Treatment Considerations for COVID-19 in Pregnancy

SMFM Webinar
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Disclosures

I have nothing to disclose
Learning Objectives

Upon completion of this webinar, the participant will be able to:

- Describe the WHO levels of disease severity for COVID-19 infections
- Apply obstetric management considerations to common clinical scenarios based on level of disease severity
Outline

- Define levels of COVID-19 severity
- What we know about outpatient management
- Outpatient areas of inquiry
- What we know about inpatient management
- Inpatient areas of inquiry
Defining COVID-19 severity

- Asymptomatic/pre-symptomatic
- Mild illness
- Moderate illness
- Severe illness
- Critical illness
A framework for patient management – by severity

- **Asymptomatic/pre-symptomatic**

- **Mild illness:** COVID mild enough to be managed at home

- **Moderate illness:** COVID evidence of lower respiratory disease by clinical assessment or imaging with SpO2 >93% on room air at sea level
A framework for patient management – by severity

- **Severe illness:** COVID with ≥1 of:
  - SpO2 ≤ 93% on room air at sea level
  - Respiratory rate > 30
  - Ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) < 300
  - Lung infiltrates > 50%

- **Critical illness:** respiratory failure, septic shock, multi-organ dysfunction
Step 1 – Triage disease severity

Assess Patient’s Symptoms
Symptoms typically include fever ≥38°C (100.4°F) or one or more of the following:
• Cough
• Difficulty breathing or shortness of breath
• Gastrointestinal symptoms

No → Routine Prenatal Care

Yes → Conduct Illness Severity Assessment

• Does she have difficulty breathing or shortness of breath?
• Does she have difficulty completing a sentence without gasping for air or needing to stop to catch breath frequently when walking across the room?
• Does patient cough more than 1 teaspoon of blood?
• Does she have new pain or pressure in the chest other than pain with coughing?
• Is she unable to keep liquids down?
• Does she show signs of dehydration such as dizziness when standing?
• Is she less responsive than normal or does she become confused when talking to her?

No Positive Answers → Assess Clinical and Social Risks

• Comorbidities (Hypertension, diabetes, asthma, HIV, chronic heart disease, chronic liver disease, chronic lung disease, chronic kidney disease, blood dyscrasia, and people on immunosuppressive medications)
• Obstetric issues (e.g., preterm labor)
• Inability to care for self or arrange follow-up if necessary

No Positive Answers → Low Risk

• Refer patient for symptomatic care at home including hydration and rest
• Monitor for development of any symptoms above and re-start algorithm if new symptoms present
• Routine obstetric precautions

If no respiratory compromise or complications and able to follow-up with care → Admit patient for further evaluation and treatment. Review hospital or health system guidance on isolation, negative pressure and other infection control measures to minimize patient and provider exposure

If yes to respiratory compromise or complications → Moderate Risk

See patient as soon as possible in an ambulatory setting with resources to determine severity of illness. When possible, send patient to a setting where she can be isolated. Clinical assessment for respiratory compromise includes physical examination and tests such as pulse oximetry, chest X-ray, or ABG as clinically indicated. Pregnant women (with abdominal shielding) should not be excluded from chest CT if clinically recommended.

Any Positive Answers → Elevated Risk

Recommend she immediately seek care in an emergency department or equivalent unit that treats pregnant women. When possible, send patient to a setting where she can be isolated. Notifying the facility that you are referring a PUI is recommended to minimize the chance of spreading infection to other patients and/or healthcare workers at the facility. Adheres to local infection control practices including personal protective equipment.

Abbreviations: ABG, arterial blood gases; CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus. Healthcare providers should immediately notify their local or state health department in the event of a PUI for COVID-19 and should contact and consult with their local and/or state health department for recommendations on testing PUIs for COVID-19.
Outpatient: What we know (Asx/Mild disease)

• Limited prenatal care widely adopted for all patients

• Telehealth visits effective means to social distance while checking in on PUI/positive patients

• 1st / 2nd, much of 3rd trimester – can delay appt until outside infective window

• If need to be seen – Consider “COVID” specific clinic
  • Subject matter experts – RN, MA, front desk, MD
  • Cohorting PUI/Covid patients away from non-infected women
Outpatient: What we know (Asx/Mild disease)

- Consider detailed anatomy US for 1st and early 2nd trimester infection³

- Consider growth US 1-3 weeks after quarantine ends / no longer infectious (not earlier than 28 weeks)³

- Antenatal testing not indicated outside usual indications³
Outpatient: What remains unclear...

• When is a patient no longer infectious?

Per CDC⁴:

- **Test-based strategy:**
  - No fever, no symptoms AND 2 neg swabs>24hrs apart

- **Non-test based strategy:**
  - >3d with no fever or sx (w/o meds) AND ≥7 days since sx onset

- **Asx patients:**
  - >10 days since positive test
Outpatient: What remains unclear.

What about moderate disease – to admit or not admit?

ADMIT:
- Other respiratory pathology
- Immunocompromised

STAY HOME:
- Otherwise healthy

**Remember: Goal 02 sat in pregnancy is >95% **
Inpatient: OB issues what we know: (Asx/Mild)

PPE necessary
Minimize providers in room

COVID-19 NOT indication for delivery\textsuperscript{3,5}
COVID-19 NOT indication for CS or OVD\textsuperscript{3,5}
Inpatient: OB issues what we know: (Asx/Mild)

Delayed cord clamping OK⁵

No skin to skin

Consider mother/baby separation⁶

Breastmilk safe³,⁵
Inpatient: OB issues what we don’t know: (Asx/Mild)

What we don’t know:

- Are there early warning signs for women who will worsen in labor? (D-dimer⁷, low wbc, high CRP⁸)

- Which moms are at risk to decompensate PP?

- Is there a sinister synergy with preeclampsia?
Inpatient: OB issues what we know: (Mod dz)⁹

**Patient in Labor**

- **Mat/fetal compromise**
  - **Early epidural**
    - YES
    - Maternal SpO2>93%
      - NO....
  - NO

**General**

- Emergency cesarean
  - YES
  - O2<93%
  - Regional
    - O2>93%
Inpatient: OB issues what we know: (Severe disease)⁹

- Mat/fetal compromise
  - Maternal SpO₂ > 93%
    - Regional
    - General
  - Emergency cesarean
    - O₂ > 93%
    - O₂ < 93%
  - Assess BP
  - Hypertension
    - PreX protocol
    - Care escalation, ICU, *Consider delivery
  - Hypotension

*Society for Maternal-Fetal Medicine*
Inpatient: Non-OB Admission (Mod disease)
Inpatient: Non-OB admission (Severe/Critical disease)\textsuperscript{10}

Critical care management

- NIV or HFNC
- Restrictive fluid resuscitation
- Awake prone position (With alveolar collapse)

If no alleviation:
- IMV
- Lower tidal volumes
- Lower inspiratory pressures
- Prone position >16h
- Conservative fluid management strategy
- Higher PEEP
- ECMO
- ......
Inpatient: Non-OB admission (Severe/Critical disease)

What we know:

- BMZ → Avoid ALPS, Recommend BMZ* (unless critical - then case-by-case)\(^3\)
- Ppx Anticoagulation in cases of immobility
- Work with ICU to account for pregnancy physiology\(^12\)
- ECMO in pregnancy → fetal survival ~65-70% (depending on indications)\(^11\)
### Inpatient: Remote from delivery (Severe/Critical disease) – Rx?

<table>
<thead>
<tr>
<th>Medication</th>
<th>What is the data?</th>
<th>Pregnancy data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine (+/- Azithromycin)(^{15,16})</td>
<td>“Insufficient clinical data to recommend either for or against using chloroquine or hydroxychloroquine for the treatment of COVID-19 (AIII)”(^{22})</td>
<td>Compatible in pregnancy and breastfeeding</td>
</tr>
<tr>
<td>Remdesivir (^{13,19})</td>
<td>“Insufficient clinical data to recommend either for or against using the investigational antiviral drug remdesivir for the treatment of COVID-19 (AIII)”(^{22})</td>
<td>No safety published data (23 pregnant patients included in Ebola RCT, Ob outcomes not published)</td>
</tr>
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## Inpatient: Remote from delivery (Severe/Critical disease) – Rx?

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<td>Tocilizumab, sarilumab (IL-6 inhibitor) ¹⁴, ²⁰, ²²</td>
<td>“Insufficient clinical data to recommend either for or against the use of <strong>Interleukin-6 inhibitors</strong> for the treatment of COVID-19 (AIII)”²²</td>
<td>Limited preg data, not a/w anomalies, likely ok with breastfeeding</td>
</tr>
<tr>
<td>Convalescent Plasma¹⁷,¹⁸,²²</td>
<td>“Insufficient clinical data to recommend either for or against the use of <strong>convalescent plasma</strong> for the treatment of COVID-19 (AIII)”</td>
<td><em>IVIG well-tolerated (nothing specific)</em></td>
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Inpatient: Remote from delivery (Severe/Critical disease) – Rx?

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<td>Hydroxychloroquine (+/- Azithromycin)(^{15,16})</td>
<td>shown to inhibit replication of SARS-CoV2 in vitro, ?mod</td>
<td>Compatible in pregnancy and breastfeeding</td>
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<td>Tocilizumab, sarilumab(^{14,20})</td>
<td>Case series – better outcomes in severe disease, ongoing RCTs</td>
<td>Limited preg data, not a/w anomalies, ?SAB risk, likely ok with breastfeeding</td>
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<td>Convalescent Plasma(^{17,18})</td>
<td>Used in other respiratory epidemics, no covid data, ongoing RCTs</td>
<td>*IVIG well-tolerated (nothing specific)</td>
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At present, no drug has been proven to be safe and effective for treating COVID-19\(^{22}\)
Inpatient: Remote from delivery (Severe/Critical disease)

What we don’t know?

- What about fetal monitoring in these cases?
- Does delivery impact disease course?
- Proning in pregnancy... even the non-intubated patient\textsuperscript{10,21}
In summary...

Asx/Mild infections → outpatient ok

Obstetric admission with mild/asx → most uncomplicated

Obstetric admission with mod/severe disease → Maternal status guides MOD

COVID admission → .....
References

8. CRP: https://www.medrxiv.org/content/10.1101/2020.03.21.20040360v1
9. https://www.ajog.org/action/showPdf?pii=S0002-9378%2820%2930430-0
On to Dr. Gaw...then Questions
Other questions...

Intrapartum fever:
- Vitals often ‘normally’ abnl
- Clinical judgement → ?IAI

POC testing on L+D
- Reasonable when possible
Other questions...

Vaccine:
- Many candidate vaccines out there (>100)
- Planning to initiate human testing later this year
- Wide diversity of platforms in public / private sector
- Unprecedented scale and speed of R+D