

PREGNANCY RISKS MANAGEMENT IN THE CONTEXT OF COVID-19 OUTBREAKAbdifatah Mohamed Nuh^{1,2}, Yan You^{1,2} and Min Ma*^{1,2} Ph.D.¹Department of Obstetrics, Affiliated Hospital of Yangzhou University, Yangzhou, Jiangsu Province, 225000, China.²Yangzhou University Medical College, Yangzhou, Jiangsu Province, 225000, China.***Corresponding Author: Min Ma Ph.D**

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Article Received on 22/04/2020

Article Revised on 12/05/2020

Article Accepted on 01/06/2020

ABSTRACT

In late December 2019, a series of novel corona virus isolates have been found from human being presenting with unexplained pneumonia in Wuhan China and officially named as Severe Acute Respiratory Syndrome-Corona Virus-2. This virus causes Corona Virus Disease 2019 has raised concerns in the community about the potential risks to the maternal health and the optimal management of the pregnant women, fetus and neonate, as well as the care providers in the neonatal period. At present, evidences for viral vertical transmission from mother to fetus or from mother to neonate is obscure and are based on few case sample sizes and case reports. In this review we discuss the available knowledge on mother to child transmission, clinical outcomes, and the concerns about imaging modalities to diagnose pneumonia. Unlike in SARS and MERS outbreaks of corona viruses where by significant worse maternal outcomes were reported in pregnant women affected compared with non-affected pregnant women, reported data suggest that outcome is similar among COVID-19 pregnant women and unaffected. As the global pandemic continues and knowledge expands regarding this outbreak, additional information and scientific evidences will be available on clinical characteristics, potential effects of SARS-Cov-2 on pregnant women, and to their neonates.

KEYWORDS: SARS-Cov-2, COVID-19, Severe Acute Respiratory Syndrome, pregnancy, SARS, MERS, Vertical Transmission, Outcome.

INTRODUCTION

Severe Acute Respiratory Syndrome (SARS) emerged in China and Middle East during the outbreak in 2003 and 2013 respectively. These outbreaks were later confirmed to be caused by corona virus family and were named as Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-Cov). Both viruses are known to have emerged from animals such as bats, camel, cattle and cats.^[1,2] In December 2019, about two decades from these two previous epidemics, a series of genetically similar human corona virus were isolated from the respiratory epithelium of unexplained pneumonia patients in the Wuhan seafood market. This virus was later confirmed to be the major cause of disease outbreak and has been named the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) on February 11 2020.^[3] This virus causes acute lung disease with a potential to life-threatening respiratory outcome, leading to a condition that has been named as "coronavirus disease 2019" (COVID-19).^[4] The spread of Corona Virus Disease-19 has been so rapidly and widely around the world and becomes one of the significant global health pandemic in recent times. Several studies reported that nearly 85% of cases are mild, 10% moderately and 5% become critically ill that may require ICU.^[5,6] Advanced ages and comorbidities

predispose the patient to develop into critical condition and possibly death.

In view of the current COVID-19 pandemic, the information regarding clinical features, intrauterine transmission risks of COVID-19 pneumonia in pregnant women is obscure. Answer to this gap is of paramount importance for formulating the principles of obstetric treatment for pregnant women with COVID-19 infection. Recently, Liu et al reported clinical course and outcome of 13 pregnant patients with COVID-19 showing high complication rates. Five of their patients (38%) had to be delivered by an emergency cesarean (including one stillbirth) due to a variety of indications, and six (46%) had preterm delivery. One women had multiple organ failure and was on life support with extracorporeal membrane oxygenation at the time of reporting.^[7] Another published case series of 9 pregnancies with COVID-19 by Chen et al. reported a cesarean section rate of 100 % but no stillbirth or neonatal death.^[8]

However, pregnant women are faced with immunocompromised status and physiological adaptive changes during pregnancy. Under normal circumstance, such changes could influence their susceptibility to COVID-19 infection than the general population. For

example, previous relatively similar epidemics of SARS and MERS resulted to poor maternal and fetal outcomes such as morbidity, mortality, maternal-fetal transmission and even perinatal deaths.^[9-11] The report from these studies indicated that some women required mechanical ventilation, while some neonates developed fetal distress. At present, there is insufficient understanding whether COVID-19 pregnant women are more severely affected, whether intrauterine transmission or from women to neonate might occur and which management standard should be followed. This review intends to give an up-to-date account of this gap.

VERTICAL TRANSMISSION RISKS

Major concern is the speculation that SARs-Cov-2 can be transmitted vertically from women to fetus hence causing congenital COVID-19 pneumonia. Several preliminary case series have reported contrasting reports regarding risks of women to child transmission of SARS Cov-2. Importantly, both of these data are generated from limited sample sizes.

The study by Siyu Chen and colleagues which evaluated clinical features and outcomes of five pregnant women who were waiting term deliveries concluded that these deliveries were uneventful and the perinatal outcomes to both women and neonates were impressive.^[12] While this study indicates favorable results, general conclusion is limited by its small cohort. Another study of 10 pregnant women who tested positive of COVID-19 shows that none of the neonates tested positive for SARS-Cov-2 at 72 hours post birth.^[13] Another study whose main focus was to investigate the possibility of intrauterine transmission of SARS-Cov-2 tested the amniotic fluid, cord blood and neonatal swab. In order to ascertain the contamination free sample, six COVID-19 pregnant women at term underwent Caesarean section and all the samples were taken in the operating room. In this study, all samples tested negative for SARS-Cov-2.^[8] Outside China, according to the National Website of Ministry of Health and Medical Education of Iran, three infants born to COVID-19 pregnant women at term and none of them tested positive for SARS-Cov-2. On the other hand, with increased understanding of the pathogenesis of COVID-16 pneumonia infection, a body of few studies recently published is indicating the possibilities of intrauterine infections of SARS-Cov-2. Recent study exploring the mechanism of SARS-Cov-2 infection has revealed that this virus enters the host cells via the angiotensin-converting enzyme II receptor (ACE2), the virus specific expressed on cell surface and hence augment infection in human cells.^[14,15] There is update understanding that high levels of ACE2 mRNA receptors and protein expression are expressed in reproductive organs such as uterus, testis, spermatids and placenta.^[16]

CLINICAL OUTCOME FOR MATERNAL AND CHILD HEALTH

Pregnancy is an important risk factor for developing other diseases including diabetes, hypertension and depressed immunity. Notably, viral infections may worsen the pregnant outcome and increase the suffering of the pregnant woman. In 2003, the case series of 12 pregnant suffered from SARS.^[17] In this case series, the fatality rate was 25%. However, it is not precise how potentially the viral infections would adversely affect the pregnant outcomes. Studies report that pregnancy outcomes due to viral infections are largely depending on the gestational age at presentation.^[17] The newly emerged viral respiratory pneumonia caused by SARS-Cov-2 have been reported to cause suffering in many patients across the globe. Pregnant women are not excluded to get infected. Recently both Chen et al and Zhu et al reported small series of pregnant women at their third trimester to have delivered healthily unaffected babies in which there were no maternal or neonatal deaths.^[8,13] To date, 32 women affected by COVID-19 in pregnancy, including one with a twin pregnancy, have been reported, delivering 30 infants.^[8,13,18] Twenty-seven delivered by Cesarean and two by vaginal delivery. Women who delivered did so within 13 days of onset of illness; three pregnancies were ongoing. In cases in which maternal morbidity and mortality were reported (n=23), two women required intensive care unit (ICU) admission and mechanical ventilation and one developed multi organ dysfunction and was still on extracorporeal membrane oxygenation (ECMO) when her case was reported. When reported (n=17), all symptomatic women had viral changes apparent on computed tomographic (CT) chest imaging. There were no maternal deaths to date.^[8]

No scientific data exist regarding the effect on fetuses of maternal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during the first or second trimester of pregnancy, and data are limited regarding infections that occur during the third trimester. However, reports of newborns with fetal distress or requiring admission to the intensive care unit^[8,13] and a stillbirth after maternal coronavirus disease 2019 (COVID-19)^[7] in the third trimester suggest the possibility of COVID-19-induced placental pathology.

Infection of the maternal side of the placenta inducing acute or chronic placental insufficiency resulting in subsequent miscarriage or fetal growth restriction was observed in 40% of maternal infections with Middle East respiratory syndrome coronavirus and severe acute respiratory syndrome coronavirus.^[17,19] Additional study of pregnant women with COVID-19 is warranted to determine if SARS-CoV-2 can cause similar adverse outcomes. Serious morbidity occurred in 2/32 women with COVID-19, both of whom required ICU care. Compared with SARS and MERS, COVID-19 appears less lethal, acknowledging the limited number of cases reported to date and one woman who remains in a critical

condition. Preterm delivery affected 47% of women hospitalized with COVID-19, which may put considerable pressure on neonatal services if the UK's reasonable worst-case scenario of 80% of the population being affected is realized. Based on this review, the RCOG (in consultation with the RCPCH) developed guidance for delivery and neonatal care which recommends that delivery mode be determined primarily by obstetric indication and recommends against routine separation of COVID-19-affected women and babies.

Taken together, we currently face a pandemic with a novel virus, and considerable uncertainty remains regarding SAR-CoV-2 infections and consequences of infection during pregnancy.

Several questions remain about pregnant women and their newborns. Preliminary information suggests that pregnant women are not more severely affected than the general population^[20] however, the numbers of pregnant women reported have been small, and comparison is needed with other people women of similar age rather than with all persons with COVID-19, a population that is older (median age is approximately 50 years) and has underlying conditions. A small study that compared pregnant women with a matched control group of other people women of similar age suggests that pregnant women with SARS may have an increased risk of severe disease and death.^[21] Whether intrauterine or perinatal transmission occurs is also unknown. Among the small number of pregnancies reported thus far, no evidence of transmission to the neonate has been observed; however, these women were nearly all infected in the third trimester and most underwent cesarean delivery.^[7,8,13] The effects of the virus earlier in pregnancy are completely unknown; no neonates have been delivered to women infected in the first and second trimesters of pregnancy. The paucity of evidence challenges some of the key decisions that need to be addressed. For example, one question that has arisen is whether pregnant health care workers should receive special consideration. During the 2009 H1N1 influenza pandemic, in which pregnant women were more likely to develop complications than other people women.^[22,23] The CDC recommended that pregnant women should strictly adhere to the same measures that were recommended for all health care personnel, although certain work accommodations, such as avoidance of aerosol generating procedures on infected patients, could be offered as an option.^[24]

MODE OF DELIVERY

The choice of mode of delivery is influenced by medical indications such as maternal chronic or acute diseases, advances in technology, social and cultural changes, and, in particular, legal change. In general, pregnant women may give birth their neonates through one of the four methods: natural delivery, assisted delivery, Cesarean section due to medical factors, and Cesarean section due to social factors. The new coronavirus 2019 (COVID-19)

pneumonia is transmitted from person to person via respiratory droplets that come in contact to smooth and thin membranes such as mouth, eyes and nostrils. The most important question is whether the COVID-19 could be transmitted vertically to the fetus from the pregnant women and cause a clinically significant infection.^[25] It is this question that creates worries to the COVID-19 expectant women, family members, obstetrician, nurses, and the rest of healthcare providers. Recently, a finding from nine cases suggested that there is no evidence for intrauterine infection caused by vertical transmission in women who develop COVID-19 pneumonia in late pregnancy.^[8] These nine pregnant women were in their third trimester and underwent a caesarean section. The indications for a caesarean section was influenced by the presence of either severe pre-eclampsia, a history of caesarean sections, and fetal distress. Importantly, the obstetricians were uncertain about the risk of intrapartum women-to-child transmission if vaginal delivery was opted.

IMAGING TESTS PROTOCOL

According to the COVID-19 pneumonia management protocol, chest imaging is critical for the complete evaluation of COVID-19, limited reports concluded that this test should not be withheld in pregnant women. Both X-ray and computed tomography (CT) use radiation. Impact on the fetus is related to the gestational age at the time of the examination and the dose of radiation exposure. The suggestion is that, routine diagnostic imaging doses are much lower than 1 Gy, the threshold for early embryonic injury. There have been no reports of fetal malformations, restricted growth, or miscarriage.^[26] The minimum radiation dose associated with developmental delay is above 610 mGy.^[27-29] According to data cited in clinical guidelines from the American College of Radiology^[30] and the American College of Obstetrics and Gynecology^[31] when pregnant women undergo a single chest X-ray examination, the fetus will receive a radiation dose of 0.0005–0.01 mGy. CT is associated with a fetal radiation dose of 0.01–0.66 mGy.^[30] [During the CT examination, intravenous iodine contrast agent can enter the fetal circulation and amniotic fluid through the placenta, but animal studies have shown that it has no teratogenic or mutagenic effects.^[32,33] Due to a favorable risk–benefit ratio, X-ray, and CT should be used for pregnant women as clinically necessary, with informed consent. Abdominal shielding and limiting exposure times to the minimum necessary may reduce the total fetal radiation dose.

CONCLUSION

At present, this review has found clinical symptoms and outcome is similar among COVID-19 pregnant women to those in other people. Moreover, the information regarding the optimal management of COVID-19 pregnant women is similar to those in general obstetric care. Although there is no current evidence of increased risks pregnant women affected by COVID-19 as compared to unaffected group, studies on potential

outcome of the virus in women with maternal co-morbid like preeclampsia, gestational diabetes, gestational hypertension should be extended. As the global pandemic continues and knowledge expands regarding this outbreak, additional information and scientific evidences will be available on clinical characteristics, potential effects of SARS-Cov-2 on pregnant women, and to their neonates.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgments

The study is funded by Jiangsu Province mass entrepreneurship and innovation program, and Yangzhou Green and Golden phoenix plan.

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