Review methods were amended after registration. Please see the revision notes and previous versions for detail.

Citation

Orene Greer, Ee Von Woon, Nishel Mohan Shah, Susanna Price, Mark R Johnson, Claudia A. Hardy, Juan Mauricio Pardo-Oviedo. A living systematic review and meta-analysis characterising treatment regimes, clinical outcomes and complications associated with extracorporeal life support (ELS) for critical COVID-19 in women in pregnancy and the puerperium compared to non-pregnant women of reproductive age and comparing materno-fetal outcomes to pregnant women without COVID-19. PROSPERO 2022 CRD42022266537 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022266537

Review question

1. To characterise the prevalence, treatment regimes, clinical outcomes and complications of COVID-19-related extracorporeal life support (ELS) as therapy for women in pregnancy/ puerperium compared to non-pregnant women of reproductive age with COVID-19.

2. To characterise maternal and fetal clinical outcomes for pregnant and puerperal patients with critical COVID-19-managed by ELS compared to pregnant women without COVID-19.

Searches

Electronic bibliographic databases searched include MEDLINE, EMBASE, The Cochrane Library, Health Technology Assessment Database, Web of Science, Global health, Maternity and Infant Care, the Cochrane Central Register of Controlled Trials (CENTRAL), covid?19.cochrane.org, EU Clinical Trial Register. In addition, national and international health registries will be searched such as: the ELSO registry, UKOSS, WHO (World Health Organization) COVID-19 database, WHO International Clinical Trials Registry, China National Knowledge Infrastructure (CNKI), and Wanfang databases, National Institutes of Health clinical trials registry.

Additionally, the reference lists of eligible studies and review articles, key journals, conference proceedings, internet resources e.g., Google Scholar and contact with study investigators will be performed.

Search dates will be from inception to 10/02/2022).

The search will not be restricted to any language. Selected studies studies, however, will be in English and Spanish.

Searches will be re-run prior to the final analysis.
No unpublished studies will be sought.
Additional search strategy information can be found in the attached PDF document (link provided below).

Types of study to be included

Inclusion criteria:

Abstracts where outcome data is reported;

Case reports;

Case series;

Cohort studies;

Case-control studies;

National and International medical registries and clinical data surveillance systems;

RCTs;

Health registries.

Additional inclusion criteria:

Studies involving confirmed PCR positive infection for SARS-CoV-2 in:

Women in pregnancy or puerperium (up to six weeks after delivery) diagnosed with critical COVID-19 managed with ELS;

and women of reproductive age (18-50 years) diagnosed with critical COVID-19 managed with ELS (as controls in case-control studies).
AND
Healthy pregnant women without COVID-19.

Exclusion criteria:

Studies with pregnancy as an exclusion criterion.

Studies involving suspected unconfirmed infections with SARS-CoV-2;

Male patients;

Incomplete datasets;

None of the research outcomes are reported.

Condition or domain being studied

Prevalence, treatment regimes, clinical outcomes and complications in pregnant and puerperal women managed with ELS for critical COVID-19.

Participants/population

Inclusion criteria:

Confirmed PCR positive infection for SARS-CoV-2 in:

Women in pregnancy or puerperium (up to six weeks after delivery) diagnosed with critical COVID-19 managed with ELS;

Women of reproductive age (18-50 years) diagnosed with critical COVID-19 managed with ELS (as controls in case-control studies).

AND
Healthy pregnant women without COVID-19.

Exclusion criteria:

Suspected unconfirmed infection with SARS-CoV-2;

Male patients.

Intervention(s), exposure(s)

ELS for PCR positive COVID-19 of patients who are either pregnant (any gestation) or upto 42 days after pregnancy (of any gestation).

Comparator(s)/control

Inclusion criteria:
i) Non-pregnant women of reproductive age diagnosed with critical COVID-19 managed with ELS when compared to women in pregnancy/ puerperium with critical COVID-19 managed with ELS (in case control studies and RCTs);

ii) Women in pregnancy or puerperium without COVID infection - when compared to women in pregnancy/ puerperium with critical COVID-19 that have been managed with ELS (in case series, case-control studies, cohort studies and RCTs).

Context

Studies worldwide set in ICU centres providing ECMO (extracorporeal membrane oxygenation).

Main outcome(s)

ELS outcomes:
Prevalence of ELS including VV and VA ECMO in pregnant/ puerperal women and non-pregnant women of reproductive age with critical COVID-19;
Duration in days from positive test PCR when escalated to ELS;
Duration in days from commencement of symptoms when escalated to ELS;
Duration in days of noninvasive ventilation prior to ELS;
Duration in days of mechanical ventilation prior to ELS;
In-hospital mortality;
ELS regime;
Successful wean off ELS or successfully discharged from hospital (e.g., discharged with left ventriclar assist device);
ELS - related complications.
Maternal clinical outcomes:
Duration on ECMO from admission to discharge or death (measured in days);
Duration on ECMO from admission to discharge/ death according to trimester/ postnatal week at admission (measured in days). (Patients will be grouped into 1st trimester, 2nd trimester, 3rd trimester and weeks 1-2 postpartum and weeks 2-6 postpartum.);

Gestation at delivery and timing of delivery in relation to commencement and cessation of ELS (measured in days) in pregnant patients.

Fetal clinical outcomes:

Live birth;

Mean gestation at delivery.

Measures of effect

1. Outcome measures will be reported as proportions of the total sample number for case reports and case series.

2. Outcome measures will be reported as proportions of the total sample number for cohort studies.

3. Odds ratio will be the effect measure for the case-control studies and any RCTs.

Additional outcome(s)

Maternal:

Rates of composite morbidity: thrombosis/ ARDS/ DIC and haemorrhage/ super-imposed bacterial pneumonia/ cannulation complications;

Maternal mortality at 56 days?.

Fetal:

Birthweight;
Apgar scores at delivery.

Event rates of:
Admission to the neonatal intensive care unit;
Stillbirth or miscarriage;
Neonatal death.
NICU admission and duration (measured in days).

Measures of effect

Maternal:

Odds ratio for dichotomous data and standardised mean difference as compared to non-pregnant women of reproductive age.

Fetal:

Odds ratio for dichotomous data and standardised mean difference as compared to healthy women in pregnancy and the puerperium (UKOSS/ national statistics/ background rates).

Data extraction (selection and coding)

Five reviewers will be involved in developing the search terms and applying the full literature search. Study selection will be performed by four reviewers (two pairs - one pair reviewing English language studies independently and one pair reviewing Spanish language studies independently) and disagreement will be resolved by consensus.

Studies will be uploaded to a study management software such as Covidence or EPPI-Reviewer for study screening, data extraction which will be performed independently by four reviewers. Data analysis will be performed in Revman or EPPI-Reviewer by each reviewer according to their pairings. Consensus will be reached by discussion.

Study investigators will be contacted for unreported data relevant to the study.

Study characteristics such as author, country, study design, sample number, study objective, patient demographics and clinical data will be reported.

Risk of bias (quality) assessment

The following will be applied:

The Joanna Briggs Institute (JBI) for case reports;

Newcastle-Ottawa Scale (NOS) for case series;

ROBINS-I tool will be used for case-control studies;

ROB-2 will be used for RCTs.

Strategy for data synthesis

Clinical outcomes of case reports and case series will be presented as proportions of the total sample number and presented as a narrative synthesis for case reports and a quantitative synthesis for case series using pooled proportions and the random effects methods as for cohort studies below.

Event rates from cohort studies will be presented quantitatively by determining maternal and clinical outcomes and determining outcomes according to gestation week or in weeks postpartum at commencement of ECMO as well as gestation in weeks at delivery.

Case-control study data and any RCTs will be presented quantitatively with dichotomous data presented as odds ratios using the random effects model and continuous data presented as standardised mean difference with the 95% confidence interval.

Analysis of subgroups or subsets

Analysis of clinical outcome will be performed for demographic variables for all participants: age, BMI, co-morbidities, ethnicity and illness severity as per SOFA or APACHE score.
?Subgroup analysis: VV Vs. VA?.

Contact details for further information

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Organisational affiliation of the review

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Review team members and their organisational affiliations [1 change]

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Type and method of review

Epidemiologic, Intervention, Living systematic review, Meta-analysis, Narrative synthesis, Prognostic, Systematic review

Anticipated or actual start date

10 February 2022

Anticipated completion date

31 January 2023

Funding sources/sponsors

None

Conflicts of interest

None known

Language
English, Spanish

Country
Colombia, England

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Adult; COVID-19; Critical Care; Critical Illness; Disease Management; Extracorporeal Membrane Oxygenation; Female; Fetal Viability; Fetus; Humans; Infant Health; Infant, Newborn; Maternal Health; Postpartum Period; Pregnancy; Pregnancy Outcome; Pregnant Women; Prevalence; Prognosis; SARS-CoV-2; Treatment Outcome

Date of registration in PROSPERO
04 January 2022

Date of first submission
04 January 2022

Stage of review at time of this submission
The review has not started

Stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Revision note
The protocol has been updated to correct an error made in the first submission in documenting the affiliation of Dr Claudia Hardy.

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.
The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions
04 January 2022
04 January 2022