Pregnancy related risks associated with COVID-19

A rapid review

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Pregnancy related risks associated with COVID-19
Table of Contents

EXECUTIVE SUMMARY ................................................. iv
Methods........................................................................ 1
Results ........................................................................... 2
References ....................................................................... 3
EXECUTIVE SUMMARY

This should not be longer than 1-2 pages and should include the following:

Objectives: The purpose of this review was to provide evidence on the following:

Key Question:
1. Has there been a change in the rate of pregnant persons admitted to the ICU/developing severe COVID outcomes?

Supporting Questions:
2. What is the risk of pregnant women acquiring COVID-19, developing severe illness, being hospitalized, requiring ICU admission or death?
   a) Does the risk differ between trimesters?
   b) Does the risk differ between COVID-19 genomic variants (e.g., variants of interest, concern or high consequence)?
   c) What risk factors related to pregnancy, based on intersecting conditions of social and/or material disadvantage or certain health conditions (e.g., obesity, diabetes, hypertension, chronic respiratory illness), are associated with a higher risk?
3. What is the association of physiological changes during pregnancy (e.g., increased risk of thromboembolic events, natural state of immunosuppression) with increased risk of acquiring COVID-19, developing severe illness, being hospitalized, requiring ICU admission or death?

Design: Rapid review

Method: We searched four bibliographic databases (Medline, Embase, CovidLit and CochraneCovid). One reviewer selected studies for inclusion, extracted data and assessed the quality of systematic reviews using the AMSTAR tool.

Results: Numerous evidence syntheses have been identified that provided evidence on the key questions. All were ‘low’ to ‘critically low’ quality. Additional primary studies (n = 95) were identified that were not captured by previous evidence syntheses (mostly cohort and case-controlled studies).

Conclusion: While there are many evidence syntheses, their poor quality and lack of including numerous potentially relevant studies, reflects the need for more well-conducted evidence syntheses to answer the questions of relevance to this review.
Methods

The primary research questions for this review were as follows:

**Key Question:**
1. Has there been a change in the rate of pregnant persons admitted to the ICU/developing severe COVID outcomes?

**Supporting Questions:**
2. What is the risk of pregnant women acquiring COVID-19, developing severe illness, being hospitalized, requiring ICU admission or death?
   d) Does the risk differ between trimesters?
   e) Does the risk differ between COVID-19 genomic variants (e.g., variants of interest, concern or high consequence)?
   f) What risk factors related to pregnancy, based on intersecting conditions of social and/or material disadvantage or certain health conditions (e.g., obesity, diabetes, hypertension, chronic respiratory illness), are associated with a higher risk?
3. What is the association of physiological changes during pregnancy (e.g., increased risk of thromboembolic events, natural state of immunosuppression) with increased risk of acquiring COVID-19, developing severe illness, being hospitalized, requiring ICU admission or death?

We utilized a hierarchical approach to the evidence synthesis with a focus on previously conducted systematic reviews (SRs), scoping reviews (ScRs), rapid reviews (RRs), meta-analyses (MAs), and clinical practice guidelines (CPGs)/ policy guidance statements (e.g., from governmental organizations or specialized societies). In addition, we identified primary clinical studies (CS) that were not captured by the previously conducted reviews. Lastly, we highlighted some key findings from Editorials, Commentaries, Opinions, and Narrative reviews (ECONs) that provided additional insight for the key questions.

**Search strategy for identification of studies**
We searched general health bibliographic databases [MEDLINE (Ovid) and EMBASE (Ovid), and COVID-19 specific databases [LitCovid (https://www.ncbi.nlm.nih.gov/research/coronavirus/) and Cochrane Covid (https://covid-19.cochrane.org/)]. Searches were conducted from May 17-19, 2021. Each database was searched using an individualized search strategy; example of Medline search is available in Appendix 1. Finally, the reference lists of relevant narrative and systematic reviews and included studies were hand-searched for relevant citations. We performed reference management in EndNote™ (version X9, Thomson Reuters, Carlsbad, CA, USA).

**Study selection**
We used a two-stage process for study screening and selection using standardized and piloted screening forms. One reviewer screened the titles and abstracts of search results to determine if a

Pregnancy related risks associated with COVID-19
Pregnancy related risks associated with COVID-19

citation met the inclusion criteria. Full texts (if available) of all the selected citations were examined by one reviewer.

The population of interest for this review was limited to pregnant individuals irrespective of trimester. Non-pregnant, fetal, and newborn populations were not within the scope of this review. The diagnosis of COVID-19, requirements for hospital or ICU admission were author-defined. We also did not limit to studies that only include women with laboratory-confirmed infections. Lastly, we did not limit studies to any geographic location but will limit to only English-language publications for feasibility.

Data abstraction and management
One reviewer summarized the findings from included study reports. We tabulate the results and the evidence is presented descriptively. Data management was performed using Microsoft Excel™ 2010 (Excel version 14, Microsoft Corp., Redmond, WA, USA).

Assessment of methodological quality and potential risk of bias
Due to the expedited nature of this rapid review, and that most of the evidence was expected to come from lower quality, single-arm observational studies, we did not assess the methodological quality or potential risk of bias of the included observational studies. However, we did assess the quality of systematic reviews (as defined by Cochrane) using the AMSTAR 2 tool.

Results

From 12,758 citations identified through the search strategy, 192 studies met the inclusion criteria: 69 SRs/CPGs, 95 CS, 28 ECONs (Figure 1). The included studies are summarized in the associated Excel Workbook (Evidence Summary.xlsx) and is divided based on key question and evidence source. All the systematic reviews were ‘low’ to very ‘critically low’ quality studies.

Overall, the quality of the evidence from previous evidence synthesis is weak and decision-making should consider looking closely at higher-quality primary studies (e.g., prospective, longitudinal studies).
References


Pregnancy related risks associated with COVID-19


Pregnancy related risks associated with COVID-19
European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2020:1-8.


Pregnancy related risks associated with COVID-19


Pregnancy related risks associated with COVID-19
Pregnancy related risks associated with COVID-19


Pregnancy related risks associated with COVID-19
Pregnancy related risks associated with COVID-19


Pregnancy related risks associated with COVID-19

Figure 1. Modified PRISMA flow-chart

Records identified through database searching and other sources (n = 12,758) →
Duplicate records excluded (n = 6,577) →
Excluded based on study design/ publication type/ Non-English publication (n = 826) →
Unique records screened for eligibility (n = 5,355) →
Records excluded for not meeting inclusion criteria (n = 4,652) →
Full-text articles assessed for eligibility (n = 703) →
Full-text articles excluded: (n = 511) →
Studies included in the review (n = 192) (SRs/ CPGs = 69) (CS = 95) (ECONs = 28)
Appendix 1. Medline (Ovid) Search Strategy

1. exp Coronavirus/ or exp Coronavirus Infections/ (96880)
2. (OC43 or NL63 or D614G or 229E or HKU1 or hcoV* or ncov* or covid* or sarscov* or sars-
cov* or sarscoronavir* or sars-coronavir* or 2019ncov* or 19ncov* or novel cov* or 2019novel
cov* or severe acute respiratory syndrome corona*).ti,ab,nm,ot,ox,rx,px. (138705)
3. ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus*
or corona virus* or betacoronavirus* or CoV)).ti,ab,kf,ot. (42496)
4. ((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or
outbreak* or crisis)).ti,ab,kf,ot. (7974)
5. ((wuhan or hubei) adj5 pneumonia).ti,ab,kf,ot. (335)
6. (COVID-19 or SARS-CoV-2).rx,px,ox,rn. or (COVID-19 or COVID-19 serotherapy or ORF7b
protein, SARS-CoV-2 or ORF6 protein, SARS-CoV-2 or ORF8 protein, SARS-CoV-2 or pediatric
multisystem inflammatory disease, COVID-19 related or envelope protein, SARS-
CoV-2 or ORF7a protein, SARS-CoV-2 or spike protein, SARS-CoV-2 or ORF3a protein,
SARS-CoV-2 or COVID-19 drug treatment or severe acute respiratory syndrome coronavirus
2 or membrane protein, SARS-CoV-2 or ORF1ab polyprotein, SARS-CoV-2 or nucleocapsid
protein, Coronavirus or COVID-19 vaccine or COVID-19 diagnostic testing).os,ps,rn,rs. (7980)
7. or/1-6 (156700)
8. limit 7 to yr="2019 -Current" (140838)
9. exp pregnant women/ or exp pregnancy/ or exp pregnancy complications/ or exp maternal
health services/ or exp prenatal care/ or exp perinatal care/ (959417) ()
10. (pregnan* or gestation* or gravidity or maternal or maternity or antenatal or ante
te partum or ante partum or prenatal or pre natal or perinatal or peri natal or obstetric*).ti,ab,kf. (921768)
11. or/9-10 (1293208)
12. 8 and 11 (3599)
13. exp animals/ not humans.sh. (4832753)
14. 12 not 13 (3576)
15. limit 14 to english language (3472)