



National COVID-19 Health and Research Advisory Committee*

Date of advice: 9 June 2021

Advice 21: Impacts of COVID-19 during pregnancy on newborn health

Focus

The Chief Medical Officer has requested a rapid review of the evidence on the direct impacts of COVID-19 during pregnancy on newborn health.

To enable the provision of rapid advice, systematic reviews of the literature were considered to summarise the observed clinical characteristics and neonatal outcomes that occur at birth due to women having COVID-19 during pregnancy.

Notes

This report is point in time and may need further review as more evidence is available.

This report was developed by an NCHRAC working group led by Professor Bart Currie, and included Professor Jonathan Carapetis and external expert Professor Caroline Homer.

Search strategy

A search of PubMed on 17 May 2021, using the terms: COVID-19 pregnancy newborn outcomes, [limited to English] revealed 37 systematic reviews. Search dates of the systematic reviews ranged from 13 March 2020 to 31 October 2020. Eight were not considered for further analysis as: one was a protocol; one full text article was only available in Spanish; three focused on vertical transmission; and three on maternal health and did not discuss neonatal outcomes.

The remaining 29 reviews, of varying quality, are summarised at [Attachment 1](#).¹⁻²⁹ This includes the PregCOV-19 project, a series of living systematic reviews (LSR), conducted by the University of Birmingham, involving pregnant and postnatal women at risk, suspected, and diagnosed to have COVID-19 and synthesise the relevant evidence on prevalence, risk factors, mother-to-child transmission, diagnosis, treatment of the disease.²

In addition, attention is drawn to the recently released consensus policy brief on maternity care during the COVID-19 pandemic provided at [Attachment 2](#).³⁰

* NHMRC is providing secretariat and project support for the Committee, which was established to provide advice to the Commonwealth Chief Medical Officer on Australia's health response to the COVID-19 pandemic. The Committee is not established under the NHMRC Act and does not advise the NHMRC CEO.

Out of Scope:

- Examination of maternal health outcomes.
- Maternal treatments for COVID-19 during pregnancy.
- Indirect impacts on newborn health that arise from public health changes.
- Long-term sequelae in the child due to SARS-CoV-2-infection in pregnancy.

Approach

The clinical features of pregnant women infected with SARS-CoV-2 and their newborn outcomes in the 29 systematic reviews have been summarised to identify if there are any adverse health outcomes that are documented to occur at a statistically significant higher rate than the background rates.

It should be noted that:

- No formal assessment of the quality of the systematic reviews included has occurred.
- The reviews predominantly analysed data from case-report, case-series, cross-sectional, case-control, and cohort.
 - Risk of bias due to study types and asymptomatic/patients with mild disease not presenting to hospital.
 - The majority of primary studies analysed by the authors of the systematic reviews were considered to be of poor methodological quality. Tools used included the Newcastle Ottawa Scale, the Joanna Briggs Institute and that described by Murad et al.³¹⁻³³
 - Management of pregnancy for SARS-CoV-2 infected mothers varied between regions and has changed as the pandemic progressed.
- A large proportion of the primary studies looked at data from single health care facilities across China. Most systematic review authors have attempted to remove duplicate data.

Given the above limitations, care needs to be taken with the interpretation of the presented evidence.

Definitions:

- Preterm birth is less than or equal to 36 completed weeks i.e. <37 weeks.
- Vertical transmission is mother-to-child transmission, which may include in utero, intrapartum and early postnatal pathways depending on the definition used in each study.

Summary of findings

Maternal factors of potential relevance to the neonate

The World Health Organisation (WHO) has reported that with SARS-CoV-2 infection there is no apparent difference in the risk of developing clinical symptoms between non-pregnant and pregnant women of reproductive age. However, the evidence shows that women infected with SARS-CoV-2 are at significantly higher risk for caesarean section and preterm birth.

Pregnant women are more susceptible to respiratory pathogens^{34,35} due to the anatomical structure and physiological adaptive alterations of the respiratory system that change during pregnancy, such as increased oxygen consumption and oedema of the respiratory tract.^{36,37} Studies carried out with pregnant women diagnosed with other highly pathogenic coronaviruses causing severe acute respiratory syndrome (SARS) in 2002 to 2003 have described that this infection can increase the risk of maternal death, miscarriage, preterm delivery, and intrauterine growth restriction.³⁸⁻⁴⁰

High rates of caesarean section were consistently reported. A precautionary approach is thought to contribute to the high rate of caesarean section for women with COVID-19 compared to non-COVID-19. This was generally attributed to a lack of formal guidelines on management of SARS-CoV-2 positive pregnant women during the early stages of the pandemic.²² Regional differences were reported, with higher rates of caesareans observed in China compared to the US and Europe.²² Caesarean section can be clinically indicated where maternal SARS-CoV-2 infection during pregnancy results in hypoxemia or respiratory failure, leading to fetal distress, stillbirth, and preterm labour, and/or the need of maternal ventilation.²⁷ It is not clear what proportion of the increased rates of caesarean section are due to precautionary measures for feared vertical transmission, fetal distress or for maternal stabilisation.²⁴

Transmission and neonatal infection

On 8 February 2021, WHO issued a scientific brief on the categorization of the timing of mother-to-child transmission of SARS-CoV-2. Despite reports of vertical transmission in the literature, a lack of a systematic classification systems and sample collection timing has meant that the WHO has been unable to make a firm conclusion on vertical transmission or the potential mechanism.⁴¹

This review of the literature did not reveal any definitive evidence on vertical transmission of SARS-CoV-2. The following key points are based on the summary of systematic reviews at Attachment 1:¹⁻²⁹

- False negatives of SARS-CoV-2 nucleic acid tests have not been ruled out in cases of newborns of SARS-CoV-2 positive mothers who were asymptomatic but experienced adverse outcomes such as thrombocytopenia and abnormal liver function.¹
- It is important to exercise caution and consider serology results of neonates in conjunction with SARS-CoV-2 nucleic acid test due to the higher false-negative rate in the latter and the asymptomatic presentation of many neonates.
- Newborn infants may be infected in the first few hours of life, but as very few are severely affected it is likely that the benefits of contact with the mother and the ability to breast feed outweigh the potential benefits of separation.
- The rate of infection is no greater when the baby is born vaginally (as compared to caesarean), breastfed or kept with the mother.

The Australian COVID-19 Clinical Evidence Taskforce has developed guidelines on the management of pregnant/postpartum women and their newborns.⁴² The Lancet Infectious Diseases Guidelines⁴³ recommend the following for symptomatic cases:

- Prioritise vaginal delivery when possible
- Delayed clamping of the umbilical cord if possible
- No early cleaning of the newborn
- Newborn surveillance in isolation
- PCR testing of the newborn
- Decision making on mother-newborn separation and breastfeeding should be individually discussed by an interdisciplinary team including neonatologists, paediatric infectious disease specialists, infection control and hygiene team and obstetricians.

The American Academy of Paediatrics and Centers for Disease Control and Prevention guidelines recommends the use of measures to reduce the risk of infection between the mother and newborn including facemasks, and hand/breast hygiene before feeding.⁴⁴ The current WHO recommendation (as outlined in their most recently published guidelines on clinical management of COVID-19) is that if infection prevention measures are taken, the benefits of breastfeeding outweigh the risks of any potential mother to child transmission.⁴⁵ Keeping mothers and babies together is important. Kangaroo care (early, prolonged skin-to-skin contact with a parent and exclusive breastfeeding) is particularly critical for babies born preterm or at low birthweight.^{42,46}

Outcomes of neonates of SARS-CoV-2 positive mothers

Based on the summary of systematic reviews at [Attachment 1](#), most infants born to COVID-19-confirmed mothers were reported as asymptomatic with low rates of transmission of SARS-CoV-2. SARS-CoV-2 positivity in mothers does not change the rates of intrauterine fetal death or neonatal death.¹⁶ Adverse clinical impacts for neonates to SARS-CoV-2 positive mothers have been reported, although generally the outcomes are favourable.^{4,9} Reported clinical presentation of affected^a newborns included (in order of decreasing frequency):

- Fever
- Preterm birth
- Low birth weight
- Reduced Apgar scores immediately post birth and 5-10min later
- Pneumonia
- Respiratory distress syndrome +/- requiring NICU admission
- Lymphocytopenia and thrombocytopenia (often in asymptomatic babies)
- Intrauterine and neonatal death.

High risk of preterm birth was consistently reported in newborns to SARS-CoV-2 positive mothers. One systematic review found the risk of pre-term birth to be 19% higher for mothers with SARS-CoV-2 than expected in the general population.²¹

Though fetal and neonatal mortality is low, COVID-19 infection of mothers can be associated with adverse neonatal outcomes. Severe maternal disease and prematurity are associated with, and thought to be primary contributors, to adverse neonatal outcomes.²² Hypoxemia

^a Affected newborns include those born to SARS-CoV-2 positive mothers. SARS-CoV-2 infected infants have not been separated from this analysis.

and respiratory failure in mothers with severe COVID-19 cases can lead to fetal distress, preterm labour and stillbirth.²² Risk factors for severe COVID-19 in pregnancy include:²

- Pre-existing comorbidities
- Non-white ethnicity
- Chronic hypertension
- Pre-existing diabetes, high maternal age
- High body mass index.

Infection in newborns of SARS-CoV-2 mothers is uncommon, with one review observing positive RT-PCR in only 3.9% of the cohort.¹⁰

Outcomes of SARS-CoV-2 positive neonates

Neonatal morbidity and mortality are suspected to be due to prematurity rather than SARS-CoV-2 infection of newborns.²⁷ Abnormal Apgar scores, neonatal asphyxia, stillbirth and neonatal death rates have been found to be similar with infected or uninfected newborns born to SARS-CoV-2 positive mothers. NICU admission was more common in infected newborns however this likely to reflect the policy of unit than the neonatal problem.²² In a study that included 12 cases of newborns infected with SARS-CoV-2: respiratory symptoms (42%), gastrointestinal symptoms (25%) and fever (25%) were observed. One neonate required invasive ventilation and two received antibiotics.⁴⁷

Overall, prognosis of infected newborns is good, although it is important to note that unlike older children, approximately two thirds of neonatal cases are symptomatic.^{10,48}

Other considerations

In addition to the adverse outcomes described above, newborns of SARS-CoV-2 infected mothers may show subclinical abnormalities on radiology and blood tests and should be carefully monitored by treating clinicians. Abnormal radiological finding, lymphocytopenia and thrombocytopenia have been repeatedly reported in seemingly healthy babies born to SARS-CoV-2-infected women.²⁸

Attachments

Attachment 1: Summary of systematic review findings

Attachment 2: Improving provision and experiences of maternity care during the COVID-19 pandemic – lessons from the COVMAT study Policy Brief 1.

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