

IMPACT OF COVID-19 PANDEMIC ON FETUS AND NEWBORN: A SYSTEMATIC REVIEW

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ABSTRACT

Background: The COVID-19 pandemic has reported the potential infection to children, including newborns. The data for the intrauterine transmission of Covid-19 during pregnancy and its impact is still limited. This study aimed to investigate the impact of the Covid-19 pandemic on fetus and newborns.

Subjects and Method: A systematic review was conducted by searching from PubMed, Google Scholar, JAMA, and ScienceDirect conducted in April 2020. The keywords were "child health" AND "COVID-19" OR "newborn" AND "novel coronavirus" AND "infection" OR "intrauterine transmission AND COVID- 19 AND Review". The data were reported systematically.

Results: The reviewed articles were cohort retrospective, case report, review, and systematic review. Intrauterine transmission of Covid-19 in pregnancy remained uncertain. Some studies reported the confirmation of infected Covid-19 in newborns within <2 hours to 2 days of birth. Supportive therapy was given according to the clinical conditions of newborns.

Conclusion: There is a lack of evidence in the intrauterine transmission of Covid-19 in pregnancy. The infected newborns with Covid-19 are confirmed within <2 hours to 2 days. Supportive therapy is conducted according to the clinical conditions of newborns.

Keywords: newborns, Covid-19, infection

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BACKGROUND

To date, more than one million people had been infected with the acute respiratory syndrome caused by coronavirus 2 (COVID-19 / SARS-CoV-2). In the early stages of the epidemic, older adults were the group most likely to be infected. Furthermore, the infection had been reported in infants under 1 year of age (Zhang et al., 2020). As the epidemic progressed, there was little understanding of the transmission route of COVID-19 in newborns, so many women gave birth by cesarean section because of concerns about infection. The condition raises the most important question regarding whether COVID-19 can be transmitted from pregnant

women to the fetus and cause clinically significant infection (Y. Chen et al., 2020).

This concern was because COVID-19 infection can develop into pneumonia. Pneumonia can be fatal, and it is estimated that 1 toddler dies every 20 seconds from pneumonia. In fact, because of the large number of pneumonia deaths, pneumonia is referred to as "the forgotten pandemic" (MOH RI, 2011).

The above background made the authors interested in reporting a review regarding the effect of COVID-19 on fetuses and newborns based on various published case reports.

SUBJECTS AND METHOD

1. Study Design

A systematic review was conducted in April 2020, using various databases, including PubMed, Google Scholar, JAMA, and ScienceDirect. The keywords used included: “child health” AND “COVID-19” OR “new-born” AND “novel coronavirus” AND “infection” OR “intrauterine transmission” AND “COVID-19” AND “Review.” This article followed the writing rules of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

2. Inclusion Criteria

Articles published in English or Indonesian, Free full text, or articles that can be downloaded for free (open access) were included in this study. The study design included were case reports, case series, systematic reviews, and cohorts of pregnant women and newborns and infants affected by COVID-19.

3. Exclusion Criteria

The excluded articles were articles written in Chinese, Japanese, Spanish, and Arabic language, subjects less than 19 years old, articles with quasi-experimental designs, and the Randomized Controlled Trial.

4. Strategies for Quality Assessment and Data Synthesis

All identified studies were independently assessed by all authors for relevance by title and abstract. Then, the full-text version of all the relevant possibilities, disagreements between the authors was resolved via a discussion forum. Most of the articles that do not fall into the qualitative criteria will be discussed in this article and used as literature sources.

5. PICO

The population of this review was newborns. The intervention was the exposure of COVID-19 in pregnant women. The comparison was babies born to mothers who were not exposed to COVID-19. Outcomes were

emergencies that occurred shortly after birth for up to 7 days.

RESULTS

The effect of COVID-19 on fetuses and newborns were studied in case reports. Chen et al. (2020) reported that a total of nine third trimester pregnant women with COVID-19 were confirmed in the age range of 26-40 years. Pregnancy complications were arising after the onset of infection COVID-19, including fetal distress (in two of nine patients) and premature rupture of membranes (in two out of nine).

The possibility of infection with COVID-19 (SARS-CoV-2) was tested in amniotic fluid, umbilical cord blood, neonatal throat swabs, and breast milk samples. The results showed that all babies were negative for COVID-19 shortly after birth, so there was no evidence for intrauterine COVID-19 infection caused by vertical transmission of the placenta at the end of pregnancy (Chen et al., 2020). However, research conducted (Zhang et al., 2020) on newborns to neonatal showed that 4 babies out of 4 mothers who experienced COVID-19 infection during pregnancy were confirmed to have contracted COVID-19. A nasopharyngeal or swab was taken To detect neonatal infection during hospitalization. The quantitative real-time polymerase chain reaction was used according to the recommended protocol.

A systematic review conducted (Zaigham and Andersson, 2020) reported that the first symptom in newborns with COVID-19 infection was shortness of breath observed in six neonates. Other early symptoms were fever, thrombocytopenia accompanied by abnormal liver function, tachycardia, vomiting, and pneumothorax.

The study of Fan et al. 2020 stated that neonates' symptoms were low-grade fever, abdominal distension with lymphocytopenia on the 3rd day, and the day after the chest X-

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ray described a diffuse haze. Besides, some continue to develop mild neonatal pneumonia with lymphocytopenia, which was

treated with antibiotics.

Table 1. Summary Sources

No	Author (Year)	Study Design	Results
1.	Chen et al. (2020)	Retrospective cohort	9 patients underwent cesarean section in the third trimester. All babies were born alive. No neonatal asphyxia was observed with an APGAR score of 1 minute 8–9 and an APGAR score of 5 minutes 9–10. Amniotic fluid, umbilical cord blood, neonatal throat swabs, and breast milk samples from six patients were tested for SARS-CoV-2, and all samples tested negative for the virus.
2.	Zhang et al. (2020)	Case report	Identifying 4 infections in newborns in China on March 13. Age range between 30 hours and 17 days. Two newborns had fever, 1 had shortness of breath, 1 had a cough and 1 had no syndrome. Supportive care was provided for all 4 newborns. Neither one requires intensive unit maintenance or mechanical ventilation. Neither had severe complications. Three newborns recovered at the end of the study and were discharged 16, 23, and 30 days in the hospital.
3.	Zhu et al. (2020)	Case reports	Six preterm births with symptoms reported: shortness of breath (n= 6), fever (n= 2), thrombocytopenia accompanied by abnormal liver function (n= 2), tachycardia (n= 1), vomiting (n= 1), and pneumothorax (n= 1). Six newborns had a Pediatric Critical Illness Score <90.
4.	Wang et al. (2020)	Case report	APGAR score at 1 and 5 minutes: 8 and 9. Mild clinical manifestations in infants.
5.	Xia et al. (2020)	Case Series	Of 20 infants reported: Fever ($\geq 37.3^{\circ}\text{C}$) 12/20 (60%), cough 13/20 (65%), diarrhea within 3/20 (15%), vomiting 2/20 (10%), tachypnea 2/20 (10%), and cyanosis 1/20 (5%).
6.	Yang et al. (2020)	Case report	19 newborns negative for SARS CoV-2. Ten breastmilk samples tested for SARS-CoV-2 RT-PCR were negative. The SARS-CoV-2 RT-PCR test resulted from throat swabs, gastric fluids after birth, urine, and feces of all newborns were negative. APGAR scores 8 and 9 at 1 and 5 minutes. No fetal distress was found.
7.	Khan et al. (2020)	Case series	Three of 17 newborns were preterm; birth weight from 2300g - 3750g. The APGAR score for the 16 newborns was 9 - 10. Only two newborns were suspected of having COVID-19; five reported neonatal pneumonia.
8.	Li et al. (2020)	Case-control	Two babies were born prematurely. The prevalence of prematurity was similar (23.5% and 21.1%) between A and B significantly higher than that of controls (C: 5.8% and D: 5.0%). Low birth weight was more frequent in groups A and B (17.6% and 10.5%) than in the control group (2.5%). There were no significant differences in the main neonatal indicators between groups. Of the three newborns with intrauterine fetal distress, two of the mothers with confirmed COVID-19, one also had sinus tachycardia. One case of fetal distress from group B, but no other comorbidities

DISCUSSION

From these findings, fetuses and newborns of mothers with confirmed COVID-219 can show clinical symptoms. However, Schwartz (2020), in his analysis of 38 infected pregnancies, found no evidence for intrauterine transmission, although there was still much evidence to study this. Lymphocytopenia and thrombocytopenia had occurred repeatedly. There were radiological findings in infants infected with SARS-CoV-2 but appeared healthy, so they should also be cautious. Therefore, we encourage doctors to closely monitor newborns to mothers with COVID-19. The physical distancing between mother and baby and breastfeeding are treatment options. Isolation measures for both mother and baby must be considered.

A report suggested symptomatic supportive care was provided for all infected newborns. Intensive care or mechanical ventilation is not always necessary. The infant was considered to be recovered after two consecutive negative nucleic acid tests (examined with an interval of ≥ 24 hours). The average care required for infants in the hospital was 16, 23, and 30 days, respectively (Zhang et al., 2020).

The review results showed that the transmission of COVID-19 to fetuses and newborns via intrauterine transmission is not yet certain. However, it had been reported that many newborns transmitted COVID-19 within < 2 hours to 2 days after birth. Separation of the treatment room and prevention of direct breastfeeding from infected mothers are things that must be done to reduce the risk of worsening the situation. However, exclusive breastfeeding is still an intake option for babies. Supportive therapy is given according to the rules and symptoms experienced by the baby.

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