




# Rapid Review: Is there an increased risk of adverse maternal or fetal outcomes in women exposed to COVID-19 during pregnancy?

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# Executive Summary

## Background

Evidence on maternal, fetal, and neonatal outcomes associated with COVID-19 is lacking. Understanding the implications of COVID-19 infection during pregnancy may be used to guide obstetric care for patients with COVID-19.

This rapid review was produced to support public health decision makers' response to the coronavirus disease (COVID-19) pandemic. This review seeks to identify, appraise, and summarize emerging research evidence to support evidence-informed decision making.

This rapid review is based on the most recent research evidence available at the time of release. This version includes evidence available up to May 7, 2020.

In this rapid evidence review, we provide the most recent research evidence to answer the question: **Is there an increased risk of adverse maternal or fetal outcomes in women diagnosed with COVID-19 during pregnancy?**

## Key Points

- There is little to no evidence of adverse outcomes associated with pregnancy among women with COVID-19. Evidence quality is low to moderate; findings are consistent.
- Several reviews and studies report a high rate of cesarean deliveries among women with COVID-19, although the clinical indications for cesarean in these cases are not well described, and the limited available evidence suggests that vaginal delivery can be safe. Evidence quality is low to moderate; findings are consistent.
- Some reviews report rates of pre-term birth between 21-39% of cases. The extent to which this rate is elevated compared to non-COVID-19 rates is not reported. Evidence quality is low to moderate; findings are consistent.
- There is no evidence of vertical transmission. Evidence quality is low to moderate; findings are consistent.

## Overview of Evidence and Knowledge Gaps

- Evidence specific to COVID-19 is lacking and this question should be reviewed again as more information is available from around the world.
- Evidence on maternal, fetal and neonate outcomes among women with COVID-19 infection in the first and second trimesters is lacking.
- It is not known whether COVID-19 infection resulted in clinical indication for cesarean delivery or whether clinician preference determined the method of delivery.
- It is not known whether the reported rate of cesarean delivery or pre-term delivery for women with COVID-19 infection is significantly higher than usual at these sites.
- Study designs tend to be weak (case series, case reports or case controls).
- Although several syntheses exist, there is a large amount of overlap of single studies within the reviews. For example, the same observed case of neonatal death was reported in three reviews. Similarly, the high rate of cesarean delivery may be overestimated due to the same deliveries being reported in multiple reviews.

## Methods

### Research Question

Is there an increased risk of adverse maternal or fetal outcomes in women diagnosed with COVID-19 during pregnancy?

### Search

On 7 May 2020, the following databases were searched for evidence pertaining to the relationship between risk for adverse maternal or fetal outcomes and COVID-19 during pregnancy.

- Cochrane [Coronavirus \(COVID-19\) Special Collections](#)
- Cochrane [Rapid Reviews Question Bank](#)
- Joanna Briggs [Institute COVID-19 Special Collection](#)
- Oxford [COVID-19 Evidence Service](#)
- Oxford [COVID-19 Evidence Service: Current Questions Under Review](#)
- [Turning Research Into Practice \(TRIP\)](#)
- [Guidelines International Network \(GIN\)](#)
- [LitCovid](#)
- World Health Organization [Global literature on coronavirus disease](#)
- [CovidReview](#)
- [Prospero Registry of Systematic Reviews](#)
- [COVID-19 Evidence Alerts](#) from McMaster PLUS™
- [Public Health +](#)

A copy of the search strategy is available on request.

### Selection Criteria

The search first included recent, high-quality syntheses. If no syntheses were found, single studies were included. English-language, peer-reviewed sources and sources published ahead-of-print before peer review were included. Grey literature and surveillance sources were excluded.

	Inclusion Criteria	Exclusion Criteria
Population	Pregnant women	Adolescents
Intervention	COVID-19	
Comparisons	No COVID-19	
Outcomes	Mortality Miscarriage Preterm labour	

## Data Extraction and Synthesis

Data on study design, setting, location, population characteristics, interventions or exposure and outcomes were extracted when reported. We synthesized the results narratively due to the variation in methodology and outcomes for the included studies.

We evaluated the quality of included evidence using critical appraisal tools as indicated by the study design below. Quality assessment was completed by one reviewer and verified by a second reviewer. Conflicts were resolved through discussion.

<b>Study Design</b>	<b>Critical Appraisal Tool</b>
Synthesis	Health Evidence™ <a href="#">Quality Appraisal Tool</a>
Case Control	Critical Appraisal Skills Programme (CASP) <a href="#">Case Control Checklist</a>
Case Series	Joanna Briggs Institute (JBI) <a href="#">Checklist for Case Series</a>

Completed quality assessments for each included study are available on request.

## Findings

This document includes five completed and seven in progress syntheses and three single studies, for a total of 15 publications included in this evidence review. The quality of the evidence included in this review is as follows:

		Total	Quality of Evidence
Syntheses	Completed Reviews	5	1 Low 4 Moderate
	In Progress Reviews	7	-
Single Studies	Completed	3	1 Low 2 Moderate

### Warning

Given the need to make emerging COVID-19 evidence quickly available, many emerging studies have not been peer reviewed. As such, we advise caution when using and interpreting the evidence included in this rapid review. We have provided a summary of the quality of the evidence as low, moderate, or high to support the process of decision making. Where possible, make decisions using the highest quality evidence available.

**Table 1: Syntheses**

Reference	Date Released	Description of included studies	Summary of Findings	Quality Rating: Synthesis	Quality Rating: Included Studies
Elshafeey F, Magdi R, Hindi N., Elshebiny, M., Farrag, N., Mahdy... Nabhan, A. (2020). <a href="#">A systematic scoping review of COVID-19 during pregnancy and childbirth</a> <i>Int J Gynaecol Obstet</i> . Epub ahead of print, 2020.	Apr 24, 2020 (Search to Apr 19, 2020)	Scoping review of 33 studies from around the world, published between December 8, 2019 and April 19, 2020, reporting on clinical characteristics, maternal and perinatal outcomes of 385 pregnant women with COVID-19. Study designs included case control, case reports, case series.	Included cases were predominantly mild: 368 (95.6%) mild; 14 (3.6%) severe; and 3 (0.8%) critical. 17 women were admitted to intensive care, including 6 who were mechanically ventilated and 1 maternal mortality. 252 women gave birth: 69.4% cesarean and 30.6% vaginal births. Outcomes for 256 newborns included 4 RT-PCR positive neonates, 2 stillbirths, and 1 neonatal death. No evidence of vertical transmission. Limited data suggest that pregnant women have a clinical presentation and severity similar to non-pregnant adults, and adverse maternal and perinatal outcomes were rare.	Low	Not reported
Yang Z, Wang M, Zhu Z, & Liu Y. (2020). <a href="#">Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review</a> <i>J Matern Fetal Neonatal Med</i> . Epub ahead of print.	Apr 20, 2020 (Search to Mar 26, 2020)	Systematic review of 18 studies from around the world, published between January 1, 2020 and March 26, 2020, reporting on maternal, fetal, and neonatal outcomes of 114 pregnant women infected with (COVID-19). Study designs included case control, case reports, case series.	91% had cesarean delivery. In terms of fetal and neonatal outcomes, stillbirth (1.2%), neonatal death (1.2%), preterm birth (21.3%), low birth weight (<2500 g, 5.3%), fetal distress (10.7%), and neonatal asphyxia (1.2%) were reported. No direct evidence of intrauterine vertical transmission.	Moderate	Low

			The clinical characteristics of pregnant women with COVID-19 are similar to those of non-pregnant adults. Fetal and neonatal outcomes appear good in most cases. <b>Limitation: Available data only include pregnant women infected in their third trimesters.</b>		
Della Gatta AN, Rizzo R, Pilu G, & Simonazzi G. (2020). <a href="#">COVID19 during pregnancy: a systematic review of reported cases</a> . <i>Am J Obstet Gynecol</i> . Epub ahead of print.	Apr 17, 2020 (Search to Mar 16, 2020)	Systematic review of 6 studies from around the world, published prior to March 16, 2020, reporting on clinical outcomes for 51 pregnant women infected with COVID-19. Study designs included case series, case reports, and retrospective studies.	39% had preterm birth; 96% had cesarean delivery with unclear indications. No evidence of vertical transmission. 1 fetal death occurred in a critically ill patient. Clinical outcome has been generally favorable for both mothers and neonates.	Moderate	Low to moderate
Parazzini, F., Bortolus, R., Mauri, P.A., Favilli, A., Gerli, S. & Ferrazzi, E. (2020). <a href="#">Delivery in pregnant women infected with SARS-CoV-2: A fast review</a> . <i>Int J Gynecol Obstet</i> . 150(1).	Apr 10, 2020 (search to Mar 31, 2020)	Rapid review of 13 studies from around the world, published between January 1 to March 31, 2020, of clinical maternal characteristics, mode of delivery and neonatal outcomes for 64 pregnant women infected with COVID-19. Study designs included case reports and retrospective clinical series.	Pneumonia was present in 80.3% women, oxygen support was needed by 82.9%, and 6.5% were admitted to a critical care unit (among limited cases for which the information was available). 39.6% had preterm birth; 48.4% had cesarean delivery due to worsening of maternal conditions. In all reported cases the 5-minute Apgar score was greater than 7 and generally 9 or 10. Zero or low rate of vertical or peripartum transmission through cesarean delivery; no data available for vaginal delivery. Risk of transmission during breastfeeding is unknown.	Moderate	Not reported

			Overall, risk of adverse maternal and fetal outcomes is low.		
Zaigham, M. & Andersson, O. (2020). <a href="#">Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies.</a> <i>Acta Obstet Gynecol Scand.</i> Epub ahead of print.	Apr 7, 2020 (Search to Apr 4, 2020)	Systematic review of 18 studies from around the world, published between December 8, 2019 and April 4, 2020, of clinical manifestations and maternal and perinatal outcomes for 108 pregnant women with lab-confirmed COVID-19 infection. Study designs included case reports and case series.	68% presented with a fever at admission. 91% had cesarean delivery. The majority of mothers were discharged without any major complications. However, severe maternal morbidity as a result of COVID-19 and perinatal deaths were reported, with 3% of women requiring admission to maternal ICU, and 1 case of perinatal death. No clear evidence for vertical transmission.	Moderate	Low



## Table 2: In-Progress Syntheses

Title	Anticipated Release Date	Description of document
Novoa, R., Quintana Munoz, W., Llancari Melendez, PA., & Ventura Laveriano, W. <a href="#">Maternal clinical characteristics and perinatal outcomes of pregnant women infected by coronavirus (COVID-19). A systematic review.</a> PROSPERO 2020 CRD42020176534	Apr 30, 2020	This review will look to answer two questions: 1) What are the clinical characteristics of COVID-19 infection in pregnant women; and 2) What are the perinatal outcomes of COVID-19 infection in pregnant women?
Poon, L., Yang, H., del Mar, M., & Juan, J. <a href="#">Maternal, fetal and neonatal characteristics and clinical outcomes in cases of COVID-19 infection during pregnancy: a systematic review.</a> PROSPERO 2020 CRD42020181557	May 25, 2020	The research question looks to answer, "What is the effect of SARS-CoV-2 infection (COVID-19 disease) in pregnancy, mother, fetus and newborn".
Ramos, M. <a href="#">COVID-19 in pregnant women: a systematic review.</a> PROSPERO 2020 CRD42020179843	May 30, 2020	The research question for this review is, "What evidence is available about COVID-19 in pregnant women?" The primary outcomes are hospitalization, mortality, medical complications and readmission and secondary outcomes include clinical management and delivery arrangements.
Aparecido Foratori-Junior, G., Mosquim, V., & de Carvalho Sales-Peres, S.H. <a href="#">COVID-19 and its relation with pregnancy and neonates: a systematic review.</a> PROSPERO 2020 CRD42020177354	Sep 24, 2020	This review will look to synthesize evidence on the symptoms of COVID in pregnant women and in their newborn children as well as the impacts on delivery and the possibility of vertical transmission.
Fen, LY., Lei, GX., Han NC., Peng Mei, YN., & Amin, Z. <a href="#">A systematic review of neonates and COVID-19.</a> PROSPERO 2020 CRD42020183500	Dec 31, 2020	This review will address four questions: 1) What are the maternal and neonatal serological results (i.e. IgM and IgG) in reported COVID-19 pregnancies; 2) What are the immunological profiles of mothers and neonates in reported COVID-19 pregnancies; 3) What is the effect of gestational age at maternal COVID-19 infection on neonatal outcomes and 4) What are the neonatal outcomes of perinatally acquired infection compared to postnatally acquired infection?
Bahri, N., Sashti, S., Fathi Najafi, T., & Reza Tohidinik, H. <a href="#">Assessment of the possibility of vertical transmission of COVID-19: a systematic review and meta-analysis protocol.</a> PROSPERO 2020 CRD42020173886	Mar 1, 2021	This review will assess the possibility of vertical transmission of COVID.
Cochrane Ireland. (2020). <a href="#">COVID and pregnancy: MTC transmission, outcomes</a>	Not reported	No details provided

**Table 3: Single Studies**

Reference	Date Released	Study Design	Population	Comparator	Setting	Summary of findings	Quality Rating:
Liao, J., He, X., Gong, Q., Yang, L., Zhou, C. & Li, J. (2020). <a href="#">Analysis of vaginal delivery outcomes among pregnant women in Wuhan, China during the COVID-19 pandemic.</a> <i>Int J Gynecol Obstet.</i> 150(1).	Apr 29, 2020	Case control	10 pregnant women with COVID-19	53 pregnant women without COVID-19	Wuhan, China	There were no differences in outcomes (gestational age, postpartum hemorrhage, and perineal resection rates, birth weight of neonates and neonatal asphyxia rates) between the two groups. Neonates delivered by pregnant women with COVID-19 tested negative.	Low
Yan J., Guo J., Fan C., Juan J., Yu X., Li J... Yang, H. (2020). <a href="#">Coronavirus disease 2019 (COVID-19) in pregnant women: A report based on 116 cases.</a> <i>American Journal of Obstetrics and Gynecology</i> 223(1); 111.e1-111.e14	Apr 23, 2020	Case series	116 pregnant women with COVID-19	None	China	50.9% presented with fever. 21.2% had preterm birth. No evidence of vertical transmission, and low risk of spontaneous abortion or spontaneous preterm birth.	Moderate
Qiancheng X., Jian S., Lingling P. Lei, H., Xiaogan, J., Weihua, L... Lei, Z. (2020). <a href="#">Coronavirus disease 2019 in pregnancy</a> <i>Int J Infect Dis.</i> 95, 376-383.	Apr 27, 2020	Retrospective case control	28 pregnant women with COVID-19	54 reproductive-aged non-pregnant women with COVID-19	Wuhan, China	No difference between pregnant and non-pregnant women in severity of COVID-19, and little data to support the likelihood of vertical transmission. Pregnant women in the third trimester delivered live births without documented perinatal complications, except 1 preterm birth.	Moderate

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