2018) despite ingesting breast milk with detectable ZIKV RNA. Blood samples for Zika IgG and IgM serology testing on January 5 and 30, 2018 were negative. Parents were also tested for anti-Zika IgG and IgM drawn on December 26, 2017, showing IgG positive and IgM negative for both. We noted that the absence of ZIKV infection to the baby could possibly be due to antibody against ZIKV in the breast milk and that the baby at the time of the study is 10 months old, with more local gastrointestinal immunity than perhaps days-old infant.

There has been limited evidence to confirm ZIKV transmission through breastfeeding and early post-partum cases of infants infected with ZIKV were most likely via transplacental or during delivery.[5-7] Our study demonstrates that breast milk contains the ZIKV RNA by RT-PCR consistent with other previous case reports.[8,9] In our study, breast milk does not appear to be infectious to the baby through breastfeeding, even though it was daily fed to baby for 11 days. In cases where infants were infected with ZIKV, no developmental sequelae or permanent deficit demonstrated at 30 months.[10] Therefore, breastfeeding should be encouraged despite suspicion or confirmed maternal infection. Variables which may affect viral transmission through breastfeeding such as immune status, milk conditioning, viral load, and the presence of viable ZIKV need to be investigated to ensure validity of the recommendation. As of now, ZIKV transmission via the gastrointestinal system is not observed. Limitations to this study include the fact that baby's serum was not tested by RT-PCR; however, we believe that serological assays and urine RT-PCR provide adequate sensitivity for detection of ZIKV.[11]

Author Contributions

PH interpreted the data and wrote the paper, SW conceived and designed the analysis, RB collected the data, SP performed the analysis, SB performed the analysis, CR performed the analysis, PR collected the data and TH performed critical revision.

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