Prognosis of COVID-19 in pregnancy: Protocol for an overview of systematic reviews

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ABSTRACT

Objective

We aim to map and summarise the current evidence about COVID-19 prognosis in pregnant women.

Design

This is the protocol of an overview of systematic reviews.

Data sources

We will conduct comprehensive searches in PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), grey literature, and L·OVE (Living Overview of Evidence). L·OVE is a platform that maps PICO evidence questions from Epistemonikos database. In response to the COVID-19 emergency, L·OVE was adapted to expand its COVID-19 repository evidence as a way to gather it in one place. The search will cover the period until the day before submission to a journal.

Eligibility criteria for selecting studies and methods

We adapted an already published common protocol for multiple parallel systematic reviews and overviews of systematic reviews to the specificities of this question.

We will include all systematic reviews about COVID-19 in pregnant women.

Two reviewers will independently screen each study for eligibility, extract data, and assess the risk of bias.

Ethics and dissemination

No ethics approval is considered necessary. The results of this overview will be widely disseminated via peer-reviewed publications, social networks and traditional media.

Keywords

COVID-19, severe acute respiratory syndrome coronavirus 2, Coronavirus Infections, Systematic review, Overview, Pregnant Women, Gravidity, Pregnancy

INTRODUCTION

COVID-19 is an infection caused by the SARS-CoV-2 coronavirus [1]. It was first identified in Wuhan, China, on December 31, 2019 [2]; eight months later, more than fifteen million cases of contagion had been identified across the globe [3].

While most cases result in mild symptoms, some might progress to pneumonia, acute respiratory distress syndrome and death [4–6]. In general population severe cases of COVID-19 are about 14% and 5%, critical [7]. Major risk factors for worst prognosis are the presence of diabetes, cardiovascular and respiratory disease [8]. The case fatality rate reported across countries, settings and age groups is highly variable, but it ranges from about 0.5% to 10% [9]. In hospitalised patients it has been reported to be higher than 10% in some centers [10].

Pregnant women are a special group of concern in this outbreak. Physiological changes in immunologic, cardiovascular, and respiratory systems may increase the severity of respiratory diseases, especially during the third trimester [11–13]. Scarce data about SARS and MERS suggests that coronaviruses infections during pregnancy are associated with adverse perinatal outcomes, with high rates of maternal and perinatal mortality, cesarean section, and preterm birth [14,15].

Cases of pregnant women with COVID-19 have already been reported in several primary studies and systematic reviews [16–18]. However, there are still controversies about maternal prognosis and perinatal outcomes in pregnant women with COVID-19.

Using innovative and agile processes, taking advantage of technological tools, and resorting to the collective effort of several research groups, this overview of systematic reviews aims to map and summarise the current evidence on prognosis of COVID-19 in pregnant women.

METHODS

This manuscript complies with the ‘Preferred Reporting Items for Systematic reviews and Meta-Analyses’ (PRISMA-P) guidelines for reporting systematic reviews and meta-analyses [19]. A protocol stating the shared objectives and methodology of multiple evidence syntheses (systematic reviews and overviews of systematic reviews) to be conducted in parallel for different questions relevant to COVID-19 was published elsewhere [20]. This protocol was adapted to the specificities of the question assessed in this overview of systematic reviews.

Search strategies

Electronic searches

Our literature search will be devised by the team maintaining the L·OVE platform (<https://app.iloveevidence.com>), using the following approach:

1. Identification of terms relevant to the population and exposure components of the search strategy, using Word2vec technology [21] to the corpus of documents available in Epistemonikos Database.
2. Discussion of terms with content and methods experts to identify relevant, irrelevant and missing terms.
3. Creation of a sensitive boolean strategy encompassing all the relevant terms
4. Iterative analysis of articles missed by the boolean strategy, and refinement of the strategy accordingly.

Our main search source will be Epistemonikos database (<https://www.epistemonikos.org>), a comprehensive database of systematic reviews and other types of evidence [22] with more than 300.000 systematic reviews, and over 400.000 studies included in those reviews. We will supplement this with information from Pubmed, EMBASE, the WHO International Clinical Trials Registry Platform and other 30 sources relevant to COVID-19. The list of sources that have been added to Epistemonikos is continuously expanded. This list of sources regularly screened by Epistemonikos for COVID-19 is updated regularly on our website [23].

In sum, Epistemonikos Database acts as a central repository. Only articles fulfilling Epistemonikos criteria are visible by users. The remaining articles are only accessible for members of COVID-19 L·OVE Working Group.

The searches will cover from the inception date of each database until the day before submission. No study design, publication status or language restriction will be applied to the searches in Epistemonikos or the additional searches.

The following strategy will be used to search in Epistemonikos Database. We will adapt it to the syntax of other databases.

((coronavir* OR coronavirus* OR "corona virus" OR "virus corona" OR "corono virus" OR "virus corono" OR hcov* OR "covid-19" OR covid19* OR "covid 19" OR "2019-nCoV" OR cv19* OR "cv-19" OR "cv 19" OR "n-cov" OR ncov* OR "sars-cov-2" OR "sars-cov2" OR (wuhan* AND (virus OR viruses OR viral)) OR (covid* AND (virus OR viruses OR viral)) OR "sars-cov" OR "sars cov" OR "sars-coronavirus" OR "severe acute respiratory syndrome" OR "mers-cov" OR "mers cov" OR "middle east respiratory syndrome" OR "middle-east respiratory syndrome" OR "covid-19-related" OR "SARS-CoV-2-related" OR "SARS-CoV2-related" OR "2019-nCoV-related" OR "cv-19-related" OR "n-cov-related") AND ((pregnan* OR gestation* OR primigravid* OR "mid-pregnancy"))

Other sources

1. We will conduct cross-citation search in Google Scholar and Microsoft Academic, using each included study as the index reference.
2. We will review the reference list of each included study.
3. We will review the reference list of other broad synthesis identified by our search.

Eligibility criteria

Types of studies

We will include all systematic reviews assessing prognosis of COVID-19 in pregnant women, including those reviews broader in scope than this overview that present separate data for our group of interest.

We will consider as a systematic review any secondary research including only primary studies, with an explicit search strategy in at least two databases.

We will exclude primary studies, clinical practice guidelines, overviews and other evidence synthesis studies including secondary studies.

Types of participants

We will include studies assessing pregnant women.

Type of exposure

We will include studies assessing the impact of SARS-CoV 2 infection. We will exclude any information on studies evaluating other coronavirus infections.

Types of outcomes

We will not use the outcomes as an inclusion criterion during the selection process. Any article meeting all the criteria except for the outcome criterion will be preliminarily included and evaluated in full text.

We used the core outcome set COS-COVID [24], studies contained in the COMET-initiative [25] repository, the existing guidelines and reviews and the judgement of the authors of this overview as an input to select the primary and secondary outcomes, as well as to decide upon inclusion. The review team will revise this list of outcomes, in order to incorporate ongoing efforts to define Core Outcomes Sets (e.g. COVID-19 Core Outcomes [26]).

Primary outcome

- All-cause mortality (Maternal and Neonatal)

Secondary outcomes

- *Maternal:*
 - Admission to intensive care required
 - Mechanical ventilation support required
 - Preterm delivery <37 weeks
 - Preterm delivery <34 weeks
 - Preterm rupture of membranes (PROM)
 - Cesarean delivery

- *Infant:*
 - Stillbirth
 - Neonatal admission to special care and/or intensive care unit
 - Mechanical ventilation support required
 - APGAR score
 - Infection status of the newborn (or products of conception)

Selection of studies

The results of the literature search in Epistemonikos database will be automatically incorporated into the L-OVE platform (automated retrieval), where they will be de-duplicated by an algorithm comparing unique identifiers (database ID, DOI, trial registry ID), and citation details (i.e. author names, journal, year of publication, volume, number, pages, article title and article abstract).

In L-OVE platform two researchers will independently screen the titles and abstracts yielded by the search against the inclusion criteria. We will obtain the full reports for all titles that appear to meet the inclusion criteria or require further analysis to decide about their inclusion.

We will record the reasons for excluding reviews in any stage of the search and outline the study selection process in a PRISMA flow diagram adapted for the purpose of this project.

Extraction and management of data

Using standardised forms, two reviewers will extract data independently from each included systematic review. We will extract all data from systematic reviews and not from primary studies.

We will collect the following characteristics of included systematic reviews: publication date, search sources and strategies, number of included studies, number of relevant included studies to our overview, assessment of evidence quality of included studies, elements of the systematic review question (patients, exposure definition and assessed outcomes), source of funding of the study and the conflicts of interest disclosed by the investigators. We will also extract synthesised results from systematic reviews, either narrative or quantitative depending on how systematic reviews present their results.

Assessment of overlap

We will build a matrix of evidence using Epistemonikos to visually examine the overlap of primary studies included along the different systematic reviews. Primary studies will be presented in the columns and systematic reviews in the rows. We will calculate the corrected covered area (CCA) for quantifying this overlap [27]. We will consider overlap as low if CCA is below 5%, moderate if CCA is between 5% and 10%, high if CCA is between 10% and 15%, and very high if CCA is above 15%. We will consider overlap degree when discussing our results.

Quality assessment

Two authors will independently assess the quality of each included systematic review using ROBIS [28]. We will display this assessment graphically.

We will not assess quality of evidence of the included primary studies in the systematic reviews.

Data synthesis

We will present the results of the included systematic reviews narratively. We will not conduct a quantitative synthesis.

We will present the characteristics of each included systematic review in a table and we will summarise their results by maternal and perinatal outcomes defined above. We will graphically present overlap of primary studies and risk of bias assessment.

NOTES

Acknowledgements

The members of the [COVID-19 L·OVE Working Group](#) and [Epistemonikos Foundation](#) have made it possible to build the systems and compile the information needed by this project. Epistemonikos is a collaborative effort, based on the ongoing volunteer work of over a thousand contributors since 2012.

Roles and contributions

GR conceived the common protocol for all the reviews being conducted by the COVID-19 L·OVE Working Group. LV, NM, CV, LO, JP and GR drafted the manuscript, and all other authors contributed to it. The corresponding author is the guarantor and declares that all authors meet authorship criteria and that no other authors meeting the criteria have been omitted.

The COVID-19 L·OVE Working Group was created by Epistemonikos and a number of expert teams in order to provide decision makers with the best evidence related to COVID-19. Up-to-date information about the group and its member organisations is available here: epistemonikos.cl/working-group

Competing interests

All authors declare no financial relationships with any organisation that might have a real or perceived interest in this work. There are no other relationships or activities that could have influenced the submitted work.

Funding

This project was not commissioned by any organisation and did not receive external funding.

Epistemonikos Foundation is providing training, support and tools at no cost for all the members of the COVID-19 L·OVE Working Group.

Ethics

As researchers will not access information that could lead to the identification of an individual participant, obtaining ethical approval was waived

Data sharing

All data related to the project will be available. Epistemonikos Foundation will grant access to data.

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