



Risk Of Intrauterine Vertical Transmission Of Sars-Cov-2 During Pregnancy: A Literature Review

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Abstract: COVID-19 is an acute respiratory disease because of SARS-CoV-2. The transmission of it happens very fast and someone with a low immunity is likely to get infected. Therefore, pregnant women is one of the population that have a higher risk to get infected. A lot of complications can happens because of the virus. Another problem that can accure is a finding of SARS-CoV-2 on newborn babies. So, there's a question about the possibility of intrauterine vertical transmission. The literature review is sourced from various research articles, study cases, and reputable website that published on 2020. The searching method of the sources used a keywords, inclusions and exclusion criterias. The final sources used 11 articles that already checked using critical appraisal tools. Based on the explanation from various sources. Intrauterine vertical transmission can happen. This conclusion is based on the evidences of SARS-CoV-2 discovery through placenta and the finding of IgM on placenta as a respond to the virus.

Keywords: COVID-19, pregnant women, intrauterine vertical transmission, neonatus

I. INTRODUCTION

Since the last December of 2019 the world has been shaken by the discovery of Corona-Disease-19 (COVID-19). It is an acute respiratory disease because of a virus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). As the development of the disease was really fast, up until January 30th 2020 the World Health Organization has declared the whole condition as a pandemic. The statement was based on the number of cases that growing rapidly day by day. Till December 15th 2020, the total number of positive cases was reported around 70 million and the number of death was around 1,6 million cases. 2 While in Indonesia on the same day, the total number of positive cases was reported around 600 thousand and the death was 18 thousand cases. 3 This situation causes a fear, especially for pregnant women because it's is reported by the Indonesian Association of Obstetrics and Gynecology (POGI) Jakarta that pregnant women are 13.7% more prone to exposure to COVID-19 than women who are not pregnant.1 In addition, based on several reported cases, early neonates were found with positive PCR results, WHO stated that 2.5% of COVID-19 cases occurred in children aged 0-5 years. This certainly raises fear and the question of whether SARS-CoV-2 can be transmitted by intrauterine vertical transmission.

SARS CoV-2 virus transmission can occur through droplets with a maximum distance of 1.8 meters. 4 But other findings also explain that transmission can occur in other ways, because viruses are still found in various types of biological fluids (saliva, feces, and blood). 5 The incubation period for SARS-CoV-19 is 5 days.6 These two opinions may support the possibility that this virus can be transmitted vertically intrauterine. As explained by Dashraath (2020), SARS-CoV-2 was found in the placenta of both babies born with COVID-19. However, other studies have also shown negative PCR results for babies born to mothers with COVID-19.7 The research above shows contradictory results and emphasizes that the vertical transmission of COVID-19 from mother to fetus is still a matter of debate. Therefore, writing this study aims to explore some literature regarding the occurrence of intrauterine vertical transmission. This study is expected to provide useful information about the spread of SARS-CoV-2 to the fetus, so that preventive measures can be taken.

II. METHOD

This literature review is sourced from various research articles and case reports published in Indonesian and English from 2020. The sources are accessed through Pubmed, Scienedirect, Goggle Scholar and reputable websites, such as WHO and the Indonesian Ministry of Health. The keywords used in the article search were “COVID-19”, “Vertical Transmission”, and “Intrauterine”. The selection of sources was based on predetermined inclusion criteria, namely the study population was women who detected positive SARS-CoV-2 during pregnancy. The source showed the results of examining SARS-CoV-2 infection within 72 hours in newborns. In addition, exclusion criteria were also set on sources that explained the vertical transmission of COVID-19 outside the perinatal period.

III. RESULTS

The process of searching for sources that have been found through keywords and meeting the inclusion and exclusion criteria will be continued with the critical appraisal stage. This stage is carried out to prove that the sources used are feasible and relevant. In the end, 11 articles were determined to be used as the source of the literature review. These sources use systematic review research methods, cohort studies and case studies with research processes carried out in various different places, namely China, America, and Europe.

Researchers/Year	Title	Methods	Total Sample of Mothers	Total Sample of Neonatus with COVID-19
Baud, D., Greub, G., Favre, G., Gengler, C., Jatou, K., Dubruc, E., & Pomar, L. (2020).	<i>Second-Trimester Miscarriage in a Pregnant Woman with SARS-CoV-2 Infection.</i>	Study Case	1	1/1
de Melo, G. C., & de Araújo, K. C. G. M. (2020).	<i>COVID-19 infection in pregnant women, preterm delivery, birth weight, and vertical transmission: A systematic review and meta-analysis.</i>	Systematic Review of Cohort Study	405	108/405
Diriba, K., Awulachew, E., & Getu, E. (2020).	<i>The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a systematic review and meta-analysis.</i>	Systematic Review of Cohort Study	207	56/207
Kirtsman, M., Diambomba, Y., Poutanen, S. M., Malinowski, A. K., Vlachodimitropoulou, E., Parks, W. T., Erdman, L., Morris, S. K., & Shah, P. S. (2020).	Probable congenital sars-cov-2 infection in a neonate born to a woman with active sars-cov-2 infection.	Study Case	1	1/1
Kotlyar, A. M., Grechukhina, O., Chen, A., Popkhadze, S., Grimshaw, A., Tal, O., Taylor, H. S., & Tal, R. (2020).	<i>Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis.</i>	Systematic Review of Cohort Study	936	27/936

Madewell, Z. J., Yang, Y., Jr, I. M. L., Halloran, M. E., & Dean, N. E. (2020).	SARS-CoV-2infection of the placenta.	<i>Case Report</i>	1	1/1
Malhotra, Y., Rossberg, M. C., Bajaj, K., Shtern, A., & Moore, R. M. (2020).	<i>Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vertical Transmission in Neonates Born to Mothers With Coronavirus Disease 2019 (COVID-19) Pneumonia.</i>	<i>Cohort Study</i>	8	1/8
Nie, R., Wang, S., Yang, Q., Fan, C., Liu, Y., He, W., Jiang, M., Liu, C., Zeng, W., Wu, J., Oktay, K., Feng, L., & Jin, L. (2020).	<i>Clinical features and the maternal and neonatal outcomes of pregnant women with coronavirus disease 2019.</i>	<i>Cohort Study</i>	28	1/28
Patanè, L., Morotti, D., Giunta, M. R., Sigismondi, C., Piccoli, M. G., Frigerio, L., Mangili, G., Arosio, M., & Cornolti, G. (2020).	<i>Vertical transmission of coronavirus disease 2019: severe acute respiratory syndrome coronavirus 2 RNA on the fetal side of the placenta in pregnancies with coronavirus disease 2019– positive mothers and neonates at birth.</i>	<i>Study Case</i>	2	2/2
Pettiroso, E., Giles, M., Cole, S., & Rees, M. (2020).	<i>COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission.</i>	<i>Systematic Review of Cohort Study</i>	7	2/7
Zamaniyan, M., Ebadi, A., Aghajanpoor Mir, S., Rahmani, Z., Haghshenas, M., & Azizi, S. (2020).	<i>Preterm delivery in pregnant woman with critical COVID- 19 pneumonia and vertical transmission. Prenatal Diagnosis,</i>	<i>Study Case</i>	1	1/1

IV. DISCUSSION

Based on 11 journals that discuss the intrauterine vertical transmission of SARS-CoV-2. It was concluded that intrauterine vertical transmission of SARS-CoV-2 can occur, although the incidence rate is relatively small.⁹ This statement is proven by the finding of a positive SARS-CoV-2 case in early neonates.⁵ While the evidence that supports this relatively small incidence rate can be seen from the results of the study, that not all pregnant women with SARS-CoV-2 will give birth to babies with the virus. This is related to the main spread of SARS-CoV-2, which is still believed to be through droplets with a maximum distance of 1.8 meters with an incubation period of 5 days.

The incidence of SARS-CoV-2 infection in newborns is relatively small. It is proven in several case studies and cohort studies that show different results, such as a cases in 28 neonates with positive mothers with SARS-CoV-2, only 1 (3.2%) neonates were declared positive SARS-CoV-2.¹⁰ In this study, it is explained how the birth process is experienced, starting from the use of N95 masks on mothers and staff, followed by self-isolation in babies immediately after birth. However, the lack of information on how the examination process is carried out raises doubts about the accuracy of the results of this study. In another study conducted, also showed the same results, in 8 neonates who were tested within 24-36 hours after birth,

only one (14.3%) tested positive. The same drawbacks were also found in this study, it did not explain how the SARS-CoV-2 babies were tested.

SARS-CoV-2 vertical transmission process can be proven by immunity and placental condition. This is why pregnant women are an important population in this COVID-19 outbreak. The condition of those who are susceptible to infectious diseases is due to hormonal changes that can affect immunity. In addition, changes in the respiratory system such as increased oxygen demand and edema in the respiratory pathway facilitate the entry of respiratory pathogens. The existence of intrauterine vertical transmission was evidenced by immunity found on the results of tests carried out on two babies with positive SARS-CoV-2 cases showed the same results, namely an increase in IgM levels in the placenta.¹¹ In this study, it was explained how the conditions of both mothers showed severe symptoms and in treatment they needed a ventilator. Another finding at the Papa Giovanni XXIII Hospital, carried out tests on neonates aged two hours and the same results were obtained.¹² Basically, new IgM will appear 3-7 days after being infected by the antigen. Thus, the increase in IgM indicates a fetal response to intrauterine vertical transmission of SARS-CoV-2 that occurs. The difference in results was found in the study of 8 positive cases, only one baby with elevated IgM was found.⁹ He explained that the condition of the mother with a positive baby was in a bad condition, while the other 7 mothers were in an asymptomatic state. However, this result is still a matter of debate because the author did not include the p value as the basis for the accuracy of the research results.

SARS-CoV-2 intrauterine vertical transmission is not only associated with immunity, but also with the placenta. The role of the placenta is related to the presence of Angiotensin converting enzyme 2 (ACE2) receptors which will bind to SARS-CoV-2.¹⁴ When SARS-CoV-2 and the ACE2 receptor bind, activation of the transmembrane protease serine 2 enzyme (TMPRSS2) will occur, so that the virus can pass through cells.¹⁵ The above statement is supported by a case study conducted, which found SARS-CoV-2 in the placenta of a premature baby followed by a 24-hour positive nasopharyngeal swab.¹⁶ Although, there is a population that is lacking in this study, there are several other studies that support this statement, such as that conducted using a placenta analysis conducted on two infants with positive PCR results, SARS-CoV-2 was found on the placenta.¹² There are similarities regarding the condition of the placenta, namely the existence of disturbances in the placenta associated with complications in pregnancy experienced by the mother such as preeclampsia. Pathological conditions of placenta were also found in a systematic review of the cohort study conducted of 6 cohorts found 56 neonates with SARS-CoV-2 positive and found similar placental conditions with impaired vascular function, fibrin deposition, chronic villitis, and infarction.¹⁷ There was no risk of bias included and how the process of examining the baby made up the results of the investigators this is still in doubt. However, the management that can be done from finding the same results is preventive efforts to maintain the condition of the placenta so that intrauterine transmission does not occur.

It is concluded from the above discussion, that intrauterine vertical transmission occurs in mothers who are in poor condition requiring ventilator treatment and that the presence of pathological conditions in the placenta can also be affected. However, further research studies still need to be carried out considering the accuracy of the results of the SARS-CoV-2 examination in neonates is still in doubt due to the lack of description of the test process, lack of samples, and in several studies the explanation regarding the condition of mothers with SARS-CoV-2 positive babies is not included. The existence of further research is expected to provide an overview of the factors of transmission in the fetus, considering that not all babies with SARS-CoV-2 positive mothers also experience the same conditions. So that preventive efforts can be made.

V. CONCLUSION

Corona Disease-19 (COVID-19) is a disorder of the acute respiratory tract caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Virus. The virus spread very quickly certainly raises concerns, especially for pregnant women who have an immune system that is susceptible to infectious diseases. The main form of transmission of SARS-CoV-2 is believed to be via droplets with a maximum distance of 1.8 meters. However, it is possible that this virus can be transmitted in other ways. The finding of SARS-CoV-2 positive cases in early neonates, proves that this virus can be transmitted vertically intrauterine, although the possibility is relatively small.

The occurrence of intrauterine vertical transmission can be evidenced by positive test results found in early neonates less than 72 hours after birth. With the virus incubation period which lasts for 5 days, it can be concluded that the neonate with a positive test result has been infected with the virus since in the womb. In addition to this evidence, the discovery of SARS-CoV-2 in the placenta due to binding to the ACE2 receptor and the presence of elevated IgM in early neonates as a form of viral protective response is the basis that intrauterine vertical transmission can occur. Factors affecting transmission relate to the condition of the

mother and the condition of the placenta. However, further research still needs to be done, due to the insufficient number of studies, an explanation of the process of carrying out SARS-CoV-2 testing in infants, and the condition of your pregnancy which still raises other speculations. Another goal that is expected to be achieved with further research is preventive measures that can be done. Thus, the incidence of SARS-CoV-2 in neonates can be reduced.

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