



Short Communication

Effect of COVID-19 on pregnancy and childbirth

Priyanka Samji^{1,*}, Manoj K R¹¹Dept. of Biotechnology, Indian Institute of Technology Madras, Chennai, Tamil Nadu, India

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ABSTRACT

Considering the significance of ongoing global coronavirus pandemic, it is important to study the effect of coronavirus on pregnancy. In this review, different case studies of COVID-19 pregnant women from various hospitals of China are discussed. The symptoms of pregnant women with COVID-19 pneumonia were mainly fever and cough and except one study, there is no evidence for vertical transmission in late pregnancy. Though the conclusions from the discussed studies are limited by the small sample size, it is believed that the findings discussed in this review are important for understanding the clinical characteristics. As SARS-CoV-2 is a new virus, not much is known about its effects and it is difficult to get definitive answer for the treatment. To summarize, there is no evidence to suggest that pregnant women are more likely to contract the virus and SARS-CoV-2 might not get transmitted from the mother to the neonate.

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1. Introduction

COVID-19 or coronavirus disease 2019 has spread rapidly across the world. As on 3rd April, 2020, COVID-19 has infected 1,002,818 persons worldwide causing 52,571 deaths. In India alone, there are 2069 cases and 53 deaths reported till 3rd April, 2020. Concurrent with the sharp increase in the number of infections, the number of pregnant women and children with COVID-19 is also increasing which is a matter of concern. Coronavirus (CoV) family consists of viruses that cause common cold but can sometimes cause severe diseases such as Severe Acute Respiratory Syndrome (SARS-CoV), Middle East Respiratory Syndrome (MERS-CoV) and currently SARS-CoV-2.¹

The causative agent for COVID-19 is a new strain of coronavirus named as SARS-CoV-2 and was first discovered in humans in Wuhan, China in 2019.² Severe acute respiratory syndrome (SARS) or SARS-like coronaviruses belong to the betacoronavirus genera and their common ancestors are very much similar to the bat

coronavirus HKU9-1.³ According to the latest reports, COVID-19 virus is mainly transmitted between people through respiratory droplets and contact routes.⁴

SARS-CoV-2 is a new virus and so not much is studied about its effects on pregnant women. According to the American College of Obstetricians and Gynecologists, there is no data on COVID-19 to suggest that pregnant women are at higher risk of getting the virus as compared to non-pregnant women. It is believed that both pregnant and non-pregnant women in the same age group will develop mild to moderate symptoms if infected with the SARS-CoV-2. However, Siston et al,⁵ suggested that pregnant women are at a greater risk of harm if they get respiratory infections.

Reports from various influenza studies have suggested that during pregnancy, there are higher chances of mortality and morbidity as compared to a non-pregnant woman and similar results were also obtained for the other two coronaviruses- SARS-CoV and MERS-CoV.⁶

1.1. Effects of viral infections on pregnancy

During pregnancy, women undergo a lot of physiological changes in their immune, cardiovascular and respiratory

* Corresponding author.

E-mail address: priyankaji.gupta@gmail.com (P. Samji).

systems and therefore a small amount of stress in that situation might worsen the situation.⁷ Various studies have shown that respiratory viral infections during pregnancy have been associated with problems such as low birth weight and preterm birth. Further, high fever early in pregnancy might increase the risk of certain birth defects.^{8,9}

Viral diseases pose a grave threat to pregnancy via intrauterine transmission to the fetus. Viruses such as Ebola, Zika and TORCH agents (a term used for Toxoplasma, Other, Rubella, Cytomegalovirus, Herpes) can get congenitally transmitted to the fetus. Except herpes virus, most of these viruses enter the fetus through the hematogenous route in which the virus circulating in the mother's blood stream reaches the placenta and from there it enters the chorionic villous tree and finally to fetal blood vessels.⁵

During SARS epidemic, out of 12 pregnant women infected with the SARS-CoV, three died during pregnancy, 2 had intrauterine growth restrictions in 2nd and 3rd trimester, 4 had miscarriages in the first trimester, and finally 1 normal and 3 induction deliveries were carried out and there was no vertical transmission.⁶

During MERS-CoV epidemic, 11 pregnant females got infected and 91% of them had adverse clinical outcomes such as premature delivery, intensive care treatment for newborns, maternal and perinatal death and there was not a single case to suggest the vertical transmission of the MERS virus.¹⁰

1.2. Pregnancy outcome in SARS-CoV-2 infected females in China

Currently, there is no data about the outcome of pregnancy in SARS-CoV-2 infected females from other countries, so in this review, only the clinical case studies of SARS-CoV-2 infected pregnant women from various hospitals of China are discussed.

Zhu et al. studied the clinical features and outcomes of 10 neonates born to 9 mothers with confirmed SARS-CoV-2 infection in 5 Chinese hospitals from January 20 to February 5, 2020.¹¹ Most of these COVID-19 patients had fever, cough and only 1 patient had diarrhea. These mothers delivered 8 male and 2 female infants, out of these 10 (8 singletons and 2 twins), four were full-term infants and 6 were born premature, one was a large-for-gestational-age (LGA) infant and 2 were small-for-gestational-age (SGA) infants. Out of these 10 infants, 6 had a Pediatric Critical Illness Score (PCIS) of less than 90 with symptoms such as shortness of breath, fever, thrombocytopenia along with rapid heart rate, abnormal liver function, vomiting and pneumothorax. Out of these 10 infants, 9 were eventually cured and discharged, however, 1 infant died and pharyngeal swab specimens from these 9 neonates on days 1 to 9 after birth showed negative results for SARS-CoV-2 confirming that there was no vertical transmission.

In another single-centered study in Tongji Hospital in Wuhan, China, all the COVID-19+ pregnant females from January 1 to February 8, 2020 were assessed for clinical features, treatments, maternal and fetal outcomes.¹² The mean age of the patients was 32 years and the mean gestational age was 39 weeks with clinical symptoms such as fever (86%), cough (14%), shortness of breath (14%) and diarrhea (14%). All the 7 pregnant women received antiviral treatment, oxygen therapy in isolation and had caesarean section within 3 days of clinical symptoms. Following delivery, all the mothers and neonates born were good except one which tested positive for CoV-2 (but the viral nucleic acid tests of the placenta and cord blood were negative) at 36 h after birth. The authors concluded that the maternal, fetal and neonatal outcomes were good but one has to remember that these pregnant women were infected in late pregnancy and these results were achieved with intensive and active management.

In another case, a 28-year-old female in the 30th week of pregnancy with a travel history to Wuhan reported to the hospital with intermittent fever for one week.¹³ Initially, she tested negative for SARS-CoV-2 but the CT scan of the chest demonstrated left-sided subpleural patchy consolidation and right-sided ground-glass opacities and further SARS-CoV-2 RT-PCR results of her sputum proved that she was positive that put her into isolation at that hospital and then transferred to the intensive care unit (ICU) in a negative pressure isolation room. Due to the abnormal CT scan and low levels of lymphocytes and albumin, several multidisciplinary doctors were consulted and she was treated with antiviral drugs. In spite of the treatment, there was a reduction in the fetal movement and no change in fetal heart rate, and even after putting for ventilator support, there was no improvement which prompted doctors to go for emergency caesarean section under combined spinal-epidural anesthesia in a designated negative pressure isolation room. The patient delivered a preterm male infant weighing 1.83 kg and he was kept in the isolation ICU for observation without any contact with his mother and was given formula instead of breast milk ever since. After three days, both the child and the mother tested negative for SARS-CoV-2 again further suggesting that there is no vertical transmission of SARS-CoV-2.

Further, a study reviewed the clinical data and CT examinations of 15 COVID-19 + pregnant women with pneumonia in hospital from January 20 to February 10, 2020.¹⁴ The most common symptoms observed in these COVID-19 + pregnant women were fever (13/15 women), cough (9/15 women) and lymphocytopenia (12/15 patients). Pregnancy and delivery did not increase the severity of COVID-19 pneumonia. Eleven out of 15 women had successful deliveries (10 caesarean and one vaginal delivery), and four patients were still pregnant at the end of the study period. None of the neonates were SARS-CoV-

2 + and there were no reports of neonatal asphyxia, death, stillbirth and abortion.

In a cohort studied.¹⁵ 33 neonates born to mothers with COVID-19 in Wuhan Children's Hospital, China were studied. Out of 33, four showed symptoms of shortness of breath and 3 tested positive for SARS-CoV-2 and all three were delivered by caesarian section due to maternal distress and pneumonia. All these COVID-19 neonates had fever, lethargy and pneumonia which subsided later on by treatment with antibiotics and proper ventilation. The nasopharyngeal and anal swabs of all the 3 neonates tested positive for SARS-CoV-2 on days 2 and 4 but negative on days 6-7 of their lives. It is likely that the sources of SARS-CoV-2 in the neonates' upper respiratory tracts or anuses were maternal in origin, suggesting the vertical transmission from mother to the neonate.

Till now, none of the studies have shown that the chance of miscarriage is increased in SARS-CoV-2 infection during pregnancy, however, it was observed that women with the SARS-CoV infection were found to have a slightly higher risk of miscarriage, but of course only in those who were having some other complications.⁶

2. Conclusions

Most of the studies discussed here have analyzed the outcomes in pregnant women in the last trimester. None of the studies had pregnant women in the first and second trimesters, so the effects of SARS-CoV-2 infection on first two trimesters are not known. Further, most of the pregnant women enrolled in these studies had very mild to moderate symptoms, so it is not clear how the pregnancy will be affected if the symptoms are moderate to severe. In addition, very less number of patients were enrolled in all the studies discussed here. It is important to include a big cohort to study the course of SARS-CoV-2 infection systematically in pregnant females.

COVID-19 pneumonia in pregnancy is a complicated situation and so a multidisciplinary team of medical experts consisting of obstetricians, infectious diseases experts, anesthetists, ICU, pediatricians, internal medicine experts, nosocomial infection control experts and of course psychologists is required to manage and fully treat these patients.¹⁶ None of the medical staff should have SARS-CoV-2 infection during the entire treatment period and the entire staff should be trained for strict isolation and protection measures such as hand hygiene, use of protective equipment, safe waste management, environmental cleaning, and sterilization of medical equipment. If a pregnant female has finished full term, then after consultation with a multidisciplinary team, delivery might be a better option due to safety considerations. If possible, delivery should be performed in a designated negative pressure isolation room and the entire medical staff involved should wear protective gears including gown, N-95 mask, eye protection

and gloves.¹⁷ Based on WHO guidance and lack of clinical evidences, use of corticosteroids for COVID-19 is not recommended during pregnancy.¹⁸ Only those drugs or alternative medicines which have shown effectiveness with no side effects on the fetus should be used. Antibiotics can be used to prevent secondary bacterial infections only after operation. Most important, utmost care and precautions should be taken in handling the infant to avoid any possible transmission of infection including contact, droplet and airborne. Breastfeeding can be little bit risky due to the close contact between the infected mother and the child, so it is advised to wear a mask while feeding the baby.¹⁹ Some infected cases in China demonstrated viral shedding in faeces, suggesting that SARS-CoV-2 might also be present in other body parts, so precautions should be taken during delivery.¹⁵

To summarize, this review is an attempt to understand and learn from the clinical case histories of SARS-CoV-2 + pregnant women. It also aims to make people aware that it is very important to screen pregnant women and follow strict preventive measures. If at all they are found to be COVID-19 positive, then they should be quarantined, regularly and thoroughly checked for any complication and a multidisciplinary team should be consulted to perform the delivery. Neonates should be closely monitored and it is advised that these neonates should be separated from the COVID-19 mothers for at least 14 days if possible.

3. Source of Funding

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4. Conflict of Interest

None.

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Author biography

Priyanka Samji Scientist

Manoj K R Junior Research Fellow

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