Covid-19 During pregnancy

SOHEILA RANJBAR.MD
OBSTETRICIAN & GYNECOLOGIST
WWW.DRRANJBAR.COM
TEHRAN. FARMANIEH HOSPITAL

SEP 2021
Coronaviruses (COVs) are positive-stranded RNA viruses with a crown-like appearance under an electron microscope (coronam is the Latin term for crown) due to the presence of spike glycoproteins on the envelope. The Subfamily Orthocoronavirinae of the Coronaviridae family order Nidovirales classifies into four genera of COVs:

- Alphacoronavirus (alphaCoV)
- Betacoronavirus (betaCoV)
- Deltacoronavirus (deltaCoV)
- Gammacoronavirus (gammaCoV)
COURSE During PREGNANCY

- Pregnancy DO NOT increase the risk for acquiring SARS-CoV-2 infection

- But worsen the clinical course of COVID-19 compared with non-pregnant individuals of the same age

- Most infected mothers recover without undergoing delivery
Pregnancy complications

- Delivered before 37 weeks.
- Delivered by cesarean.
- Fever and hypoxemia in severe
- Fetal death, still birth, IUFD, IUGR

Pneumonia and fever may increase the risks:

- Preterm labor
- Premature rupture of membranes
- Abnormal fetal heart rate patterns
Classification of disease severity

- **Asymptomatic** or **Presymptomatic** infection – Positive test for SARS-CoV-2 but no symptoms.
- **Mid illness** – Any signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea or abnormal chest imaging.
- **Moderate illness** – Evidence of lower respiratory tract disease, dyspnea by clinical assessment or imaging and a saturation of oxygen ($\text{SaO}_2 > 93\%$) on room air at sea level.
- **Severe illness** – Respiratory frequency $>30$ breaths per minute, $\text{SaO}_2 \leq 93\%$ on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ($\text{PaO}_2/\text{FiO}_2 < 300$ mmHg), or lung infiltrates in ct scan $>50\%$.
- **Critical illness** – Respiratory failure, septic shock, and/or multiple organ dysfunction.
Most Frequent Symptoms

- Fever
- Cough
- Dyspnea
- Sore throat
- Fatigue
- Myalgia
- Rhinorrhea/nasal congestion
- Anorexia, nausea/vomiting
- Headache
- Possibly abnormalities in smell and/or taste.
- Lymphopenia
- Modest increase in liver enzymes
- Thrombocytopenia
Asymptomatic or pre-symptomatic

- Positive COVID-19 test result with no symptoms
- Mild disease
- Flu-like symptoms: fever, cough, myalgia, without dyspnea, shortness of breath, or abnormal chest imaging
Protocols for outpatient care

- Asymptomatic/ Mild
- Limited prenatal care for all patients
- 1st, 2nd and most of 3rd trimester visits can be delayed,
- Monitored closely by their obstetric care providers for worsening symptoms
- Daily self-assessments
- **Tele-health**
- Reliable feedback mechanism for early detection of a worsening condition.
Reasons to call a **health care provider** or **emergency medical services**

- Worsening shortness of breath
- Tachypnea
- Unremitting fever
- Inability to tolerate oral hydration or needed medications
- Oxygen saturation < 95% either at rest or on exertion
- Persistent pleuritic chest pain
- New onset confusion or lethargy
- Cyanotic lips, face, or fingertips
- Obstetrical complaints, such as preterm contractions, vaginal bleeding, or decreased fetal movements
Follow up

- There is no guidance about the timing of frequency for follow up outpatient care.
- At least once within 2 weeks of diagnosis of COVID-19.
- These visits can either be through telemedicine or specialized COVID-19 clinics where available.

**Antenatal testing (NST, biophysical profiles)**:
- Usual indications, with consolidating
- Consolidate visits: eg, clinic and ultrasound on the same date and in the same location
When is a patient not infectious

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

- **Non-test based strategy**
  > 3 days with no fever or symptom (w/o meds) AND > 7 days since symptom onset.

- **Asymptomatic patients**
  > 10 days since positive test.
Moderate disease

- Evidence of lower respiratory tract disease;
- Clinical assessment; dyspnea,
- Pneumonia on imaging,
- Abnormal blood gas results
- Refractory fever of 39 C/102 F or greater not
- No Alleviated with acetaminophen
- Oxygen saturation >93% on room air
Severe disease

- Respiratory rate > 30 (bpm)
- Hypoxia with oxygen saturation <= 93%
- Ratio of PaO2/FIO2 < 300 (mmHg)
- Lung involvement on imaging ct > 50%
The pulmonary phase is characterized by immune dysregulation

- A pulmonary microvascular injury (ENDOTHELIALITIS), with activation clotting and a pro-coagulant state together with the characteristic of an organizing pneumonia.

- It should be noted that SARS-CoV-2 as compared to all other respiratory viruses, upregulates cytokines and chemokines while at the same time down regulating the expression of interferon alpha (the host's primary antiviral defense mechanism).

- The ground glass infiltrates as peripheral and patchy, and do not resemble the dependent air space consolidation (sponge/baby lung) seen with “typical ARDS”. Extravascular lung water index (EVLWI) is normal or only slightly increased; this is by definition excludes non-cardiogenic pulmonary edema (ARDS).

- The hypoxia is due to severe ventilation/perfusion mismatch likely due to the microvascular narrowing, thrombosis and vasoplegia.
Critical disease

- Multi-organ failure or dysfunction
- Shock
- Respiratory failure requiring mechanical ventilation or high-flow nasal cannula
Three core pathologic Processes lead to multi-organ failure and death in COVID-19

1) Hyper-inflammation ("Cytokine storm") – a dysregulated immune system whose cells infiltrate and damage multiple organs, namely the lungs, kidneys and heart. It is now widely accepted that SARS-CoV-2 causes aberrant T lymphocyte and macrophage activation resulting in a "Cytokine storm".

2) Hyper-coagulability (increased clotting) – the dysregulated immune system damages the endothelium and activates blood clotting, causing the formation of micro and macro blood clots. Clotting activation may occur directly due to increased expression of Factor Xa as well as endothelial injury with the release of large aggregates of van Willbrand factor. These blood clots impair blood flow.

3) Severe Hypoxemia (low blood oxygen levels) – lung inflammation caused by cytokine storm, together with microthrombosis in the pulmonary circulation severely impairs oxygen absorption resulting in oxygenation failure.
Inpatient care

- Moderate Illness
- Severe illness or oxygen saturation less than 95%,
- Comorbid conditions: un-controlled HTN or DM,
- Fever $>39$ C despite use of acetaminophen,
- Cytokine storm syndrome
- Multi-organ failure, unremitting fever, lymphocytopenia, and blood high ferritin levels.
جدول آزمایش‌های بیماران بستری در بیمارستان

<table>
<thead>
<tr>
<th>آزمایش</th>
<th>شرایط بالینی بیمار</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC (افزایش نوتروفیل به لنفوسیت = بیش از 3.5 تا 5.5 / 10 gr/dl = HB / 10)</td>
<td></td>
</tr>
<tr>
<td>ESR (نوع کمی)</td>
<td></td>
</tr>
<tr>
<td>CRP (نوع کمی)</td>
<td></td>
</tr>
<tr>
<td>BUN/Cr, CPK, ALP, SGPT, SGOT</td>
<td></td>
</tr>
<tr>
<td>P, K, Na, Mg &gt; 3mg/dl, Ca, FBS</td>
<td></td>
</tr>
<tr>
<td>Ferritin (بیش از 100 تا 300)</td>
<td></td>
</tr>
<tr>
<td>ECG (اندازه QT در پرونده بیمار ثبت شود)</td>
<td></td>
</tr>
<tr>
<td>ABG, Troponin, LDH, FDP, D-dimer</td>
<td></td>
</tr>
<tr>
<td>Ferritin</td>
<td></td>
</tr>
<tr>
<td>IL6</td>
<td></td>
</tr>
<tr>
<td>NT-proBNP</td>
<td></td>
</tr>
<tr>
<td>INR-PTT, PT</td>
<td></td>
</tr>
<tr>
<td>Pr/Cr &gt;0/3</td>
<td></td>
</tr>
<tr>
<td>Pr/Cr &gt;0/3</td>
<td></td>
</tr>
<tr>
<td>Fibrinogen</td>
<td></td>
</tr>
<tr>
<td>U/A</td>
<td></td>
</tr>
<tr>
<td>BUN/Cr</td>
<td></td>
</tr>
<tr>
<td>در صورت بروز علائم نارسایی حاد کلیوی (افزایش کراتینین سرم بیش از 3/از حد پایه)</td>
<td></td>
</tr>
<tr>
<td>در صورت ادرار</td>
<td></td>
</tr>
<tr>
<td>در صورت ادرار</td>
<td></td>
</tr>
<tr>
<td>در صورت ادرار</td>
<td></td>
</tr>
<tr>
<td>در صورت ادرار</td>
<td></td>
</tr>
<tr>
<td>در صورت ادرار</td>
<td></td>
</tr>
<tr>
<td>در صورت ادرار</td>
<td></td>
</tr>
<tr>
<td>Fibrinogen</td>
<td></td>
</tr>
<tr>
<td>IL6</td>
<td></td>
</tr>
<tr>
<td>NT-proBNP</td>
<td></td>
</tr>
<tr>
<td>INR-PTT, PT</td>
<td></td>
</tr>
<tr>
<td>Pr/Cr &gt;0/3</td>
<td></td>
</tr>
<tr>
<td>فيروزیت، لنفوسیت، فیبروسیت و سلول اپیتیلیال برونشیال تولید می‌شود</td>
<td></td>
</tr>
<tr>
<td>شک به عفونت ثانویه باکتریال</td>
<td></td>
</tr>
<tr>
<td>HVC; HBV, HIV</td>
<td></td>
</tr>
<tr>
<td>تست‌های تشخیصی</td>
<td></td>
</tr>
</tbody>
</table>
BNP, NT-pro B-type Natriuretic Peptide

- B-type natriuretic peptide (BNP) is a hormone produced by your heart.
- N-terminal (NT)-pro hormone BNP (NT-pro BNP) is a non-active prohormone that is released from the same molecule that produces BNP. Both BNP and NT-pro BNP are released in response to changes in pressure inside the heart. These changes can be related to heart failure and other cardiac problems. Levels go up when heart failure develops or gets worse, and levels go down when heart failure is stable.
- In most cases, BNP and NT-pro BNP levels are higher in patients with heart failure than people who have normal heart
Timing of Delivery in Asymptomatic or Mildly Symptomatic Pregnant Patients

- COVID-19-positive status is not an indication for delivery, and delivery should be reserved for routine obstetrical indications. COVID-19-positive status is not an indication for C/S.

- 37 to 38 6/7 WKS without other indications for delivery: expectant management can be considered until "14 days after (PCR) result was positive or until 7 days after onset of symptoms"

- Or 3 days after resolution of symptoms

- At 39 weeks of gestation or later delivery can be considered to decrease the risk of worsening maternal status.
In the ICU, severely ill patients with COVID-19

- None pregnant patients are often managed in the prone position; the left lateral position is an alternative but may not be as effective.
- Permissive hypercapnia (PCO2 <60 mmHg) and extracorporeal membrane oxygenation (ECMO), if indicated for management of ARDS, do not appear to be harmful to the fetus, but data are limited.
- High positive end-expiratory pressure strategies (>10 mmHg), if considered, require close ongoing maternal and fetal monitoring because they decrease preload and cardiac output.
- Multi organ failure: mental status, liver, kidney, heart insufficiency.
Timing of Delivery for Critically ill patients

Pregnant Patients Should be individualized based on:

- Maternal status, Concurrent pulmonary disease (eg, cystic fibrosis, asthma, sarcoidosis, Critical illness)
- Ability to wean off the ventilator and ventilator mechanics
- Gestational age at time of delivery
- Shared decision-making with the patient or healthcare proxy.
- The timing of delivery requires carefully weighing the benefits and risks for the patient and fetus, and the decision to deliver requires close communication between the maternal-fetal medicine and critical care teams.
In the third trimester, the pressure of the uterus can decrease expiratory reserve volume, inspiratory reserve volume, and functional residual capacity, and increase the risk of severe hypoxemia in pregnant patients, especially those who are critically ill.
Venous thromboembolism prophylaxis

- Routine pharmacologic venous thromboembolism prophylaxis in patients hospitalized with COVID-19 is recommended unless there is a contraindication (e.g., bleeding, severe thrombocytopenia and less than 12 hours to delivery time).

- We initiate prophylaxis in all pregnant/postpartum women with COVID-19 admitted to the hospital for management of an antepartum or postpartum obstetric or medical disorder or because of the severity of COVID-19 alone.

- Unfractionated heparin is generally preferred in pregnant women who might be proximate to delivery because it is more readily reversed than low molecular weight heparin.

- Low molecular weight heparin (e.g., enoxaparin 40 mg daily) is reasonable in women unlikely to be delivered within several days and those who are postpartum.
Dexamethasone

- Dexamethasone 6 mg daily for 10 days or until discharge is recommended for severely ill nonpregnant patients who are on supplemental oxygen or ventilatory support. Glucocorticoids may also have a role in the management of refractory shock in critically ill patients with COVID-19.

- For a preterm delivery at 24+0 and 33+6 weeks of gestation within seven days, we suggest initiating therapy with the usual doses of dexamethasone (four doses of 6 mg given intramuscularly 12 hours apart) or betamethasone (two doses of 12 mg given intramuscularly 24 hours apart) to induce fetal pulmonary maturation followed by either methyl prednisolone (40 mg orally daily) or hydrocortisone (80 mg intravenously twice daily) to complete the maternal steroid course.

- Methyl prednisolone is a choice drug for pulmonary phase in covid-19

- Methyl prednisolone + vitamin C prevent AFOP-intra alveolar fibrin deposition.
Inhibits SARS-CoV-2 RNA-dependent RNA polymerase, which is essential for viral replication

Metabolism of remdesivir to remdesivir triphosphate (RDV-TP) demonstrated in multiple cell types

RDV-TP acts as an analog of adenosine triphosphate (ATP) and competes with the natural ATP substrate for incorporation into nascent RNA chains by the SARS-CoV-2 RNA-dependent RNA polymerase, which results in delayed chain termination during replication of the viral RNA

First day 200 mg and the rest 4 days 100 mg/ day with normal saline

Side effects : تهوع، استفراغ، افزایش قند خون و انزیم های کبدی و برادیکاردی در مادر
Actemra is a monoclonal antibody that reduces inflammation by blocking the interleukin-6 receptor. In the case of COVID-19 infection, the immune system can become hyperactive, which may result in worsening of disease. Actemra does not directly target SARS-COV-2. Actemra is a prescription medication given by intravenous infusion that is FDA-approved for multiple inflammatory diseases, including rheumatoid arthritis.

Under today’s EUA, the FDA is authorizing the emergency use of Actemra for the treatment of certain hospitalized patients with COVID-19. Actemra is not approved as a treatment for COVID-19.

Favipiravir tablet 200mg is contraindicated during pregnancy.
Ivermectin

- Pregnancy Considerations: Adverse events have been observed in animal reproduction studies. Although use in pregnancy is likely low risk, other agents are currently recommended for the treatment of pediculosis pubis or scabies in pregnant women.

- Breast-Feeding Considerations: Ivermectin is measurable in low concentrations in breast milk. The manufacturer does not recommend treating women who intend to breastfeed unless the risk of delayed maternal treatment outweighs the potential risk to the nursing infant.

- Although use is likely low risk, other agents are currently recommended for the treatment of pediculosis pubis or scabies in breastfeeding women.
Should pregnant women be vaccinated

- WHO recommends the use of the COVID-19 vaccine in pregnant women when the benefits of vaccination to the pregnant woman outweigh the potential risks. To help pregnant women make this assessment, they should be provided with information about the risks of COVID-19 in pregnancy, the likely benefits of vaccination in the local epidemiological context, and the current limitations of safety data in pregnant women.
Breast-Feeding Considerations

- The decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother.

- Vaccination should be injected for lactating moms and it is safe for infants and IgA and IgG passed through the breast milk.
و در حال حاضر بیشتر از سیتی‌های اول و دوم حق ماه پس از واکسیناسیون کامل اجرا می‌شود.
درهمه و کسیناسیون در دوران شیردهی پس از زاگمان تجویز گرست 42 روز پس از زاگمان انجام شود.

قطع شیردهی پس از واکسن کرونا توصیه می‌شود.

WHO توصیه کرده است که کسیناسیون را توصیه می‌کند.

تزئین اکسونولگولوژی، واکسن کرونا و واکسن عارضه‌گویی دوگانه تراکمی با واکسن کرونا کرده است.

گروه سنی مادران باردار از سن 35 تا 44 سال بالاتر

مادران در جریان شایانی و حمله کنترل و پیگیری مادران در دوران بارداری و در کرونا و آنفلوانزا واکسن دوگانه می‌خورند.

مادران باردار در شرایط که عصب‌پروران عصب‌پروران در جریان واکسن کرونا و یا مراکز عصب‌پروران می‌توانند کرونا شایانی بگذرانند.

مادران باردار با علت بیماری‌های بیولوژیک از 35 تا 44 سال بالاتر

مادران با بارداری دوقلوی، بچه‌بایی و بارداری با

IVF مادران با بارداری دوقلوی، بچه‌بایی و بارداری با

مادران باردار با بیماری عارضه‌گویی زیستی شامل: میگنزون، میتئون، نامزون، نامژارد 35/12.5 میلی‌گرم. مصرف اکسونولوژی، واکسن کرونا و واکسن عارضه‌گویی دوگانه تراکمی با واکسن کرونا کرده است.
چه یک جهان باشد چه صد جهان
تو را چون جان به مر، دارم
مردی نیست

با سپاس از همراهی شما و يوجدتان

و گهر سه شیلی رگنر
جرج مخصوص زنان، زایمان و نازلی
لیپ راکل، هیسترو سکپر و لایزر تزریق

ج راح و می خ صص ر ی ان ، ر ای مان  و ی ار ان ی
لای اراسکون ی، هی سی روسکون ی و لی ر ر ب ران ی