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Article

Sars-Cov-2 RNA and Spesific Antibodies in Breast Milk, Should Mother Breastfeeding? : A Literature Review

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A B S T R A C T

Introduction: Covid-19 is becoming a serious problem worldwide. The spread of disease occurs very quickly, viral mutations are fast and massive. Rules and guidelines change rapidly. WHO and UNICEF recommend exclusive breastfeeding, even though mothers are confirmed because the benefits are considered greater than the risks. The aim of this study are to answer questions, about whether this virus can transmit vertically through breast milk, and how to properly guide the breastfeeding process in the pandemic. **Methods**: The source of this literature review is accessed through Scopus, PubMed, and various reputable websites published in 2019-2021. Article search by keyword usage, inclusion criteria and exclusion. **Results**: 508 articles filtered to prove that the source used is viable and relevant, finally determined 12 articles. The prevalence of Covid-19 incidence in neonates from confirmed mothers was reported in some studies but there is no evidence that transmission is vertical through breast milk. SARS-CoV-2 RNA is found in some reports but there is nothing to confirm whether it is an active virus or just remnants of RNA that cannot infect. Beside RNA, Sars-Cov-2 specific antibodies were also found to protect neonates. **Conclusion**: Active transmission of Covid-19 vertically from breast milk has not been detected, should not be an indication of formula feeding or separation baby with mother. The findings of IgA, IgG, and IgM-specific antibodies can be passive protection, because until now no vaccination has been recommended for neonate groups.

I. INTRODUCTION

The SARS-CoV-2 virus was first detected in Wuhan, China at the end of 2019. The Covid-19 pandemic is taking place worldwide. Progress in the mutation of the virus is fast and massive. Rules and guidelines can change quickly following the development of the virus. This disease can attack anyone, including breastfeeding mothers, so that the limitations imposed on breastfeeding practices are created. Guidance regarding the breastfeeding process is needed both for mothers who are breastfeeding and their families and health workers who are directly involved in services.

In order to reduce child morbidity and mortality, the United Nations Children's Fund (UNICEF) recommends that children should only be given Mother's Milk (ASI) for at least 6 months. Safe and proper solid food should be given after the child is 6 months old, and continued breastfeeding until the child is 2 years old (UNICEF, 2018). Breast milk is beneficial for both mother and baby.

One study has reported that breastfeeding women experience difficulties due to the pandemic, have to struggle to find support, feel anxious about how safe breastfeeding is, and feel alone about this problem (Brown and Shenker, 2021). Choosing to give formula milk instead of breast milk is caused by anxiety and lack of information which causes confusion, and they have not received satisfactory answers to their questions. The choice of giving formula milk during a pandemic due to lack of support from around is supported by the research of DeYoung and Mangum, (2021) as many as 74.71% showed that they received free formula milk samples either sent free to the house, got from the pediatrician's office, received free formula at hospitals, from friends, organizations, and through advertisements on social media. The rest don't get free samples.

They hoped to receive information and support from health workers, they stated that health workers were not communicative (Aşcı, Demirgöz Bal and Ergin, 2021; Oncel et al., 2021). There has been pressure during the pandemic to separate newborns and mothers with Covid-19, ban skin-to-skin and use formula instead of breastfeeding presumably to lower the risk of infection for newborns and medical staff (Tran et al., 2020; Pacheco et al., 2021; van Veenendaal et al., 2021; Speyer, Marryat and Auyeung, 2022)

The International Confederation of Midwives (ICM) expressed concern about violations of the human rights of women, neonates and midwives with the increasing cases of caesarean sections, declining rates of Early Breastfeeding Initiation (IMD) and the implementation of mother and baby isolation (ICM, 2020). Until now there is not enough data to conclude that Covid-19 is transmitted vertically through breast milk.

II. METHODE

The method in preparing this literature review is sourced from various research articles and case reports in English, published in 2019-2022. Sources are accessed through Scopus, PubMed and reputable websites, such as WHO and UNICEF. The keywords used in the article search are "breastfeeding", "lactation", "Covid-19", and "Corona" combined with each other using Boolean operators or and and. The selection of sources is based on predetermined inclusion criteria, namely the study population is women who detected SARS-CoV-2 positive during breastfeeding whose breast milk was examined by the laboratory, articles published in the last 3 years, in

English, and full text open access. Meanwhile, the exclusion criteria are in addition to scientific articles.

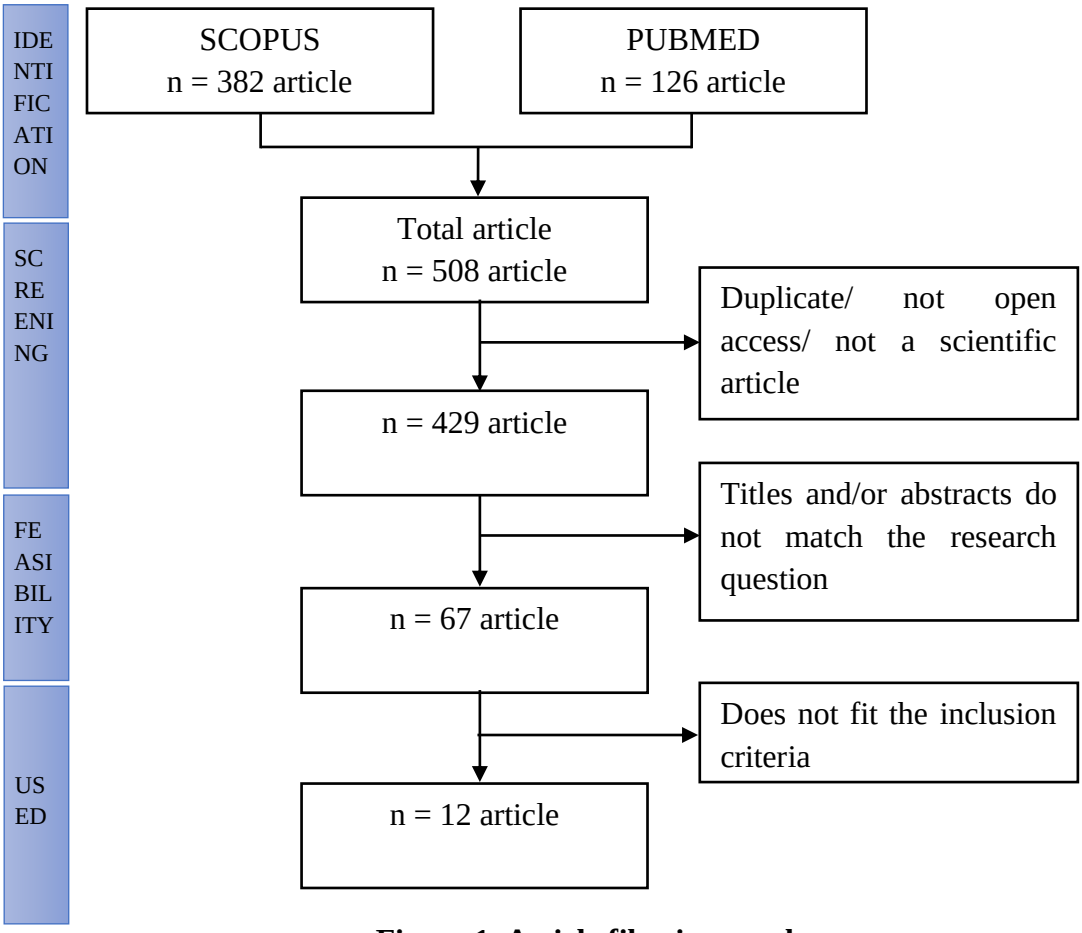

Figure 1. Article filtering results

III. RESULT

From a total of 508 articles, a screening was carried out to prove that the sources used were feasible and relevant. Until finally, it was determined that 12 articles would be used as sources for this literature review.

Such sources use a variety of methods. The study was conducted in a variety of different places, namely China, America, Honduras, Korea, Turkey, Italy, Portugal, Australia, Canada, France, Switzerland, Spain, Peru, India, Iran, United Kingdom, Italy, Belgium, Brazil, Netherlands, Romania and Germany.

A. A. Prevalence of Covid-19 incidence in neonates born to mothers infected with SARS-CoV-2

According to the data collected, the incidence of neonates infected with SARS-CoV-2 where their mothers are also infected, according to the data collected, is very rare, and when there are no symptoms. The results of a study by Tran et al., (2021) out of 120 babies born to mothers with Covid-19, none of the babies tested positive for the virus at the examination 14 days after birth, they continued to do IMD, were treated in rooming in and were exclusively breastfed . This is supported by a study conducted by Biasucci et al., (2020) of 15 infected mothers, all

babies who were born showed negative results through nosopharyngeal swab tests on day 3 and day 7, as well as research by Ronchi et al., (2021) in Italy, where out of 62 neonates born to mothers with SARS-CoV-2 infection who carried out rooming-in and breastfeeding under standard protocols, negative results were obtained for all neonatal nosopharyngeal swab examinations. Dumitriu et al., (2021) also found no transmission in 101 babies from mothers infected with Covid-19, baby care was carried out in rooming-in and babies were directly breastfed.

Another study found that there were infants who were infected, where their mothers were also positive for Covid-19 but the routes of nutrition and treatment patterns were not explained. Research by Mitoulas et al., (2020) stated that out of 205 babies born to mothers who were positive for Covid-19, 6.3% were found to be infected and did not cause symptoms. Capozza et al., (2021) reported results from 2 hospitals in Italy, 3/179 (1.67%) newborns were positive for SARS-CoV-2 and 5/156 (3.2%) babies were positive at 1 month of life. All infected infants were reported asymptomatic. According to Walker et al., (2020), which was compiled from 49 articles, 28 out of 666 neonates born to mothers who were confirmed to have Covid-19 were also reported to be infected, 7 were directly breastfed, 3 were formula milk, 1 was given expressed breast milk and 17 neonates were not. the method of providing nutrition is known. Newborns can be infected in the first few hours of life, but the method of transmission is unclear, whether through maternal droplets during breastfeeding or through breast milk. The infection rate is not greater when the baby is breastfed or allowed contact with the mother. Infected babies also do not show symptoms (asymptomatic) and the benefits of contact with the mother and breastfeeding are greater than babies separated from their mothers.

However, the search conducted by Tran et al., (2020) results are in contrast to the research above. 10 newborns in Romania tested positive, even though the mother was negative. The fact that some neonates have been infected after being separated from their mothers suggests that separation may not offer significant protection, nor should Covid-19 be an indication of formula feeding or separation of infants from mothers.

B. Detection of SARS-CoV-2 RNA in breast milk

Several studies have reported findings of SARS-CoV-2 in breast milk samples tested from mothers infected with Covid-19. Citu et al., (2021) from Romania reported that out of 889 pregnant women, there were 76 women with Covid-19, of which 1.01% detected the SARS-CoV-2 virus in the PCR swab examination of breast milk samples. Caparros-Gonzalez et al., (2020) in the 49 studies he reviewed, out of 329 infected pregnant women, with a total of 331 neonates (2 mothers gave birth to twins), 10 babies were reported to be directly breastfed and found SARS-CoV-2 RNA in 7 breast milk samples tested qRT-PCR at 8-72-96 hours after birth, 5 cases reported positive neonates but it was not clarified whether the neonates were positive before or after breastfeeding.

Descriptive study by Thanigainathan et al., (2021) of 30 mothers positive for Covid-19, Breast milk samples were collected by manually expressing them using aseptic techniques. Oropharyngeal swabs from the same neonates were also sent for RT-PCR on day 2 and day 5 of life. On the results of the 2nd day examination there was 1 positive result for SARS-CoV-2, then on the re-examination of the 5th day the milk from the same mother was all negative and all paired neonatal oropharyngeal swabs were also negative for SARS-CoV-2. Mothers and babies live in the same room and mothers exclusively breastfeed their babies. The use of masks, hand hygiene and disinfection of frequently touched surfaces were carried out by mothers. Other findings that support the presence of SARS-CoV-2 RNA in breast milk were presented by Pérez-bermejo et al., (2021), of the 30 articles included, 26 articles presented findings of RNA in breast milk but there was no virus that was viable or able to transmit, Breast milk samples that tested positive for SARS-CoV-2 RNA did not contain replicable virus, the low probability of

transmission from mother to neonate through breast milk highlights the fact that the risk of transmission is very low.

This is also supported by the research of Centeno-Tablante et al., (2021) in which 340 reports were collected, 37 of which were completed with analysis of breast milk samples and 303 without collection or testing for SARS-CoV-2 in breast milk samples. Of the 37 studies reviewed that reported 77 mothers with confirmed Covid-19, there were 19 babies who were also confirmed with Covid-19, of which 10 babies were breastfed directly, 2 babies were given formula milk, 5 babies were given mixed breast milk, and 2 babies were not explained about their nutrition. . 58 samples of breast milk from confirmed Covid-19 mothers tested negative for SARS-CoV-2, while 19 tested positive.

Meanwhile, contradictory results were obtained from a study conducted by Gao et al., (2020) in Wuhan, China on 14 pregnant women who confirmed that Covid-19 had not detected SARS-CoV-2 RNA which was examined in breast milk samples. Likewise, in the analysis by Martins-Filho et al., (2020) of 8 studies in China, where out of 24 pregnant women with COVID-19 during the third trimester, biological samples from the upper respiratory tract of the neonate and breast milk showed negative results for the presence of SARS-CoV. -2 by RT-PCR test.

This is supported by the research of Pace et al., (2021) which reported that 64 breastfeeding women with Covid-19 during a 2-month period underwent RT-PCR swab examination for breast milk samples and breast skin were analyzed for SARS-CoV-2 RNA, the result was SARS-CoV -2 was undetectable in breast milk samples but was detected in 71% of breast swabs. Follow-up examination of the positive breast skin swab was carried out again, but previously the breast was washed and cleaned first. 27 out of 29 (93%) breast swabs tested were negative for SARS-CoV-2. So these findings explain that there is an association with droplet exposure when the mother coughs. It should be noted that only low titers of viral RNA were detected in positive breast skin swab samples. Breast washing appeared to be effective in removing RNA in almost all of the cases examined. Unfortunately, it was not checked whether the detected RNA poses a potential risk or if it was just viral RNA remnants.

Several case studies from Spain, Vietnam, China and the United States stated that none of the transmission of SARS-CoV-2 was reported through breast milk (Lubbe et al., 2020).

From the data set above, breast milk is considered safe and breastfeeding is supported to continue to be carried out by both negative and positive mothers, because breast milk is the best protection strategy for mothers with Covid-19 and also for their babies. Several observational study reports in China also reported that breastfeeding a baby directly by a mother with SARS-CoV-2 pneumonia showed that breast milk was safe to give (Yu et al., 2020). One case study from Australia found that when a symptomatic mother took appropriate precautions (for example, wearing a mask and washing hands), her baby did not contract the disease (Lowe and Bopp, 2020).

The results of another study stated that 6 out of 9 patients with pneumonia caused by Covid-19 did not find the presence of the virus in the amniotic fluid, blood from the umbilical cord, breast milk, and baby oropharyngeal swabs (Calil, Krebs and De Carvalho, 2020). This means that even if the virus is excreted in breast milk, there is no clear data on the duration that the virus can be found in breast milk (Bhatt, 2021).

The findings of the cases above thus state that it is unclear whether the baby was exposed through contact with the mother or confirmed health worker or was exposed through breast milk, because until now there has been no evidence to suggest that SARS-CoV-2 can be transmitted through breast milk. Even though there have been reports of detection of SARS-CoV-2 RNA in breast milk, the results of detection of the virus' genetic material do not mean that the virus is still fit to infect.

Based on the concept of nanostructure analysis, emerging viruses can be transmitted through breast milk only if the viruses are smaller than the pores of the mammary glands. Molecularly,

the coronavirus is a large virus and the size of SARS-CoV-2 is more than 100 nm6, which is larger than the pores of the mammary glands. Therefore, transmission through breast milk should not occur if there is no mammary gland pathology (Joob and Wiwanitkit, 2020).

C. Detection of SARS-CoV-2 Antibodies in Breast Milk

Breast milk from women with Covid-19 is a source of passive immunity via anti-RBD IgA. These results support recommendations that encourage breastfeeding women to continue breastfeeding during and after confirmed Covid-19. The results of a study by Pace et al., (2021) showed that 92% of milk samples from most women contained anti-RBD IgA, and concentrations increased during the initial two weeks after the onset of Covid-19 symptoms or a positive test. Breast-transmitted anti-RBD IgA persists for at least two months in 77% of women. Similar results were expressed by Gao et al., (2020) where an immunological test on the breast milk samples examined revealed IgM seroconversion on the 8th day and IgG on the 28th day. IgM and IgG antibodies against SARS-CoV-2 were detected in breast milk, blood, umbilical cord and neonatal serum. The results of the study show that passive antibodies against SARS-CoV-2 are available by drinking breast milk. Systematic review by Pérez-bermejo et al., (2021) is in line with Gao's findings, where breast milk produced by infected mothers is a source of anti-SARS-CoV-2 IgA and IgG and has the ability to sterilize SARS-CoV-2 activity, this suggests possible immune protection for the neonate. In a review article by Aros-Vera et al., (2021) also discussed 18 mothers positive for Covid-19 whose breast milk samples were examined to contain IgA and IgG SARS-CoV-2 antibodies that specifically provide protection to babies who are breastfed. In line with this, Caparros-Gonzalez et al., (2020) in his review analyzed 2 studies which reported the presence of IgG SARS-CoV-2 in positive samples of mother's milk. There is also a review by Bardanzellu et al., (2021) and a case study by Lebrão et al., (2020) which states that specific IgA in positive mothers seems to last during breastfeeding for at least 7 months, antibodies can potentially prevent SARS-CoV infection CoV-2 or to reduce symptoms and severity in infected subjects. From the reviews above it states that breast milk contains IgA, IgG and IgM antibodies which provide passive immunity, so that the potential protection of breast milk against SARS-CoV-2 must be considered, and breastfeeding activities should be supported.

D. Benefits and Recommendations for Breastfeeding

The main route of transmission of Covid-19 is from droplets from infected mothers to their babies or from infected workers to babies being treated. So that the breastfeeding process can be carried out accompanied by very strict infection control. Breastfeeding increases survival and provides lifelong health and development benefits for newborns, breastfeeding also improves maternal health (Calil, Krebs and De Carvalho, 2020; Juan et al., 2020; Lubbe et al., 2020; Mocelin, Primo and Laignier, 2020; Pereira et al., 2020; Centeno-Tablante et al., 2021).

Breast milk is the best gift a mother gives to her child and the best gift from God to a woman. Breastfeeding protects against perinatal and maternal morbidity and mortality. For babies, breast milk is an ideal food that is safe, clean and contains antibodies, has an immunological effect and is anti-infective. Breast milk provides all the energy and nutrients a baby needs and promotes healthy brain development (Calil, Krebs and De Carvalho, 2020). Babies who are breastfed tend to avoid obesity and are not prone to diabetes (WHO, 2021).

In addition, the breastfeeding process also provides protection for the mother, including being able to prevent postpartum hemorrhage, assist in the process of losing weight, reduce the risk of breast and ovarian cancer, reduce the risk of type 2 diabetes and postpartum depression. Exclusive breastfeeding also has a contraceptive effect (Calil, Krebs and De Carvalho, 2020). According to guidelines compiled by Calil et al., (2020) for mothers with confirmed Covid-19 breastfeeding options include direct breastfeeding, breastfeeding with expressed breast milk, and the option of using donor breast milk. In breastfeeding other than direct breastfeeding, it is

recommended to give using a cup or spoon. As per WHO guidelines (2020), women with confirmed or suspected Covid-19 can breastfeed if they wish to do so. WHO recommends that women continue to breastfeed with procedures to prevent transmission of Covid-19, especially by washing their hands with soap or hand sanitizer and using a medical mask during contact with babies. If the mother is not able to breastfeed the baby directly, then the mother must be supported to provide breast milk to her baby safely by means that may be available and acceptable, such as expressing breast milk or donating breast milk. In a study conducted by Pace et al., (2021) stated that cleaning and washing the breasts appeared to be effective in removing RNA in almost all cases examined.

Table 1. Research screening results

No	Researcher (Year)	Title	Methode	Number of Sample
1.	Calil, V., Krebs,V., Carvalho,W (2020)	*Guidance on breastfeeding during the Covid-19 pandemic*	Literature Review	20 article
2.	Filho, P., Santos, V., Santos, H (2020)	*To breastfeed or not to breastfeed? Lack of evidence on the presence of SARS-CoV-2 in breastmilk of pregnant women with COVID-19*	Systematic Review	24 mothers positive for Covid-19
3.	Walker,K., O'Donoghue,K., Grace, N., *et al* (2020)	*Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis*	Systematic Review	49 article
4.	Tablente, E., Rivera,M., Finkelstein,J., *et al* (2020)	*Transmission of SARS-CoV-2 through breast milk and breastfeeding: a living systematic review*	Systematic Review	46 mothers positive for Covid-19
5.	Gao, X., Wang, S., Zeng, W., *et al* (2020)	*Clinical and immunologic features among COVID-19–affected mother–infant pairs: antibodies to SARS-CoV-2 detected in breast milk*	Case Report	14 mothers positive for Covid-19
6.	Lubbe, W., Botha, E.,Vilen, H., Reimers, P (2020)	*Breastfeeding during the COVID-19 pandemic – a literature review for clinical practice*	Literature Review	Tidak dijelaskan
7.	Gonzalez, R., Morente, M., Montoro, C., *et al* (2020)	*Congenital, Intrapartum and Postnatal Maternal-Fetal-Neonatal SARS-CoV-2 Infections: A Narrative Review*	Narrative Review	49 article
8.	Bhatt, H (2021)	*Should COVID-19 Mother Breastfeed her Newborn Child? A Literature Review on the Safety of Breastfeeding for Pregnant Women with COVID-19*	Literature Review	13 article
9.	Thanigainathan, S., Kaliyaperumal, V., *et al* (2021)	*Is SARS-CoV-2 Transmitted Through Breastfeeding?*	Descriptive Studies	30 mothers positive for Covid-19
10.	Bermejo, M.,	*COVID-19: Relationship and Impact*	Systematic	30 article

	Orchando, B., Llorente, M (2021)	*on Breastfeeding—A Systematic Review*	Review	
11.	Citu, C., Neamtu, R., Sorop, V., *et al* (2021)	*Assessing SARS-CoV-2 Vertical Transmission and Neonatal Complications*	Prospective Studies	76 mothers positive for Covid-19
12.	Pace, R., Williams, J., Järvinen, M., *et al* (2021)	*Milk From Women Diagnosed With COVID-19 Does Not Contain SARS-CoV-2 RNA but Has Persistent Levels of SARS-CoV-2-Specific IgA Antibodies*	Longitudinal Studies	64 mothers positive for Covid-19

IV. DISCUSSION

The existing article sources discuss the vertical transmission of SARS-CoV-2 through breast milk as well as recommended recommendations regarding the breastfeeding process. It was concluded that vertical active transmission of Covid-19 from mother to baby through breast milk cannot be proven. If vertical transmission does occur, infected babies rarely cause symptoms, and it seems that this is not affected by the skin-to-skin process between mother and baby. breastfeeding and rooming-in care. So that the things mentioned above are still supported to be implemented for both mothers who are not infected with SARS-CoV-2 and those who are positive, because the benefits outweigh the risks that might be experienced. Mothers must be given support, especially in terms of breastfeeding and given an explanation that Covid-19 is not a contraindication for breastfeeding so that there is no cessation in the breastfeeding process. The main reason for mothers to stop breastfeeding during the Covid-19 pandemic was that there was no adequate professional/medical support, as well as the surrounding environment such as family, friends and social media. Mothers are concerned about the safety of breastfeeding during the Covid-19 pandemic (Aşcı, Demirgöz Bal and Ergin, 2021; Brown and Shenker, 2021). Another reason is physical adjustments such as difficulty with attachment, little milk coming out, and pain in the early days of breastfeeding, and there is no proper support or help about it (Debevec and Evanson, 2016). This causes stress and increases anxiety during the isolation period (Hull et al., 2020)

Breastfeeding can still be carried out by strictly adhering to the principles of infection prevention such as wearing a medical mask, limiting the distance from the baby to 2 meters except when breastfeeding or holding the baby, cleaning the breast area before breastfeeding and disinfecting surrounding objects, especially those that are often handled by the mother.

In order to reduce child morbidity and mortality, UNICEF recommends that children should only be given breast milk (ASI) for at least 6 months. Safe and proper solid food should be given after the child is 6 months old, and continued breastfeeding until the child is 2 years old (UNICEF, 2018).

V. CONCLUSION

The active transmission of Covid-19 vertically from mother to baby, should not be an indication of formula feeding or separation of the baby from the mother. In addition to the findings of SARS-CoV-2 RNA, it was also found that there were specific antibodies of IgA, IgG and IgM which can be passive protection passed from mother to baby, because until now vaccination has not been recommended for the neonatal group. Another goal that is expected to be achieved with further research is innovation in efforts to increase breastfeeding support because the benefits of breastfeeding are very large for both mothers and their babies.

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