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Coronavirus (COVID-19) infection and antenatal care in pregnancy

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Abstract

In this review, we evaluated the protection of healthy pregnant women from the COVID-19 infection caused by the new type of coronavirus SARS-CoV-2 and the antenatal care with suspected or diagnosed COVID-19 in the light of current literature.

Keywords: antenatal care, COVID-19, pregnancy, infection

1. Introduction

The new Coronavirus infection (COVID-19), also called SARS-CoV-2, rapidly expanded to the remainder of China and beyond and turned into a pandemic after being reported as an urgent global public health problem for the first time in December 2019 in Wuhan (1-3).

Coronavirus is a kind of enveloped, non-segmented, positive sense ribonucleic acid (RNA) virus and coronaviridae belongs to the nidovirales family (4). It is known that pregnant women are disproportionately affected by respiratory diseases due to increased morbidity of infection and maternal mortality. Although most of the coronavirus infections have few symptoms, two β-coronavirus epidemics caused by SARS-CoV and MERS-CoV led to severe acute respiratory syndrome and over ten thousand patients in the past 20 years. Mortality has been reported at the rate of 10% for SARS-CoV and 37% for MERS-CoV (5-10). COVID-19 is a member of the identical β-coronavirus subgroup and this virus shows approximately 80% and 50% genomic similarity for SARS-CoV and MERS-CoV, respectively (11). COVID-19 is effused by direct contact and/or droplets (body secretions, somebody's eye, nose, or mouth, or an open incision, contact with injury or abrasion). The universal mortality proportion of COVID-19 infection was reported as 3.4% (12).

Pregnancy is a special condition which makes women suitable for respiratory complications of viral infections. Respiratory tract of pregnant women infected with viruses brings the risk of developing more severe disease due to immunological changes and cardio-pulmonary systems during pregnancy. In 2009, 1% of the patients infected with H1N1 were pregnant women and 5% of all deaths related to H1N1 occurred in pregnant women (13). Both SARS-CoV and MERS-CoV infections are responsible for endotracheal intubation, acceptance to the intensive care unit (ICU), serious complications during pregnancy, including hospitalization, renal failure and death (9, 10).

Mortality rate of pregnant women infected by SARS-CoV is about 25% (9). There is no certain and clear information regarding that if pregnant women with COVID-19 infection are more sensitive than other healthy population. There is no evidence found about COVID-19 infection causing intrauterine and congenital infection. Also, it is difficult to make a final decision about this clinical condition because the COVID-19 cases in pregnant women are low (14, 15).

2. Transition types of COVID-19 infection

The disease is mainly transmitted by droplets. It is spread by the droplets emitted by ill people through coughing and sneezing with the hands of other people, and then by touching and touching the mouth, nose or eye mucosa (16). Disease transmission through droplets does not occur at a distance of more than 2 meters. It can be contagious because viruses can be identified in respiratory tract excretions of asymptomatic people (17). The incubation period is thought to be five days (2-14 days) on average. However, it has been reported that among the recent cases, there are also those without any symptoms of contact with infected people (18).

3. Clinical findings of COVID-19 infection in pregnant women

Widespread symptoms of infection are respiratory symptoms, pyrexia, cough and dyspnea. However, less common clinical findings have also been reported. Pneumonia, severe acute respiratory infection, kidney failure, and likewise death may occur in some people with more severe illness. The most common symptoms in COVID-19 patients during pregnancy

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are prexia (87.9%), dry cough (67.7%), weakness (38.1%), inability to smell and taste (34%), sputum (33.4%), dyspnea (18.6%), myalgia or joint pain (14.8%) (17).

4. Laboratory findings

The white blood cell count may change in patients with COVID-19. Leukopenia and leukocytosis have been described; nevertheless, lymphopenia is still the widespread finding. Lactate dehydrogenase (LDH) and ferritin levels elevation are frequent and furthermore, elevated aminotransferase levels are defined. Numerous patients with pneumonia have normal serum procalcitonin levels at first diagnosis. On the other hand, higher levels may be possible in patients who require ICU. Elevated D-dimer levels and severe lymphopenia have been correlated with mortality (1, 19).

5. Precautions to take during pregnancy

Pregnant women ought to come after the identical recommendations as non-pregnant people to prevent exposure to the virus.

6. Suspected or diagnosed infection during pregnancy

Clinical symptoms, laboratory and radiological findings have the same characteristics as non-pregnant individuals. The clinical course of the disease can be mild (no symptoms or flu-like symptoms), moderate-severe (dyspnea, hypoxia, or lung involvement >50% in imaging), or critical (respiratory distress, shock, and multiorgan failure) (20). Available data show that pregnancy and delivery do not worsen the clinical process of Coronavirus infection and most infected mothers recover before giving birth (21, 22). Severe inflammatory response and cytokine storm are observed in critically ill COVID-19 cases; It is not known whether the physiological immunosuppressive state of pregnancy affects the formation and effect of this response. In addition, it is advantageous for pregnant patients to be in the young age group, the risk of severe course increases in pregnant women with comorbid diseases as in other adults. In pregnant women who develop pneumonia with COVID-19 infection, although the need for intensive care unit is at the same rate as their same age women, preterm delivery and cesarean rates seem to be increased (22, 23).

7. Pregnancy complications

There are data showing that third trimester pregnancies are affected more, rather than early-term pregnancies. The frequency of cesarean section seems to be increased due to preterm labor, premature rupture of membranes, preterm delivery, preeclampsia, and fetal distress, especially in pregnant women who develop pneumonia after COVID-19 infection (24-26). In 41 pregnant patients who had COVID-19 infection, 41.1% had preterm labor at <37 weeks, premature rupture of the membrane in 18.8%, preeclampsia in 13.6% and 91.1% were delivered by cesarean section (26). A birth decision made with the thought that it will improve the mother's symptoms related to the lungs may worsen the current situation, and there is no clear information on this issue yet.

Miscarriage has not been reported for early pregnancy. Theoretically, high fever in the first trimester may affect organogenesis and lead to congenital anomalies. Since it is not yet known whether there will be an increase in the frequency of congenital anomalies with COVID-19 infection, it may be recommended to patients postpone planned pregnancies. There is no termination in patients who had COVID-19 infection in early pregnancy.

8. Vertical transition

In a review in which 38 pregnant women with COVID-19 infection and their newborns were evaluated, no vertical transition was found (27). Second day-onset pneumonia which has been associated with postnatal contact in 3 newborns are reported (28). According to the clinical data available so far, regarding the pregnancies with COVID-19 infection in the late period, there are no proof of vertical transition. Up to the present, there is not enough data on the safety of breastfeeding and separation of mother and baby. Isolation seems the best option in the presence of severe maternal infection. If the patient is asymptomatic or mildly affected, breastfeeding can be performed with protection rules.

9. COVID-19 diagnosis during pregnancy

Submit for testing in the entity of respiratory symptoms for instance fever or dyspnea, cough, or in the presence of suspected contact history; the place where the test will be performed should not be an obstetrics outpatient clinic or delivery room.

Chest radiography contains very low radiation (0.0005 to 0.01 mGy). If indicated, thorax CT can also be carried out because it contains low dose radiation (0.01 to 0.66 mGy) that does not cause fetal anomaly or pregnancy loss. Pulmonary ultrasonography is also an option to show pneumonia in pregnant women (29).

10. How should routine antenatal care be in asymptomatic pregnant?

During the examination of pregnant women without symptoms in line with the recommendations of ACOG and SMFM, it is appropriate to limit the number of people in the polyclinic room, widen the antenatal follow-up intervals, and limit obstetric ultrasonography with accurate indications such as the need for fetal anomaly screening, fetal development and placental monitoring (30, 31). In this period, applying glucose load tests to the risky group and using a cell free DNA test instead of a combined test will shorten the period of pregnant women in the hospital. If possible, pregnancy follow-up by teleconference method, home blood pressure measurements, and fetal movement follow-up are among the recommendations (32). Our recommendation is to limit the antenatal follow-ups to weeks 12, 20, 28, and 36 of gestation when ultrasound and laboratory follow-ups can be performed

in asymptomatic pregnant women without perinatal risk factors. Healthcare professionals must wear a surgical mask during outpatient clinic examination. Relatives of the patient should not be allowed inside, but video shooting may be supported. It should also be taken into account that pregnant women experience social anxiety during this period.

11. Approach to COVID-19 infected pregnant

Fetal monitoring should be arranged according to gestational age, patient's comorbid diseases, and obstetric history. Maternal oxygen saturation (SaO_2) should be kept above >95%, if SaO_2 is <95%, PaO_2 should be measured in arterial blood gas. PaO_2 should be >70 mm-Hg to provide adequate oxygen support from mother to fetus. LMWH is recommended for these pregnant women as venous thromboembolism prophylaxis (eg, enoxaparin 40 mg subcutaneously daily or 1 mg/kg [commonly rounded to the nearest 10 mg] subcutaneously every 24 hours). If delivery occurs, postpartum 10 days prophylaxis should be continued.

Hydroxychloroquine and chloroquine are used in pregnant women for treatment in moderate and severe cases. Although fetal ocular toxicity has been reported with these agents in animal studies, no such effect has been observed in humans and is also available in pregnant women with SLE disease. It can be combined with azithromycin. Since both have a risk of prolonged cardiac repolarization and QT interval, ECG and electrolyte control are required before starting. Remdesivir can also be used in pregnancy. Ribavirin and baricitinib are considered teratogenic, their use is not recommended in pregnant women. Lopinavir can be used in pregnancy; however, its effectiveness against COVID-19 has become controversial in new publications. In the use of Oseltamivir in influenza cases in pregnant women, no risk has been detected for the fetus (33). Favipravir is contraindicated in pregnant women (16).

12. Classification of severity of disease

The National Institutes of Health (NIH) classified degrees of disease severity in five groups in non-pregnant people as follows respectively (34):

-Asymptomatic or presymptomatic infection-Positive test for SARS-CoV-2 but there are no signs of illness.

-Mild illness-The presence of any clinical findings or symptoms (for instance, fever, cough, sore throat, exhaustion, headache, myalgia) without shortness of breath, dyspnea, or abnormal chest imaging.

-Moderate illness-Finding of lower respiratory disease by clinical evaluation or imaging and a saturation of oxygen (SaO_2) ≥94% on room air at sea level.

-Severe illness-Periodicity of respiration >30 breaths per minute, SaO_2 <94% on room air at sea level, rate of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300, or lung infiltrates >50%.

-Serious illness-İnsufficiency of respiration, septic shock, and/or multiple organ dysfunction.

13. Medical treatments we use to manage pregnancy complications

13.1. Antenatal betamethasone

CDC reports that glucocorticoid use should be avoided in MERS-CoV positive patients, as it may delay viral clearance and increase mortality. However, there is no explanation about the use of antenatal steroids in COVID-19 positive pregnant women with preterm birth risk.

ACOG reports that in COVID-19 positive pregnancies up to 24 + 0 to 33 + 6 weeks if it is predicted that delivery may occur within seven days, betamethasone can be used to reduce neonatal morbidity and mortality. However, since the benefit of antenatal steroids between 34 + 0 and 36 + 6 weeks is not clear, it is not recommended for COVID-19 positive pregnant women for now.

13.2. Low-dose aspirin

ACOG recommends the continuation of low-dose aspirin, which was started with an indication such as prevention of preeclampsia (35).

13.3. Tocolysis

Nifedipine is recommended as the first choice if there is an indication to initiate tocolysis to a pregnant woman with suspected or infected COVID-19. Although there are various speculations about ibuprofen, WHO emphasized that NSAIDs should not be avoided (36). Therefore, indomethacin, an NSAID, can also be used as tocolysis.

13.4. Magnesium sulfate usage

If $MgSO_4$ is intended to be used due to its fetal neuroprotective effect or for eclampsia prophylaxis, it should be kept in mind that it may cause respiratory depression and close monitoring is recommended.

13.5. Vaccination

Numerous vaccines are being evaluated for prevention of COVID-19, but pregnant/lactating people have been excluded from these trials. The first vaccines to become clinically available are based on mRNA or protein subunits and do not contain infectious virus (either SARS-CoV-2 or a vector virus). There is no routine vaccination schedule to protect pregnant women from COVID-19 infection, and there is recently no clear consensus on vaccination during pregnancy. If a person conceives of after implementation the first dose of the COVID-19 vaccine series, the second dose ought to be performed when there is an indication.

Vaccination should be timed so that patients do not receive a COVID-19 vaccine within 14 days of administration of a routine vaccination, such as the Tdap or influenza. However, anti-D immunoglobin does not interfere with the immune response to vaccines, so timing of administration for prevention of alloimmunization is based on standard clinical protocols.

As a result, although the fetal, newborn, and maternal effects of available vaccines have not been studied in

preclinical trials, experts believe they are unlikely to pose a risk for pregnant people or breastfeeding newborns based on how mRNA vaccines work, while observational studies have demonstrated that pregnant people who become infected with SARS-CoV-2 are at increased risk of severe maternal disease and adverse pregnancy outcome.

14.Approach to pregnant women recovered from COVID-19

It is important to follow up fetal development a few weeks later, especially in patients who recovered from severe infections (26). It is not known whether it will cause intrauterine growth retardation because of limited data. Fetal growth retardation and thrombotic vasculopathy in the placenta have been reported in patients with previous SARS (37).

14.1. Delivery timing in pregnant women infected with COVID-19

Delivery is not recommended for pregnant women with mild COVID-19 infection without obstetric or medical indication for preterm delivery; The possibility of transmission to the newborn is minimized by giving birth after a negative test result is acquired or after the isolation is eliminated (30).

In serious patients, many aspects should be considered while making the decision to give birth. There is insufficient information about whether the mother's respiratory symptoms will improve with birth and that delivery, when maternal symptoms are present, may increase postnatal transmission to the newborn. Also, maternal antibodies will not have time to develop passive neonatal immunity (38).

For pregnant women with COVID-19 who were hospitalized for pneumonia but were not intubated after the 32nd week, delivery can be planned. In this case, the aim is to decide to perform the birth before the mother's respiratory symptoms deepen and without maternal hypoxemia risking the fetus. However, it is not recommended before the 32nd week of gestation.

In intubated pregnant women, if the patient is stable after 32 weeks of gestation, delivery is recommended. However, this may aggravate the birth symptoms. In pregnancies less than 32 weeks, which has exceeded the viability limit, the decision should be individualized, taking into account the fetal monitorization and the mother's condition (39). The timing and type of delivery ought to be individualized according to the clinical condition of the pregnant, gestational week and the status of the fetus.

15.Negative pressure isolation chambers

Negative pressure isolation chambers are necessary for safe labor and care of newborn. Women with critical illness should be followed in isolation rooms of intensive care units that have negative pressure. Antenatal examination and delivery of pregnant patients infected with COVID-19 ought to be in the negative pressure isolation room of the delivery room (40). When managing infected pregnant women, personal preventive equipment ought to be available for healthcare professionals.

16.Conclusion

To conclude, there are some key points to consider in the management pregnant women infected with COVID 19. Management of infected pregnant woman ought to be carried out multidisciplinary with obstetrician, primatologist, intensive care specialist, anesthesiologist, midwife, virologist, neonatologist in tertiary hospitals. These women ought to be told about the possible risk of morbidities and mortalities during pregnancy.

Conflict of interest

None to declare.

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None to declare.

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