

Current Overview on the Effects of COVID-19 Disease on Maternal and Neonatal Health; Narrative Review

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ABSTRACT

The novel coronavirus infection (SARS-CoV-2 infection), which appeared in the Wuhan region of China in late 2019, spread rapidly in a short time. A few months later, it was accepted as pandemic by the WHO (World Health Organization) and became an important threat to public health. The death rate in cases occurring in China was around 2%. Although it is thought that pregnancy is not a risk factor in the course of COVID-19 disease, it is often seen in which the cases were in the third trimester. It is striking that the maternal and neonatal implications of these infected cases during the late pregnancy period were quite good. Further studies examining more cases in the first and second trimesters, in order to determine long-term results and to clarify the risk of vertical transmission are needed.

INTRODUCTION

The novel coronavirus (SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2) infection, which appeared in Wuhan, China in December 2019, spread rapidly within a short period of time and was accepted as a pandemic by WHO (World Health Organization) as of March 11, 2020 has become an important life-threatening factor.^[1,2] This new virus was firstly named 2019-nCoV (novel CoV), but was later named SARS-CoV-2. In early January 2020, it was isolated in laboratories in China.^[3] Later, it became an increasingly widespread respiratory tract infection that can cause serious pneumonia and

death worldwide. Although there is a rapid increase in the available information regarding the genetic, virological, epidemiological and clinical aspects of this disease, 7 coronaviruses are known that can cause infection in humans to date. This novel coronavirus, recently causing COVID-19 disease, has been shown to cause fatal lung pathologies.^[4] The virus can be transmitted from infected individuals through cough, sneezing droplets as well as contact with the patient's hand spoiled with the contaminated surfaces by touching the eye, mouth and nasal mucosa.^[5] It is estimated that the respiratory droplet does not go beyond about 2 meters.

Contagion has also been reported from asymptomatic individuals.^[6] Incubation time is considered to be an average of 5 days (2–14 days). However, among the some recent cases, it has been reported that there are no signs of contact with infected people.^[7] The average age is 49–56 years and additional predisposing disease was detected in 1/3 to half of the cases.^[8] Among the most common symptoms of infection are respiratory symptoms, fever, cough, and dyspnea. In more serious cases, pneumonia, severe acute respiratory infection, kidney failure or even death due to multiple organ failure may occur. The death rate in cases occurring in China is around 2%. However, this rate may vary depending on the changes in the genetic structure of the virus or the treatment. No vaccine or antiviral treatment for the virus has yet been found.^[6] An important question we have in mind is the possibility of higher susceptibility risk to SARS-CoV-2, related to physiological changes in pregnant women. However, when we look at the literature, there is no evidence that pregnant women are more susceptible to SARS-CoV-2 infection.^[9] Another question that remains unanswered is whether SARS-CoV-2 is transmitted vertically from pregnant women to the fetus. If it is being transferred, how its mechanism is occurred. This is not only an important public health problem, but it is also an obstetric management problem for both pregnant and infant. Considering the previous experience, this becomes even more important when we consider that other agents such as Zika virus, Ebola virus are transmitted vertically and threaten the life of the infected mother and fetus.^[10,11]

Current clinical features, obstetric and neonatal reflections of pregnant women with covid-19 disease

In the current literature, when the clinical symptoms of the patients in a series of 9 pregnancies with COVID-19 disease positive were examined, it was observed that they were similar to those who were not pregnant. Although 7 patients had fever, 4 had coughs, 3 had muscle pain, 2 had sore throat, 5 had lymphopenia, and 3 had aminotransferase elevation. Mechanical ventilation was not required despite pneumonia development in all cases.^[12] In another study that examined the clinical symptoms and thorax computed tomography findings of 15 pregnant women with confirmed COVID-19 disease, 19 pregnant with suspected COVID-19 disease, cough was observed in 13 cases and lymphopenia was the most common laboratory finding in 12 cases. In 10 cases, pregnancy was completed by cesarean and in 1 case, it was completed by normal vaginal delivery. The pregnancy of the other 4 cases has been continuing. Neonatal asphyxia, neonatal death, preterm birth or miscarriage has not been reported in any baby born from these pregnant women. It was found that pregnancy and birth did not aggravate the clinical course.^[13]

108 pregnant women were investigated in a review of all case reports and case series between 12 February 2020

and 4 April 2020. It has been reported that most cases are in the last trimester and are admitted to the hospital with 68% fever and 34% cough symptoms. While C-reactive protein (CRP) levels were found to be increased in 70% of cases, lymphopenia was found in 59% of cases. The delivery of 91% of the cases was performed by cesarean section and 3 pregnant women were followed up in the postpartum intensive care unit. But no maternal death has been reported. Only one neonatal death and one intrauterine fetal death were detected.^[14]

In another study comprising of 37 pregnant women and 38 newborns, 29 pregnant women were delivered by cesarean while 8 pregnant women gave normal birth. While preterm delivery was reported in 7 pregnancies between 30–33 weeks of gestation, all other pregnant had term delivery. Although no mother needed mechanical ventilation, the patients were given non-invasive oxygen support via nasal cannula only with the combination of antiviral, and antibiotic therapies. Only one patient needed to follow-up in the intensive care unit, and her baby was closely monitored in neonatal intensive care. The most common symptoms in these cases were fever, cough and chest pain, as in other studies mentioned.^[15]

Similarly, the most frequently found laboratory finding in other publications is lymphopenia. All pregnant women in the study gave birth to healthy newborns with Apgar score between 8 and 10. Asphyxia, cyanosis or any congenital anomalies have not been reported in neonates. Sample locations taken from the newborn after delivery were examined by RT-PCR from the oropharynx, umbilical cord blood, amniotic fluid and blood samples. Also, RT-PCR was examined from the breast milk sample. Considering neonatal results, there is no evidence of teratogenicity, fetal transmission through the placenta and/or breast milk after birth. When neonates with positive COVID-19 disease are examined, the transmission is thought to be via respiratory droplet due to factors such as cough from the mother or other immediate perinatal environment. Development of symptoms in neonates occurs between 5 and 17 days after birth. The most common symptoms during follow-up were vomiting, fever, cough, pneumothorax, impaired liver function tests, thrombocytopenia and pulmonary changes in thorax computed tomography (CT). All newborns born from the mother confirmed of COVID-19 disease in the study were fed with formula.^[15]

In another study in which 16 cases with pneumonia due to COVID-19 disease and 18 suspicious cases who applied for delivery in the 3rd trimester were examined, the pregnancy of 2 cases was terminated with a normal vaginal delivery while the pregnancy of other cases was terminated with a cesarean delivery. While symptoms such as fever and cough were observed in a few cases, the findings of the neonates observed were typical in thorax computed tomography. Compared to the control group, the WBC count and neutrophil counts were

low in COVID-19 patients, whereas WBC, neutrophil, eosinophil and CRP levels increased in the postpartum period. Six of the cases had preterm delivery, and none of them had respiratory failure during their hospital stay. When neonates were examined, no serious neonatal complications were observed, and no signs of disease were encountered in any of them.^[16]

In a different study examining 32 pregnant women infected with SARS-CoV-2, 7 pregnant women (22%) were asymptomatic, while 2 patients needed admission in the intensive care unit, but no maternal death was observed. Although there were limited cases when compared to infections such as SARS and MERS in the past, COVID-19 disease has been observed to be less fatal in pregnant women. Twenty-seven cases were delivered by cesarean section, and preterm delivery was observed in 15 cases (47%). It is unclear whether preterm deliveries are spontaneous or iatrogenic. Iatrogenic deliveries were mostly due to indications caused by maternal viral infection. When neonatal results were analyzed, it was observed that only one case had neonatal death. No vertical transmission was observed in neonates. Delivery patterns were determined by obstetric indications and it was not thought to be associated with pregnancy loss or intrauterine growth retardation as seen in SARS and MERS infections.^[17]

In a single-center retrospective study examining 7 cases with confirmed COVID-19 disease, pregnancy of all cases was terminated by cesarean section. Compared to the non-pregnant population, the prognosis of the patients did not show any risk increase, and none of the patients required intensive care. In all cases, birth weight and Apgar scores of newborns were within normal limits. Since 4 of the neonates did not have any symptoms, they were discharged without SARS-CoV-2 testing and it was observed that there was no problem in their follow-up. In the other 3 neonates, the SARS-CoV-2 test was performed, only one of them was positive. In the follow-up of this positive case, no fever or cough was detected, but only mild respiratory symptoms. There were no problems in the follow-up of the patient, whose symptoms were regressed and discharged after two weeks.^[18]

In a further study evaluating 9 pregnant cases and 10 neonates (one of them was twin pregnancy), 4 cases were term and 6 cases were preterm. Clinical symptoms of fever, vomiting, thrombocytopenia, impaired liver function tests, tachycardia, and pneumothorax have also been observed in neonates whose main symptom was respiratory distress. Until the publication date of the article, 5 patients were discharged by completing their treatment. While four neonates were kept under observation in the hospital for follow-up, 1 case died. The results were negative in PCR samples taken on postnatal 9th day. When the neonatal results of pregnant women with COVID-19 disease were examined, there was no definite evidence in relation to this condition, although preterm labor, fe-

tal distress and respiratory distress syndrome can cause negative results. Vertical transmission has not been proven.^[19]

As a summary; COVID-19 disease has spread rapidly around the world and has turned into a pandemic. When we look at the limited data in the literature, an increased sensitivity to COVID-19 disease in pregnant women compared to the general population has not been reported. However, it is accepted that the immune systems of pregnant women are suppressed. Therefore, pregnant women are generally more sensitive to diseases than non-pregnant women. Higher morbidity and mortality require the management of suspicious or infected pregnant women by multidisciplinary teams with sufficient knowledge and equipment in this regard, due to the high mortality rates caused by genomically similar viruses, SARS-CoV and MERS-CoV infections in pregnant women. Although there is a limited amount of information in pregnant women, there are no significant differences in terms of symptoms, radiological and laboratory findings compared to those who are not pregnant in general. In a limited number of studies on this subject, the mortality rate is around 1–4%.

There is no evidence yet that the infection has passed from the mother to the baby. Aggressive infection control management, early mechanical ventilation in progressive respiratory symptoms, oxygen therapy, avoiding excess fluid treatment, and close fetal and uterine monitoring come to the forefront in pregnancy and birth management. Since the infection is very new, there are no large case series and randomized controlled studies in neonates. Although the case definitions of neonates are similar to those in adults, neonates may be considered to be at greater risk since their immune systems are not sufficiently developed. More care should be taken in newborns who have a history of contact in severe cases or who have risk factors such as congenital heart disease and respiratory anomaly. Considering that it has similar genomic structures and clinical features, studies conducted in patients with SARS infection also have perinatal infection in pregnant women, and no evidence of its occurrence in newborns was found.^[20] In Table 1, a summary of the studies examining the relationship between COVID-19 disease, pregnancy and neonatal period is mentioned.

CONCLUSION

In the light of the available data, it is thought that pregnancy is not a risk factor in the course of COVID-19 disease, but it is often seen in the cases in the third trimester. It is striking that the maternal and neonatal effects of these infected cases, infected during the late pregnancy period are quite good. In the cases of first and second trimesters, more studies are needed in order to determine long-term results and to clarify the vertical transmission risk.

Table 1. Current literature on COVID-19 disease, pregnancy and/or neonatal period

Author	Year	Country	Title	Key findings
Liu et al. ^[13]	2020	China	Coronavirus Disease 2019 (COVID-19) During Pregnancy: A Case Series	No evidence to suggest the potential risk of intrauterine vertical transmission
Zaigham et al. ^[14]	2020	Sweden	Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies	Vertical transmission of the COVID-19 could not be ruled out. Careful monitoring of pregnancies with COVID-19 and measures to prevent neonatal infection are warranted.
Panahi et al. ^[15]	2020	Iran	Risks of Novel Coronavirus Disease (COVID-19) in Pregnancy; a Narrative Review	COVID-19 can cause fetal distress, miscarriage, respiratory distress and preterm delivery in pregnant women but does not infect newborns. There has been no report of vertical transmission in pregnancy, and it has been found that clinical symptoms of COVID-19 in pregnant women are not different from those of non-pregnant women
Li et al. ^[16]	2020	China	Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study	Severe maternal and neonatal complications were not observed in pregnant women with COVID-19 pneumonia who had vaginal delivery or caesarean section. Mild respiratory symptoms of pregnant women with COVID-19 pneumonia highlight the need of effective screening on admission
Mullins et al. ^[17]	2020	UK	Coronavirus in pregnancy and delivery: rapid review	Compared with SARS and MERS, COVID-19 appears less lethal and delivery mode be determined primarily by obstetric indication and recommends against routine separation of affected mothers and their babies.
Yu et al. ^[18]	2020	China	Clinical features and obstetric and neonatal	The maternal, fetal, and neonatal outcomes of

Table 1. (Current literature on COVID-19 disease, pregnancy and/or neonatal period)

Author	Year	Country	Title	Key findings
Zhu et al. ^[19]	2020	China	outcomes of pregnant patients with COVID-19 in Wuhan, China : a retrospective, single-center, descriptive study Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia	patients who were infected in late pregnancy appeared very good. The clinical characteristics of these patients with COVID-19 during pregnancy were similar to those of non-pregnant adults with COVID-19 that have been reported in the literature. Perinatal 2019-nCoV infection may have adverse effects on newborns, causing problems such as fetal distress, premature labor, respiratory distress, thrombocytopenia accompanied by abnormal liver function, and even death. However, vertical transmission of 2019-nCoV is yet to be confirmed

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Conflict of Interest

None declared.

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COVID-19 Hastalığının Anne ve Yenidoğan Sağlığı Üzerine Etkilerine Güncel Bakış; Derleme

2019'un sonlarında Çin'in Wuhan bölgesinde ortaya çıkan yeni koronavirüs enfeksiyonu (SARS-CoV-2 enfeksiyonu) kısa sürede hızla yayıldı. Birkaç ay sonra, DSÖ (Dünya Sağlık Örgütü) tarafından salgın olarak kabul edildi ve halk sağlığı için önemli bir tehdit haline geldi. Çin'de meydana gelen vakalarda ölüm oranı %2 civarındaydı. COVID-19 hastalığı sırasında gebeliğin bir risk faktörü olmadığı düşünülse de, genellikle COVID-19'a rastalanan vakalar üçüncü trimesterde idi. Bu enfekte vakaların geç gebelik dönemindeki anne ve yenidoğan etkilerinin oldukça iyi olması dikkat çekicidir. Uzun dönem sonuçlarını belirlemek ve vertikal geçiş riskini açıklığa kavuşturmak için birinci ve ikinci trimesterde daha fazla vakayı inceleyen daha ileri çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: COVID-19; doğum; gebelik; yenidoğan.