COVID in Pregnancy: What have we learned?

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Maternal Fetal Medicine
Medical Director: Labor and Delivery & Antenatal Inpatient Care
Sinai Health System; Toronto CA
- Hyperlinks to 667 papers
- 87,687 cases of COVID in pregnancy reported
- 96 Systematic reviews
- Reviews of M&M reports from the CDC
- National & International COVID & Pregnancy data registries
- “Living” Systematic Review: PregCOV-19
- Regularly updated key evidence & relevant management
- BMJ publication – most recent March 2021
Globally, as of 7:19pm CEST, 21 April 2021, there have been **142,557,268 confirmed cases** of COVID-19, including **3,037,398 deaths**.
World wide status of COVID:

- > 17 different variants
- Gene mutations in the spike protein region
- Greater affinity for receptor / increased replication

VOC:
- ↑ Transmissibility
- ↑ Symptom Severity
- ↑ Resistance to therapies
- ↓ Neutralization by Ab from vaccination or prior infection

(Source: Johns Hopkins University CSSE COVID-19 Data)
Wave #3 COVID in Ontario:

Current state:
67% VOC
23% SARS-CoV-2

B.11.7 UK variant 90%
B.1351 South Africa 10%
P.1 Brazil

• Increased Transmission (# people sick)
• Increased Virulence (disease severity)
Incidence of COVID in Pregnancy in Canada

March 2020 – March 29, 2021

1.16% (0.67-1.59) Pregnant population COVID +

25.2% (9-42.6) Reproductive age population COVID +

- **Pregnancy NOT a risk factor** for acquiring COVID
- **Safety measures are effective** @ protecting pregnant patients

*** 1% of pregnant population (UK)
*** 10% Pregnant population admitted for any indication (US)
How does COVID present in the pregnant patient

- No difference by GA
- No different than NON pregnant population

Overlap with pregnancy s/s
* 70% dyspnea T3

MMWR Sept 2020
Khahil et al; EClinical Medicine (2020)
Figueiro et al, J Perinat Med (2020)
University of Birmingham LSR (Sept 2020)
Maternal effects of COVID

- **Respiratory Failure**
- **Septic Shock**
- **MSOF**
- **Pneumonia**
- **Increasing signs of respiratory distress**

* Asymptomatic (~20%)
* Minimal symptoms
* Upper respiratory infection

* Most common 85-90%

* Link to pre-existing medical diagnosis or RF:

**Risk Factors:**
- * Obesity with BMI >30
- Diabetes
- Hypertension
- Increasing maternal age

**BAME:**
- Black
- Asian
- Minority Ethnic group

* Majority late T2 and T3

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**93% Canadian Experience**

**MILD**
- Asymptomatic (~20%)
- Minimal symptoms
- Upper respiratory infection

**MODERATE**
- Pneumonia
- Increasing signs of respiratory distress

**SEVERE**
- Respiratory Failure
- Septic Shock
- MSOF

**CRITICAL**

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UKOSS 2021
BMJ LSR 2021
MMWR Sept 2020
Khahil et al; EClinical Medicine (2020)
Figueiro et al, J Perinat Med (2020)
University of Birmingham LSR (Sept 2020)
Increased risk of hospitalization: 92.9% NOT HOSPITALIZED

Increased risk of ICU admission: respiratory / immune changes of pregnancy lower threshold for admission

Pregnancy exacerbates any illness

<table>
<thead>
<tr>
<th>Confirmed hospitalized for COVID indication</th>
<th>Reproductive Age Peer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnant COVID-19 positive females in BC, AB, ON(^1), and QC(^2) per 1,000 (n=1270)/%</strong></td>
<td><strong>Non-pregnant COVID-19 positive females in BC, AB, and ON per 1,000 (n=48,593)/%(^3)(^4)</strong></td>
</tr>
<tr>
<td>Number total</td>
<td>Per 1000</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>90</td>
</tr>
<tr>
<td>Admitted to ICU</td>
<td>15</td>
</tr>
</tbody>
</table>

CANCOVID-Preg
https://ridprogram.med.ubc.ca/cancovid-preg
Feb 25, 2021
Compared with NON pregnant peers:

Higher rates of:

- 5 x Hospitalization
- 2 x ICU admission
- 2 x Mechanical ventilation
- ECMO

CDC 2021
1. Most pregnant women have **mild disease**, make **full recovery** with no residual impact.

2. Overall **maternal morbidity risk “low”**
   - ICU admission 1-7%
   - Mechanical ventilation 1-4%
   - Maternal death 1%

3. **Increased rates** of hospitalization, ICU admission & mechanical ventilation compared with peers.

   Associated with pre-existing:
   - medical co-morbidity
   - BAME
   - T3

**COVID-19 during pregnancy: an overview of maternal characteristics, clinical symptoms, maternal and neonatal outcomes of 10,996 cases described in 15 countries**

**SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes**

Asma Khalil, Erkan Kalafat, Can Benlioglu, Pat O'Brien, Edward Morris, Tim Draycott, Shakila Thangaratinam, Kirsty Le Doare, Paul Heath, Shamez Ladhani, Peter von Dadelszen, Laura A. Magee
Incidence of COVID in pregnancy in Canada: now as of April 19, 2021

Increased by 400 cases in 19 days

- Reporting bias (delay)
- Added cases from BC (Wave #3)
- Reflects uptick in cases

? Is this Wave #3 different for pregnant individuals

? What is the impact of VOC on the risk of infection in pregnancy

? What is the impact of VOC on maternal disease

? What is the impact of VOC on pregnancy outcome
**Impact of VOC on Infection in Pregnancy: UK Experience**

<table>
<thead>
<tr>
<th>Oxygen saturation measured on admission</th>
<th>Symptomatic pregnant women (n=2,642) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen saturation &lt;95%</td>
<td>190 (13.5)</td>
</tr>
<tr>
<td>Oxygen saturation ≥95%</td>
<td>1,223 (86.5)</td>
</tr>
<tr>
<td>Missing</td>
<td>979</td>
</tr>
</tbody>
</table>

| Evidence of pneumonia on imaging       | 612 (23.2)                                 |
| Required respiratory support           | 475 (18.0)                                 |
| Non-invasive oxygen (nasal canulae, mask or non-rebreath mask) | 339 (12.8)                                 |
| CPAP                                   | 44 (1.7)                                   |
| Invasive ventilation or ECMO           | 71 (2.7)                                   |
| Required support but level not known   | 21 (0.8)                                   |
| Critical care received                 | 250 (9.5)                                  |
| Maternal death                         | 15 (0.6)                                   |

Admitted for COVID
Admitted for OB indication

Majority did not have respiratory compromise

BUT ..........
Impact of VOC on Infection in Pregnancy: UK Experience

Compared with Wave #1:

<table>
<thead>
<tr>
<th>Adjusted</th>
<th>Decreased Risk</th>
<th>Increased Risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic**</td>
<td></td>
<td></td>
<td>1.20 (1.08, 1.37)</td>
</tr>
<tr>
<td>Critical care received</td>
<td>1.62 (1.22, 2.16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence of pneumonia on imaging (Yes)</td>
<td>1.58 (1.30, 1.92)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Required respiratory support</td>
<td>2.58 (2.07, 3.22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen saturation &lt;95%</td>
<td>1.42 (1.01, 2.02)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

More symptomatic patients
More moderate to disease

Increased rate of critical illness
Incidence of COVID in pregnancy in Canada: now as of April 19, 2021

? Is this Wave #3 different for pregnant individuals
   YES

? What is the impact of VOC on the risk of infection in pregnancy
   Suspect increased # of COVID infections

? What is the impact of VOC on maternal disease
   Suspect increased symptomatic profile
   Suspect increased proportion of moderate-severe illness

? What is the impact of VOC on pregnancy outcome
Obstetrical impact of COVID in pregnancy

- No reports of increase in rate of **common OB complications**: PET, BP, GDM, APH ..... 

- **Increased C/S rate**
  - associated with: increasing severity of Dx leading to maternal/fetal compromise OB indications

- **Increased rate of Low Birth Weight**

**Systematic review with meta-analysis**: International data

10 000 Pregnant patients (COVID + and COVID -)

Compared with COVID – pregnant patients:  
3 x rate of C/S  
9 x rate of LBW  
* 54% rate of PPH

UKOSS (2021)  
Jafari et al (2020)  
Can COVID Feb 2021  
Khahil et al; Eclinical Medicine (2020)  
Figueiro et al, J Perinat Med (2020)  
RCOG Guideline (Oct 2020)
### Infant outcomes from March 1, 2020 until December 31, 2020 in BC, AB, ON, and QC

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Denominator</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Apgar (5 minutes)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7</td>
<td>11</td>
<td>471</td>
<td>2.3</td>
</tr>
<tr>
<td>≥7</td>
<td>460</td>
<td>471</td>
<td>97.7</td>
</tr>
<tr>
<td><strong>Birth weight (g)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (&lt;2500 g)</td>
<td>59</td>
<td>560</td>
<td>10.5</td>
</tr>
<tr>
<td>Normal (2500-4000 g)</td>
<td>460</td>
<td>560</td>
<td>82.1</td>
</tr>
</tbody>
</table>

Increased from 6% in general pregnant population in Canada
Obstetrical impact of COVID in pregnancy

- Increased rate of Preterm Birth: International rate ~17-20%
  - Canada 12% increase from 7.8%

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Symptomatic women (n=2,642)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
</tr>
<tr>
<td>Birth</td>
<td>1926 (72.4)</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>663 (25.1)</td>
</tr>
<tr>
<td>Pregnancy loss</td>
<td>53 (2.1)</td>
</tr>
<tr>
<td>Gestation at end of pregnancy (weeks)</td>
<td></td>
</tr>
<tr>
<td>&lt;22</td>
<td>43 (2.2)</td>
</tr>
<tr>
<td>22-36</td>
<td>419 (21.2)</td>
</tr>
<tr>
<td>37 or more</td>
<td>1501 (79.5)</td>
</tr>
<tr>
<td>Missing</td>
<td>16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infant outcomes</th>
<th>Infants of symptomatic mothers (n=1963)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>24 (1.2)</td>
</tr>
<tr>
<td>Live birth</td>
<td>1939 (98.8)</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>4 (0.5)</td>
</tr>
<tr>
<td>Neonatal unit admission</td>
<td>405 (20.9)</td>
</tr>
<tr>
<td>Positive SARS-CoV-2 test &lt;12 hrs of age</td>
<td>15 (0.8)</td>
</tr>
</tbody>
</table>

UKOSS (2021)
Jafari et al (2020)
Can COVID Feb 2021
Khahil et al; EClinical Medicine (2020)
Figueiro et al, J Perinat Med (2020)
RCOG Guideline (Oct 2020)

20% PTB Rate
BUT ....

Only:
20% NICU admission
0.5% Neonatal death

Majority of PTB occurring in T3- mean GA 34-35w: low risk of neonatal morbidity
<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Symptomatic women (n=2,642) N (%)</th>
<th>Symptomatic women admitted Mar-Nov 20 (n=1,437) N (%)</th>
<th>Asymptomatic women (n=2,837) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>1926 (72.4)</td>
<td>1260 (87.5)</td>
<td>2531 (91.4)</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>663 (25.1)</td>
<td>148 (10.3)</td>
<td>239 (8.4)</td>
</tr>
<tr>
<td>Pregnancy loss</td>
<td>53 (2.1)</td>
<td>29 (2.0)</td>
<td>67 (2.4)</td>
</tr>
<tr>
<td>Gestation at end of pregnancy (weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;22</td>
<td>43 (2.2)</td>
<td>25 (1.9)</td>
<td>46 (1.8)</td>
</tr>
<tr>
<td>22-36</td>
<td>419 (21.2)</td>
<td>237 (18.4)</td>
<td>262 (10.1)</td>
</tr>
<tr>
<td>37 or more</td>
<td>1501 (76.5)</td>
<td>1,018 (79.5)</td>
<td>2262 (88.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>16</td>
<td>9</td>
<td>28</td>
</tr>
</tbody>
</table>

Preterm birth rate did not change in wave #2

Preterm birth associated with severity of disease

UKOSS (2021)
Jafari et al (2020)
Can COVID Feb 2021
Khahil et al; EClinical Medicine (2020)
Figueiro et al, J Perinat Med (2020)
RCOG Guideline (Oct 2020)
Preterm birth most commonly associated with COVID infection in T3

In summary:

• Modest increase in rate of PTB - iatrogenic & spontaneous
• Linked to more moderate to severe disease
• Mean GA 34-35w: low risk for neonatal morbidity
• Most common with infection in T#3
Fetal effect of COVID in pregnancy

• Reports of infection across all GA
  - > 50% after 20w GA

• No cases:
  a. teratogenicity
  b. disruption of organ development &/or function

• No increased risk of fetal wellbeing, fetal demise (0.6-0.9%)

POTENTIAL IMPACT

Maternal respiratory illness
Maternal infection
Maternal critical illness
Direct viral effect

Hypoxemia
Inflammation
MSOF

ACE-2 found at human maternal-fetal interface & fetal organs

Khahil et al; EClinical Medicine (2020)
Figueiro et al, J Perinat Med (2020)
Placenta pathology associated with COVID in pregnancy

- No evidence of virus in AF, vaginal secretions
- No virus in neonatal blood
- IgM detected in neonatal blood

Placenta abnormalities described:
- fetal vascular malperfusion (thrombi in fetal vessels)
- maternal vascular malperfusion (failed spiral artery remodel)
- multifocal infarctions
- diffuse perivillous fibrin (residual scar after infarct)

? Due to co-morbidity/ primary dev’t
? Due to maternal hypoxic effect
? Due to direct viral effect

- Typically associated with FGR, PET, IUFD,PTB

Rationale for fetal surveillance after COVID recovery
BPP / EFW Q2-4w > 24w GA

* Limited case series
Neonatal effect of COVID in pregnancy

- 91% babies test negative (COVID + mom)
- ~9% babies tested positive

176 cases of Neonatal COVID +

- 55% babies: mild symptoms
- Similar symptom profile
- 38% admitted to NICU
  - COVID, prematurity
  - mean LOS 8 days

Late onset COVID:
1. “Rooming in” for 72h after birth
2. Breast feeding NOT a risk

Rashetti et al, Nature (2020)
RCOG Guideline (Oct 2020)
University of Birmingham LSR (Sept 2020)
**Vitals:** HR >100, RR >20, temp >38°C, O₂ sat <94% on RA

Venous blood gas

CXR

Lytes & CR: ? signs of dehydration

Lactate: >2 measure of “sepsis”

**Remember:**
Physiological changes of pregnancy can mask / compensate for maternal deterioration

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**Imaging:**

(a) Normal

(b) Bacterial Pneumonia

(c) Viral Pneumonia

(d) COVID-19 Pneumonia

Thick patchy consolidation

Ground Glass appearance

Bilateral
Pneumonia in pregnancy

- Edematous airway
- Less lung volume
- Increased secretions
- Increased minute ventilation
- Increased O₂ consumption

** Remember to interpret ABG in context of pregnancy

<table>
<thead>
<tr>
<th>Arterial blood gas measurement</th>
<th>1st trimester</th>
<th>3rd trimester</th>
<th>Nonpregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.42–7.46</td>
<td>7.43</td>
<td>7.4</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>105–106</td>
<td>101–106</td>
<td>93</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>28–29</td>
<td>26–30</td>
<td>37</td>
</tr>
<tr>
<td>Serum HCO₃ (mEq/L)</td>
<td>18</td>
<td>17</td>
<td>23</td>
</tr>
</tbody>
</table>

** RESPIRATORY CHANGES OF PREGNANCY
Predispose to ILLNESS & RAPID DETERIORATION

- Allows for O₂ shift to HbF
- Allows for CO₂ gradient from fetus to mom
Mild Disease: Upper airway disease

DOES NOT require hospitalization
- remind to self-isolation at home, O2 sat monitor
- supportive therapy: acetaminophen, cough suppression, hydration
- education: warning signs (risk of deterioration d5-10)
- education KICK COUNTs
- education: s/s PTL
- F/U phone call from PH

Regardless of GA

Moderate to Severe Disease

Indications for hospitalization:
- Shortness of breath (unable to walk across room, speak full sentence)
- Cough with blood
- Chest pain
- S/S dehydration (lytes, CR)
- Decreased level of consciousness
- Oxygen saturation < 94%
- CXR consistent with pneumonia

Illness assessment
AND
Consideration of co-morbidity
@ risk of moderate/severe disease
COVID in Pneumonia in Pregnancy

Admission Investigations: predict the course, risk of deterioration

- Prognostic bloodwork: CBC, CRP & ferritin, LDH, LFTs, PT /PTT, fibrinogen, d-dimer (not to be used to detect risk of VTE as in non-pregnant population)
- ECG, BNP, troponin... if any concern for cardiac involvement OR pre-existing cardiac disease
- 2D ECHO (maternal) if ICU admission/underlying cardiac condition
- Urine PCR, uric acid – if any concern for PET
- CT scan only if clinically indicated (rule out pulmonary embolism)

R/O Pre-eclampsia: “Mimic” or Co-morbidity

Transaminitis
↑ LDH
Thrombocytopenia
↑ CR

Overlapping symptoms

Use: PCR, Urate, BP
COVID Pneumonia management in pregnancy

**Primary principles:**

A. symptom relief supportive care
   - anti-pyrexia
   - hydration
   - analgesia

B. Rx superimposed / co-incident infections

**Fluid management:**

Encourage PO fluid; TKVO- Avoid maintenance fluid

**If critical illness (ICU management consideration)**

Conservative strategy associated with decreased duration of mechanical vent “wet lung”

Aim: negative daily balance 0.5-1.0L

If positive balance & respiratory symptoms: consider furosemide Rx

**Antibiotics:**

** Community acquired pneumonia (CAP):** Ceftriaxone + Azithromycin  (solid consolidation on CXR)

? Aspiration pneumonia: Meropenum

Ventilator acquired pneumonia (VAP): based on aspirate

** Co-existent UTI
Oxygen Therapy

PRINCIPLES

- Maternal PaO2 drives fetal PaO2 (~30 mmHg), influenced by placenta volume
- Impact of maternal PaO2 & O2 sat: varies with umbilical O2 sat, pH & PO2
- PaCO2 gradient from fetus to mom to allow diffusion
- Target maternal >94% (no evidence)

ACTION

- O2 sat < 94% (or tachypnea > 20 RR): O2 by NP at 1-6 L/min.
- O2 sat < 94% with NP at 6 L/min:
  - Simple facemask @ 6-10 L/min OR Venturi face mask @ FiO2 40%-60%
- If oxygen goals are not met by facemask
  - Non-rebreather (TAVISH) facemask (at 10-15L/min)
  - High flow nasal cannula (OptiFlow)

Awake, Non-Intubated Prone positioning:

- RCT only
- Not STD of care
Maternal Surveillance

Maternal Surveillance & Warning signs: Respiratory vitals RR, O2 sat, WOB

- **Vitals q4h**: if requiring increasing oxygen support increase vitals to q 1-2 with 1:2 RN care

If require:

- New use of oxygen support
- RR increases despite O2 sat >94%
- Increasing amount of oxygen to maintain O2 sat>94%

**WARNING SIGN OF RESPIRATORY DETERIORATION**
- Consult ICU
- Pattern of rapid deterioration ass’t with COVID

Warning signs of acute maternal deterioration / respiratory failure

- Increased O2 demands by 50% over 1-2h
- O2 sat < 94% despite O2 support
- > 4L/min O2 by facemask

**TRANSFER TO ICU**

MEOWS data:
- Change in maternal vitals ~4h before deterioration

No evidence from RCT
Expert opinion
**Mechanical Ventilation**

**Critical care decision**

**Key Points to NB:**

- Keep maternal PaO₂ > fetal PaO₂ but **can run hypoxic**
- Balance fetus against maternal cardiac output
- Hyper-oxygen: increased peripheral vascular resistance impact O₂ delivery (uterus)
- Target O₂ sat >90%

- Lowering PaCO₂: uterine vasoconstriction
- Elevated PaCO₂: affects O₂ dissociation & fetal PaO₂ changes fetal HR, MCA psv

**ARDS Management Principles:** **

**Analgesia:** Opioid

**Sedation:** Benzodiazepine- Midazolam *
- Propofol (Risk of elevated TG)*
- Ketamine (Risk UC)

**Paralysis:** Rocuronium *

* Safe if BF
** Impact on fetal monitoring

**Surveillance:** P/F Ratio

PaO₂ from the ABG

Fraction of inspired oxygen (FiO₂)

Target> 150
Prone Positioning

A. Supine Position
   Normal Lung

B. Supine Position
   ARDS Lung

C. Prone Position
   Normal Lung

D. Prone Position
   ARDS Lung

Gravity

https://www.youtube.com/watch?v=SOgwakxeyXE
Indications for VV-ECMO

Hypoxic respiratory failure despite optimal ventilation strategies

- PF ratio < 150
- pH < 7.15

** management in pregnancy
Steroids and COVID Pneumonia

**Rationale:** Steroids decrease mechanical vent days & mortality with ARDS (except influenza)

**RECOVERY Trial:** Randomized Evaluation of steroids for COVID-19 pneumonia Trial
Included pregnant and BF patients (n=6)
Rx dexamethasone 6mg PO x 10d

**Reduced rate of 28d mortality for patients:**
Mechanical ventilation RR 0.64
Supplemental O₂ RR 0.84

No impact if NOT requiring O₂ support

*not for mild disease* at home or hospital
Steroids & COVID Pneumonia: Dosing

Pre-viable gestational age (< 22w or >34w): Methyprednisolone* 32 mg IV OD x 10d or discharge from hospital

Perivable gestational age (22-25w): if considering neonatal resuscitation & risk of preterm birth

- Dexamethasone 6mg IM BID x 48 h
- Methyprednisolone 32 mg IV OD to complete 10 days or DC from hospital

Viable gestational age (25-34w GA): Dexamethasone 6mg IM BID x48 h
- Methyprednisolone 32 mg IV OD to complete 10 days or DC from hospital

Late ANC 34-36w GA: as above

Postpartum partum: Dexamethasone** 6mg IV OD x10 d or DC from hospital

* Prolonged/high dose steroid associated with fetal growth/end organ maturation
** No info on breastfeeding, methylprednisolone is safe
Remdesvir and Tocilizumab: benefit in non-pregnant population

**Remdesvir:**
- Viral RNA polymerase inhibitor
- Goal: reduce viral replication
  - *Used with Ebola in pregnancy - no impact*
  - *Breastfeeding: no information BUT poor GI absorption...*
- **Indication:** moderate Dx requiring O2 BUT not mech vent/ECMO
- **Dose:** IV 200mg x1 and then 4d of 100mg

**Tocilizumab:**
- IL-6 receptor blocker
- IL-6 driver of COVID inflammation; increased levels ass’t with critical COVID, death
- **Goal:** reduce systemic inflammation
  - *Used with rheumatic Dx in pregnancy: no birth defects, SA*
  - *Minimal detection in breastmilk*
- **Indication:** CRP >75
  - High flow nasal cannula/ventilation
- **Dose:** single IV dose of tocilizumab 8 mg/kg
# Thromboprophylaxis & COVID

**Rationale:** increased rate of VTE complications with ALL **severe-critical COVID illness** (16%)

**Mechanism**

- **Pulmonary microvascular thrombosis**
  
  * extravascular fibrin (lung) + hypoxia + inflammation = CLOT

- **Hospital based VTE**
  
  * immobility + prothrombotic state + endothelial activation + CLOT

## Antepartum at home

Continue AC if previous prescribed  
Encourage hydration, mobilize

**AC Recommended:**  
Prophylactic dose LMWH  
Weight based

## Admitted 2º COVID

AC recommended

## Admitted 2º OB reason

AC based on OB condition  
? Stockings

**New RCT:** full dose AC for moderate Dx  
? Improved outcome

## Postpartum

**Moderate-severe COVID:** AC recommended  
OB indications: AC recommended  
Mild COVID: AC not recommended
Other considerations:

Hemodynamic status:
- supine with wedge
- maintain BP > 90 systolic
- vasopressor: not contraindicated in pregnancy / BF
- “mimic” PET: use urine PCR, urate and BP to distinguish
- need 2D ECHO: critical illness link to cardiomyopathy

Glycemic control:
- If DM: monitor for DKA, monitor impact of steroid
- Improve critical care outcome if BS 7-10
- If prolonged illness: lower target based on fetal risk ** documented in DM

Medical Imaging:

<table>
<thead>
<tr>
<th>Medical Imaging</th>
<th>Dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low Dose (&lt;0.1mGy)</td>
<td></td>
</tr>
<tr>
<td>Chest X ray</td>
<td>0.0005-0.01</td>
</tr>
<tr>
<td>Head/Neck CT</td>
<td>0.001-0.01</td>
</tr>
<tr>
<td>Low-Moderate Dose (0.1-10 mGy)</td>
<td></td>
</tr>
<tr>
<td>Abdominal X Ray</td>
<td>0.1-3</td>
</tr>
<tr>
<td>CT Chest/CT pulmonary angiography</td>
<td>0.01-0.66</td>
</tr>
<tr>
<td>Nuclear Medicine (Low Dose Perfusion Only)</td>
<td>0.02-0.6</td>
</tr>
<tr>
<td>Nuclear Medicine Ventilation Scan</td>
<td>0.1-0.3</td>
</tr>
<tr>
<td>High Dose 10-50mGy</td>
<td></td>
</tr>
<tr>
<td>Abdominal/pelvic CT</td>
<td>1.3-35</td>
</tr>
</tbody>
</table>

Generally accept up to 50mGy in pregnancy
When to deliver COVID+ with critical illness

- COVID-19 infection is **NOT** a direct indication for delivery
- Decision to deliver is *individualized* based on maternal & fetal status, GA

**General principle of critical care in pregnancy:**
- Delivery will not improve maternal status
- Delivery MAY trigger deterioration

**Considerations: Why to deliver .....ESP in T3**
- Increased O₂ consumption
- Decreased functional residual capacity
- Risk of rapid decompensation
- Difficult airway

**Suggested indications for delivery with critical COVID:**
- Intrauterine infection
- DIC
- Hepatic or renal failure
- Compromised CV function due to gravid uterus
- Compartment syndrome
- Cardiac arrest
- Fetal demise
- GA of low morbidity / mortality .... > 34w

No evidence from RCT
Expert opinion
? Would delivery improve maternal status
  • decrease O2 consumption
  • increase lung volume

? Would delivery compromise maternal status
  • increased central volume: pulmonary edema
  • pulmonary hypertension: volume will trigger RV failure

? Would delivery improve fetal status
  • maternal hypoxemia /hypercapnia affects uterine blood flow/fetal oxygenation
  • risk of HIE in utero versus the risks of prematurity

General principle: Mechanical ventilation not indication for delivery if can maintain maternal oxygenation
  * consideration for GA (>34w), complexity of the delivery
  * may be indicated by OB indication: PPROM, PTL, APH, IUGR

If >36w: consider delivery as a tool to improve maternal status
may not improve based on natural Hx of the disease
? When to deliver with hypoxic respiratory failure

ECMO itself is NOT an indication for delivery

? Will delivery improve maternal status
? Will delivery improve fetal status (GA)
? Institutional considerations (location of ECMO)
When to deliver with hypoxic respiratory failure

** Each institution & OB/Critical Care Team needs to set own criteria ......

*Suggested algorithm (but should be discussed on a case by case basis)*

< 28w gestation: do NOT deliver prior to ECMO
low likelihood of fetus impairment / significant risk of prematurity

>32w gestation: consider delivery prior to ECMO
low likelihood of risk associated with prematurity * cannulate after C/S in event of deterioration

28-32w gestation: individualized discussion
pediatrics, obstetrics & intensivist
balance patient wishes, fetal status, maternal status/tolerance for delivery

45 cases in literature: (2018)
77.8% maternal survival
65% fetal survival

THEN:
9 cases with COVID: same
Fetal Surveillance in ICU

**What is the minimum surveillance requirement**
- Daily FHR confirmation

**What additional surveillance is indicated**
*Consider:* GA, maternal status, feasibility (location, maternal position)

- NST
- BPP
- Fetal Doppler study: UA, MCA, DV

**What abnormality will you act on?**

- NST: After viability & interpretable (> 25w)
  - Persistent tachycardia not explained by maternal status
  - Recurrent deep deceleration > 1h

- BPP: After viability (>25w)
  - Weekly
  - Anticipate decreased AFV, poor FT/FM/FBM due to sedation, narcotic
  - Substitute UA Doppler +/- DV
  - Deliver if abnormal DV .... If maternal status permits

- EFW: Baseline at admission for comparison after recovery

**<25w:** Daily FH
**>25w:** Daily NST
**>25w:** Weekly BPP/ UA Doppler
  Biweekly EFW

**No continuous monitoring**
Neonatal resuscitation in ICU

- In the event of a spontaneous delivery......
- In the event of perimortem C/S (*at the direction of the ICU team- may not be of benefit; consider GA)

? What will be the neonatal resuscitation plan
? What equipment is required at bedside in ICU

<22w GA: comfort care
>25w GA: full active case based on Canadian Pediatric Society Guideline
23-25w GA: previously expressed wishes / SDM request
ethical consideration if no direction: risks of prematurity

If viable: Vaginal delivery tray
C/S delivery tray (scalpel on top)
Neonatal resuscitation isolate/Code pink kit

** Education for ICU RN for s/s labor, ROM, calling an OB emergency /Code Pink
Criteria for transfer to Level III ICU for critically ill COVID + pregnant individual (ICU to ICU)

Based on risk for PTB

** Need for ICU services, access to ECLS

Maternal medical indication: as per current guidelines for ICU

** Regardless of GA

Maternal obstetrical indication:

- Gestational age >24 but < 32w GA: need level III care
- ** Gestational age: 22, 23w GA if a family/pre-expressed wish for neonatal resuscitation if spontaneous delivery
- Fetal condition requiring delivery at level III regardless of GA (> 25w)
- Maternal co-morbidity requiring delivery at level III regardless of GA (>25w)

Criteria for transfer to Level III for moderately ill* COVID + pregnant individual (OB to OB)

- Defined as: need O2, OB co-morbidity, Medical co-morbidity, + prognostic indicators (include CXR)...

** Based on risk for PTB
** As listed above
Intrapartum Management of Any COVID + /PUI patients

• Recommend hospital birth if unwell

• CEFM for OB indications only
  - no evidence that asymptomatic /mild disease associated with abnormal FHR

• Hourly assessment of maternal status
  - Fluid status: strict euvoelemia
  - Maintain O2 sat > 94%

• No contraindication for FSE, fetal scalp sample * virus not detect in AFV or blood

• Management of second stage: pushing not AGMP, but increased secretions/spray
discourage active pushing
consideration for assist VD (symptomatic, prevent prolong SS)

• Hand hygiene/Mask mom for baby contact & BF
Fever in Labor: Becoming a COVID PUI

- Temperature >37.8°C
- Give 500 cc fluid bolus (takes 30 min). **DO NOT GIVE ACETOMINOPHEN DURING THIS TIME**
- Repeat temperature 30 min after bolus completed
- If still >37.8 (or any other symptoms) .... COVID NP SWAB and CONTACT/DROPLET PRECAUTIONS

- IF > 38°C ... initiate chorioamnionitis workup and treatment ... Blood cultures, Acetaminophen, Broad spectrum ABX

- After birth- Neonate also a PUI until mom test result is available

Post COVID infection

- Serial BPP & EFW for fetal growth
- Educated re: s/s PTB
- No special precautions for intrapartum management
Help patients to understand how to protect themselves & family

- Limit visitation to household members/ bubble
- Limit outside exposures to absolutely necessary
- Self monitor: screen for symptoms daily
- Get tested if you have symptoms
- Inform your OB care provider
- Extra caution if any RISK FACTORS
- Extra caution in T3 and weeks before due date

SOCG
RCOG, ACOG
WHO
United Nations
Vitamin D Supplement and COVID

Rationale:

• Daily Vitamin D supplement shown to decrease risk of acute respiratory infections (any) - effect greatest in those who are vitamin D deficient

• Vitamin D deficiency is common - especially in reproductive age women - @ risk: dark skin, limited sun exposure (seasonal, lockdown)

• Correlation between vitamin D deficiency & the rate of COVID infection & COVID death

** no RCT proof that Vitamin D supplement decreases/prevents COVID
** Vitamin D driver of immune modulation

Recommendation: Vitamin D supplement in pregnancy
Dose: 2000 IU daily

Martineau et al; (2015)
Zemb et al, (2020)
RCOG Guideline (Oct 2020)
University of Birmingham LSR (Sept 2020)
mRNA Vaccine: Moderna, Pfizer

All COVID vaccines:
- Do not contain mercury, aluminum or formaldehyde
- PEG safe in pregnancy
- Only contraindication: allergy

Increased interval of dosing
- Greatest effect from first dose
- 2nd dose is modest effect
- Immunity effect from “herd”

Protect against getting COVID & the severity of COVID if infected
Risk of VIIT: Vaccine Induced Thrombocytopenia
1/250,000 - 1/1,000,000

- hyper-autoimmune response
- pregnancy not a risk factor for VIIT
- hypercoagulable state of pregnancy not associated
- pregnancy VTE risk > VIIT risk

- Counsel that benefit of vaccine > risk of VIIT
- Rx for VIIT: IVIG, alternatives to heparin Rx

- not tested in pregnancy / BF
- enroll in the registry https://c-viper.pregistry.com
- no complication / VIIT reported to date

Adenovirus Vaccine: AstraZeneca / Oxford Vaccine / J&J Vaccine

- Spike protein gene enveloped in a harmless virus
- 64-66% effective
- significant impact on risk of severe disease

This is injected into the patient

The vaccine enters cells, which then start to produce the coronavirus spike protein

This prompts the immune system to produce antibodies and activate killer T-cells to destroy infected cells

not tested in pregnancy / BF
enroll in the registry https://c-viper.pregistry.com
no complication / VIIT reported to date
Vaccine Guidance for Pregnant & Breastfeeding Individuals

** Pregnant & Breastfeeding individuals excluded from all vaccine trials
** Not tested DOES NOT mean not safe
** NO biologic rationale to suggest not safe
** NO systemic circulation of the vaccine
** Other vaccines are given in pregnancy: tDAP, FLU
** Goal to protect MOM but may have fetal and neonatal benefit

“Any pregnant / breastfeeding person may receive the vaccine should they choose after informed counselling”
• review of the benefits and risks of the vaccine
• review of the risk of acquiring COVID infection in pregnancy
• review of the risks / consequences of a COVID infection in pregnancy
• acknowledgment of the insufficiency of evidence for the use of COVID-19 vaccine in pregnant / breast feeding population
N= 35,691 pregnant individuals

No difference in side effects

** Fever <1%

No difference in rate of adverse RX
# CDC vSafe Registry

## Timing of first eligible dose

<table>
<thead>
<tr>
<th>Timing of First Eligible Dose</th>
<th>Pfizer</th>
<th>Moderna</th>
<th># / %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periconception: within 30 days before last menstrual period</td>
<td>55 (2.6)</td>
<td>37 (2.0)</td>
<td>92 (2.3)</td>
</tr>
<tr>
<td>First trimester: &lt;14 wk</td>
<td>615 (28.8)</td>
<td>517 (28.4)</td>
<td>1132 (28.6)</td>
</tr>
<tr>
<td>Second trimester: ≥14 and &lt;28 wk</td>
<td>932 (43.6)</td>
<td>782 (42.9)</td>
<td>1714 (43.3)</td>
</tr>
<tr>
<td>Third trimester: ≥28 wk</td>
<td>533 (25.0)</td>
<td>486 (26.7)</td>
<td>1019 (25.7)</td>
</tr>
<tr>
<td>Missing data</td>
<td>1 (&lt;0.1)</td>
<td>0</td>
<td>1 (&lt;0.1)</td>
</tr>
</tbody>
</table>

## Participant-Reported Outcome

<table>
<thead>
<tr>
<th>Participant-Reported Outcome</th>
<th>Published Incidence*</th>
<th>V-safe Pregnancy Registry†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>no./total no. (%)</td>
</tr>
<tr>
<td>Pregnancy loss among participants with a completed pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous abortion: &lt;20 wk†‡</td>
<td>10–26</td>
<td>104/827 (12.6)‡</td>
</tr>
<tr>
<td>Stillbirth: ≥20 wk†§</td>
<td>&lt;1</td>
<td>1/725 (0.1)§</td>
</tr>
<tr>
<td>Neonatal outcome among live-born infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm birth: &lt;37 wk§</td>
<td>8–15</td>
<td>60/636 (9.4)†</td>
</tr>
<tr>
<td>Small size for gestational age§</td>
<td>3.5</td>
<td>23/724 (3.2)</td>
</tr>
<tr>
<td>Congenital anomalies§</td>
<td>3</td>
<td>16/724 (2.2)</td>
</tr>
<tr>
<td>Neonatal death§†</td>
<td>&lt;1</td>
<td>0/724</td>
</tr>
</tbody>
</table>

**n= 827 completed pregnancies**
Timing of vaccination

<table>
<thead>
<tr>
<th>Gestational age at diagnosis (weeks)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;14</td>
<td>125</td>
</tr>
<tr>
<td>14-27</td>
<td>273</td>
</tr>
<tr>
<td>28-37</td>
<td>218</td>
</tr>
<tr>
<td>38-42</td>
<td>79</td>
</tr>
</tbody>
</table>

 Majority of COVID Dx in T2/T3

** Want immunity before increasing risk of infection

** 80-85% immunity >14d

Suggest optimal time ..... ANY TIME

“**The SOGC supports the use of all COVID-19 vaccines approved in Canada in any trimester of pregnancy and during breastfeeding in accordance with regional eligibility. “**
Vaccine antibodies in cord blood .... potential fetal /neonatal benefit

- 27 participants
- mRNA vaccination in T3

1:1 ratio of Cord and Maternal Ab concentration

Cord Ab concentration increased with time after vaccination
Vaccine antibodies in breastmilk .... potential neonatal benefit

- 87 breast feeding participants
- 2 doses of Pfizer vaccine while BF
- No adverse reactions, similar side effect profile
• Snap shot of the Canadian COVID experience to date
• Profile of the third wave: what we can expect based on experience from the UK
• COVID maternal disease spectrum
• COVID pregnancy outcomes
• COVID assessment & determine disposition
• COVID prognostic indicators / distinguish from PET
• COVID pneumonia & pharmacotherapies: steroid, remdesvir, tocilizumab, enoxaparin, ABX
• Management of oxygen therapy
• Maternal warning signs: when to call ICU
• ICU considerations:
  - hemodynamic parameters, glycemic control, medical imaging
  - ECMO & gestational age considerations
• Timing of delivery, fetal surveillance, neonatal resuscitation
• COVID recovered: fetal surveillance
• COVID vaccination
COVID in Pregnancy: What have we learned?

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Medical Director: Labor and Delivery & Antenatal Inpatient Care
Sinai Health System; Toronto CA