

REVIEW

Pregnancy and Coronavirus Disease 19

Mythri Shankar ^a , Nishanth KR ^b

^a Assistant Professor, Institute of Nephrourology, Bengaluru, India; ^b Associate Professor, Rajiv Gandhi University of Health Sciences, Bengaluru, India

ABSTRACT

As Coronavirus disease 2019 (COVID 19) is declared a global pandemic, management of expecting mothers and newborn care becomes a great challenge to the physicians and their families. They should follow the same guidelines as the general population to avoid exposure to the virus as much as possible. Pregnancy does not seem to increase the risk of infection nor accelerate its natural history or the severity of illness. Routine prenatal-antenatal care should be home monitored and telemedicine encouraged as much as possible. Women with comorbidities or at high risk of infection such as a recent history of travel, from a containment zone, history of primary or secondary contact should be closely monitored for symptoms. RT PCR is recommended before labor or one day before elective surgery. Supportive treatment is important in infected patients. Low molecular weight heparin can be used for thromboprophylaxis in severe illness. Data on the use of Remdesivir, Hydroxychloroquine, Lopinavir-Ritonavir are limited. There is limited data on the placental transmission of the virus. The newborn should also be immediately tested following the delivery of a COVID19 pregnant woman. If the newborn is found to be negative, strict hygienic measures according to CDC should be followed to express breast milk. According to WHO, breast milk banks are a safe alternative. Few mothers may prefer to give formula feeds, which can be administered by healthy caregivers. There is limited data regarding the transmission of the virus through breast milk.

KEYWORDS: COVID19, Pregnancy, Newborn, Prenatal care, Breast milk.

Correspondence: Dr Mythri Shankar. Institute of Nephrourology, Bengaluru, India. Email: mythri.nish@gmail.com

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INTRODUCTION

Coronavirus disease 2019 (COVID 19) is declared a global pandemic affecting more than a lakh population in more than a hundred countries. It is caused by SARS coronavirus 2 (SARS CoV 2). The first case was declared in Wuhan Province of China on December 31st, 2019. Since then the disease has spread far and wide. Millions of people are infected worldwide and lakhs of people have died as a consequence. Pregnant women may be at a higher risk due to physiologically suppressed immunity during pregnancy. Also, posing as a major challenge in the care of the newborn.

PREVENTION

Pregnant women should follow the same precautions as non-pregnant people to avoid exposure to the virus. Such as social distancing, disinfecting surfaces, performing hand hygiene, wearing masks in public places. The monitoring of women with the history of epidemiologic contact should be followed up strictly.

Pregnant women with children should be more vigilant. Mild or asymptomatic infections have been reported in the majority of infected children. They can be super-spreaders of the infection. Children from one household should not play around with children from other households. They should maintain six feet distance from other children.[1] They should practice wearing masks in public spaces.

Pregnant health care workers should avoid working in COVID19 treatment establishments. Pregnant workers in non-healthcare occupations can work till term. However, they should work in an environment with a reduced risk of exposure. Fifteen days of quarantine before the date of delivery is recommended. The individual's comorbidities and the scope of work will guide the clinician for requests of medical leave.[2, 3]

CLINICAL MANIFESTATIONS

All pregnant women should be carefully monitored for symptoms and signs, especially if they are primary or

secondary contacts of a COVID19 infected case. According to a systematic review, which included 356 studies, the most common symptom was fever (67%) followed by cough (66%), sore throat (7%), breathlessness (7%) and body ache (6%). Other symptoms were rhinorrhea, anorexia, headache, loss of taste, and smell. [4]

LAB INVESTIGATIONS

Lymphopenia (14%) was seen most commonly, followed by deranged liver function tests (5%) and thrombocytopenia (1%). Severe lymphopenia, increased total leucocyte count, increase in neutrophil count, increase in S. creatinine and blood urea levels were associated with poor prognosis, and an increase in mortality.[5] Cytokine storm caused by viral invasion is a cause for neutrophilia. Sustained inflammation causes coagulation abnormalities. Acute kidney injury can be caused by hypoxia, shock, or direct viral injury.

COMPLICATIONS

Acute respiratory distress syndrome, myocarditis, shock, disseminated intravascular coagulation [5], thromboembolic complications such as stroke, pulmonary embolism.[6]

COURSE IN PREGNANCY

According to case series and case reports, pregnancy does not enhance the chances of acquiring infection, does not alter the natural history of the disease and the rate of recovery is the same as the general population. Early delivery is not mandatory for recovery.[7][8] However, elderly pregnant women and those with comorbidities such as obesity are at increased risk of more severe disease. [9] In pregnant women with pneumonia, there is an increased risk of preterm and cesarean delivery. 295 pregnant women were studied in a systematic review [10], out of which 4.7% required ICU admission. In a study from New York, the United States, 43 pregnant patients were studied. 9.3% had severe disease and 4.7% required ICU admission [11]. In China, 147 pregnant patients were studied, illness was severe in 7% of the patients and critical in 1%.[12]

Fever and pneumonia can cause hypoxia and increase the risk of premature rupture of membranes and preterm labor. Hyperthermia is one of the symptoms of COVID19. An increase in maternal core temperature can theoretically increase the risk of congenital anomalies such as neural tube defects in the first trimester. However, data on the same are limited. The use of paracetamol for hyperthermia is safe during pregnancy.

VERTICAL TRANSMISSION

Vertical transmission is not yet proven but the possibility cannot be ruled out. Some of the ways of ensuring fetal safety are by measuring IgM cord blood levels of the virus and testing neonatal nasopharyngeal swab, placental tissue using sterile precautions immediately following delivery. Amniotic fluid can also be tested in case of a cesarean section.

Pregnant women with positive SARS-CoV 2 infection, have tested negative for vaginal and amniotic fluid till date.[13] The percentage of viremia in pregnant women with SARS-CoV2 infection is low [1%] reducing the incidence of vertical transmission and placental seeding.[14]

A few cases of possible vertical transmission have been reported. But in such cases, Ig M was positive in the neonate on day 1 or day 2. Vaginal swab and amniotic fluid testing were not done. The infection may be due to postnatal contact with the mother or the caregiver.[15]

Serological tests identify patients who have had prior infections and some patients with ongoing infection (between day 9 to day 14 of symptom onset).[16] They are not useful in the acute setting as it takes 9 to 14 days for antibodies to form. In areas of low seroprevalence, the results should be interpreted with caution. As they have low positive predictive value.[17]

Some kits have obtained emergency use authorization by the FDA.[18] These kits detect antibodies against nucleocapsid and spike antigens of SARS-CoV2. The sensitivity and specificity of these tests are uncertain. They should not be used solely for diagnosis or to rule out SARS-CoV2 infection. The catalog of serological tests is available on www.centerforhealthsecurity.org. CDC recommends using test strips with high specificity (>99.5%) and to test in patients with a high pre-test probability of having had the infection earlier. Or else, a two-step method of diagnosis can be used. Confirming the initial positive result with a subsequent different antibody test. Kits based on Ig A antibodies should not be used. The serological tests can cross-react with other coronavirus strains and hence, can have high rates of false-positive tests.[19]

APPROACH TO DIAGNOSIS

Any patient with:

- New onset of fever/chills and cough/dyspnea
- Pneumonia of unknown etiology
- With travel history prior to 14 days
- History of contact with COVID19 infected patient.
- Residing in the containment zone

should be tested with RT-PCR (reverse transcriptase – Polymerase chain reaction) for SARS-CoV2-RNA on a nasopharyngeal swab specimen. In areas where the infection is prevalent, pregnant women should be tested when they get admitted for labor or delivery. If a cesarean section is planned, testing can be done one day before the surgery.

DIFFERENTIAL DIAGNOSIS

If there is a community spread of influenza, it is reasonable to test for influenza infection as well. There can be a coinfection of influenza with SARS-CoV2. Pregnant women can have thrombocytopenia, liver dysfunction, hemolysis as part of HELLP syndrome. Patients with SARS-CoV2 infection may have similar lab abnormalities due to sepsis [20]. Such as,

- Normal or Prolonged PT INR, APTT
- Increased Fibrinogen

- Increased D-Dimer
- Thrombocytosis or Thrombocytopenia

ROUTINE OBSTETRIC PRENATAL CARE:

Prior to the visit, pregnant women should take an appointment and use the necessary precautions to reduce the degree of exposure. They should constantly monitor the fetal kick counts and inform immediately in case of decreased fetal movement. As far as possible, teleconsultation should be encouraged.

TREATMENT

Thromboprophylaxis: Pregnant women with SARS-CoV2 infection, should be started on low molecular weight heparin prophylaxis. Unfractionated heparin is preferred over low molecular weight heparin when close to delivery as it has a shorter half-life.

ANTI-VIRAL DRUGS

Remdesivir: It is a nucleotide analog that has in-vitro activity against SARS-CoV2. It is being used on compassionate grounds in pregnant women with severe disease. No reports of fetal toxicity have been found when this drug was used against Ebola Virus.[21, 22]

Hydroxychloroquine: Early randomized studies have shown no benefit. It is known to cause cardiac arrhythmias, especially when combined with other cardiotoxic drugs. Animal studies have shown that it crosses the placenta and causes ocular damage. However, it is not seen in humans. Hydroxychloroquine has been used in pregnant women with systemic lupus erythematosus and malaria.[23]

Favipiravir: It is an RNA Polymerase inhibitor. It is contraindicated in pregnancy and lactation at present. Clinical trials are underway in Asia to test the efficacy of the drug. {NIH 2020A, NIH2020B}

BREASTFEEDING

Some case reports of SARS-CoV2 being transmitted in breast milk are published [24], there are also few other studies stating otherwise i.e, no evidence of SARS-CoV2 in breast milk. [25] More data are required regarding the transmission of the virus in breast milk.

If the mother is COVID 19 positive and the newborn is negative, she can express breast milk. The expressed breast milk can be fed to the baby by a healthy caregiver. Adequate hygienic measures should be used while expressing the milk, she should clean the breast, nipple, hands with soap and water. She should wear a mask. All

AUTHORS' CONTRIBUTIONS

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the [Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals](#) of the [International Committee of Medical Journal Editors](#). Indeed, all the authors have actively participated in the redaction, the revision of the manuscript and provided approval for this final revised version.

the breast milk collection equipment should be sterilized. CDC has released guidelines for the safe expression of breast milk.[26]

Global human breast milk banks screen the donor mother, collect, pasteurize, and store breastmilk. It was set up primarily for pre-term, low birth weight babies and babies with congenital anomalies or neurological deficits to improve their immunity and prevent complications [27] In the current Coronavirus Pandemic, WHO has recommended milk from such human breast milk banks as a safe alternative if a mother is unable to feed the baby.[28]

But there are challenges faced by these milk banks such as screening of donor, safe collection of milk, handling risks, transportation, and other logistic problems which need to be taken care of.

A Virtual Communication Network of milk bank leaders started to form on March 17, 2020 and now has more than 80 members from 34 countries.[29]

If both mother and infant are positive for infection, separation is not necessary.[30]

If women choose to administer formula feed, the healthy caregiver is preferred for the same.

CONCLUSION

Pregnant women should follow the same recommendations as the general population to avoid exposure to SARS-CoV2. Clinical symptoms are similar to the general population. Women with a severe infection such as pneumonia may have complications like premature rupture of membranes and preterm delivery. Women with preterm mild COVID 19 infection do not require early delivery. Delivery can be planned once the patient becomes negative for the infection and in isolation. Only for women with severe COVID 19 illness with pneumonia, early delivery at least at 32 to 34 weeks can be planned. In areas where the infection is prevalent, pregnant women should be tested when they get admitted for labor or delivery. If a cesarean section is planned, testing can be done one day before the surgery. If the mother is COVID 19 positive and the newborn is negative, she can express the breast milk. The expressed breast milk can be fed to the baby by a healthy caregiver. Adequate hygienic measures should be used while expressing milk. WHO has recommended pasteurized milk from human breast milk banks as a safe alternative if a mother is unable to feed the baby.

SPONSORSHIP

Declared none.

COMPETING INTERESTS

The authors declare no competing interests with this study.

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