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Review Article

COVID-19 during pregnancy: vertical transmission, diagnosis and maternal-fetal complications

Mounir Moukit^{1*}, Assia El Ouardi², Abdellah Babahabib^{1,3}, El Mehdi El Hassani^{1,3},
Jaouad Kouach^{1,3}

¹Department of Obstetrics and Gynecology, Military Training Hospital Mohammed V, Rabat, Morocco

²Department of COVID-19, University Hospital Center Hassan II, Fes, Morocco

³Faculty of Medicine and Pharmacy, University Mohammed V, Rabat, Morocco

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***Correspondence:**

Dr. Moukit Mounir,

E-mail: moukitmounir@yahoo.com

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ABSTRACT

The current pneumonia outbreak of COVID-19 has been declared a pandemic by the World Health Organization on March 11, 2020. With its indiscriminate spread across continents, authors are likely to see women with COVID-19 canvassed across all trimesters of pregnancy. To date, few reports have provided information about this disease in pregnant patients. Authors conducted a literature review to summarize the results concerning intrauterine transmission, diagnostic challenges and maternal-fetal outcomes of pregnant women with COVID-19 pneumonia.

Keywords: COVID-19, Diagnosis, Maternal and fetal complications, Pregnancy, Vertical transmission

INTRODUCTION

In December 2019, a new strain of coronavirus causing coronavirus disease 2019 (COVID-19) was first identified in Wuhan, a mega city with an 11 million population in central China.¹ Over the ensuing weeks, widespread transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, has been reported in all continents. As of April 22, 2020, there are more than 1,714,000 active cases in the world and approximately 182,000 deaths. The epidemiological data showed that most cases had mild symptoms, with the overall case fatality rate of 2.3%.² Although most human coronavirus infections are mild, the SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) epidemics of the past two decades were grave; the fatality rate of SARS and MERS among pregnant patients was 25% and 40%, respectively.^{3,4} While data regarding COVID-19 continues to inform authors understanding of this disease,

clinical reports on maternal and neonatal outcomes of pregnant women with SARS-CoV-2 infection are rare and limited to small case series. In this article, authors conducted a literature review of publicly available information to summarize knowledge about the pathogen in this vulnerable population. Vertical transmission, diagnosis and maternal-fetal complications are all reviewed.

VERTICAL TRANSMISSION

Actually, emerging evidence suggests that vertical transmission is probable. In fact, two reports have published evidence of IgM for SARS-COV-2 in neonatal serum at birth.^{5,6} Since IgM does not cross the placenta, this is likely to represent a neonatal immune response to in utero infection. However, there are no confirmed cases of vertical transmission among the other neonates born to COVID-19 infected mothers, supported by an absence of virus in amniotic fluid, cord blood, placenta swabs and neonatal throat swabs.^{2,7,8}

Table 1: Fetal complications reported in the literature (case reports have been excluded).

	n	Median gestational age at birth (weeks)	IUFD	Premature birth	Low birth weight	Apgar score at 5 minutes	Still birth	Vertical transmission
Li et al ²	36	38	8%	22%	13%	10	No one	No one
Liu et al ²⁷	19	38	-	-	No one	≥8	No one	No one
Breslin et al ⁹	18	37	No one	5%	No one	≥9	No one	No one
Zhang et al ²⁴	16	38	No difference with women without COVID-19 (comparative study)				No one	No one in 10 of 16 neonates
Yang et al ²⁶	13	38	-	-	No one	-	No one	No one
Liu et al ²³	11	37	No one	-	-	≥8	No one	-
Liu et al ¹⁷	10	35	30%	60%	-	10	10%	No one
Zhu et al ²²	9	38	55%	55%	22%	≥8	No one	No one
Chen et al ¹⁰	9	38	11%	44%	22%	≥9	No one	No one in 6 of 9 neonates
Yu et al ²⁵	7	39	No one	No one	No one	≥9	No one	14%
Chen et al ⁸	4	38	No one	No one	No one	≥7	No one	No one

IUFD: Intrauterine fetal distress.

DIAGNOSIS

Clinical features of COVID-19 are similar to non-pregnant patients (fever during pregnancy or postpartum period, cough, shortness of breath, headache, anosmia). It is important to note that gestational rhinitis, usually affects a fifth of healthy women in late pregnancy and due to estrogen-mediated hyperaemia of the nasopharynx, may mask symptoms of COVID-19 and consequently causing community transmission. In addition, physiologic dyspnea due to increased maternal oxygen demands from heightened metabolism and anemia is common in pregnancy and must be distinguished from a pathologic breathlessness. In a series of 43 COVID-19-positive pregnant women identified over a two-week period, infection was often asymptomatic, supporting a role for universal testing of pregnant women being admitted to the Labor Unit.⁹ Laboratory investigations are not specific. An early study has evaluated the outcome of nine pregnant patients with COVID-19 without any specific underlying diagnosed diseases (all gestational ages ≥36 weeks). Among them, none had leukopenia (perhaps masked by the physiological increased levels of white blood cells during pregnancy) while 56% had only lymphopenia (<109 cells/L).¹⁰ Also, elevated CRP and liver cytolysis were observed in 75% and 33% respectively.¹⁰ The reverse transcriptase polymerase chain reaction (RT-PCR) test for SARS-CoV-2 from respiratory specimens is the gold standard for diagnosis. It is a quantitative test and the determination of viral load is possible. However, a previous report argued that false negatives cases might be common due to low virus titers, sampling at late stage of illness, and inappropriate swabbing sites.¹⁰ Antigen-antibody detection tests are not validated, and viral culture takes at least 72 hours to cause cytopathic effects in selected cell lines. Chest imaging is used for diagnosis of 2019 novel coronavirus

disease, as an important complement to the RT-PCR tests. Predominant radiological appearances are peripheral airspace shadowing on a plain chest radiograph and bilateral, multi-lobar ground-glass opacities or consolidation on computed tomography (CT) scan.^{11,12} The sensitivity, specificity, positive predictive value and negative predictive value of a CT chest in diagnosing this entity are 97%, 25%, 65% and 83% respectively.¹³ In pregnancy, fetal exposure to ionizing radiation during a CT chest is not associated with increased risk of teratogenicity.^{14,15}

MATERNAL COMPLICATIONS

Compared to SARS and MERS, maternal prognosis during COVID-19 infection appears more promising.^{4,16} Whilst pregnant women are not more susceptible to viral illness, changes to their cardiorespiratory and immune system increase susceptibility to severe infection, particularly in the last trimester. There have been cases reports of women with severe COVID at the time of birth that has required ventilation and extracorporeal membrane oxygenation.¹⁷ A single case report has been published a maternal and intrauterine fetal death, at 30 weeks, attributed to COVID-19.¹⁸ Recently, Breslin et al. have described a case series of 43 women tested positive for COVID-19 and showed a similar pattern of disease severity to non-pregnant women: 86% mild, 9.3% severe and 4.7% critical, although the sample size was too small to draw a definitive conclusion.⁹ A study has evaluated the risk factors related to the mortality among survivor and non-survivor patients diagnosed with COVID-19.¹⁹ Authors have stated that sepsis, respiratory failure, acute respiratory distress syndrome, heart failure, septic shock, coagulopathy, acute cardiac injury, and acute kidney injury were significantly higher in non-survivors. In addition, they have shown that the administration of

corticosteroids in non-survivors was significantly higher than in survivor group.¹⁹ Given that pregnancy is known to be a hypercoagulable state, and emerging evidence suggests that individuals admitted to hospital with COVID-19 are also hypercoagulable, it follows that infection with COVID-19 is likely to be associated with an increased risk of maternal venous-thromboembolism.^{20,21} Also, reduced mobility resulting from isolation increases this risk.

FETAL COMPLICATIONS

There are currently no data suggesting an increased risk of miscarriage or early pregnancy loss in relation to COVID-19. There are case reports of preterm birth in women with COVID-19, but it is unclear whether this was iatrogenic or spontaneous. Liu et al and Chen et al have reported other complications including fetal distress (23%), premature rupture of the membrane (7%), stillbirth (7%) and low birth weight.^{10,17} Currently, there is no evidence that the virus is teratogenic. It is notable that the majority of reported cases acquired COVID-19 in the last trimester, and there is no data when the infection is acquired in early gestational age. The situation may change and continued monitoring is recommended. Fetal complications reported in the literature are summarized in Table 1. Protracted respiratory compromise increases the risk of fetal growth restriction due to maternal hypoxia. Consequently, fetal monitoring by ultrasound is recommended. Although the data do not suggest a risk of vertical transmission, delayed clamping of the umbilical cord and skin-to-skin contact should be avoided following delivery, extrapolating from recommendations by the Canadian society of obstetricians and gynecologists guidelines for SARS in pregnancy.²⁸

CONCLUSION

Pregnant women are a vulnerable group in SARS-CoV-2 infection. The latest may increase health risks to both mothers and fetus during pregnancy. Efforts should be taken to reduce the infection rate of SARS-CoV-2 during gestational and postpartum period, and more intensive attention should be paid to pregnant patients.

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