

# Infection Prevention Strategies for Novel Coronavirus in Pregnant and Puerperal Women

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## ABSTRACT

More than two years have passed since the reported emerging infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In the last two years, various clinical studies have been carried out, and the mechanism for the onset of coronavirus infection disease-2019 (COVID-19) is being elucidated. According to previous clinical studies, pregnancies at an older age, obesity, hypertension, diabetes, etc. are considered to be risk factors for the aggravation of COVID-19. Therefore, pregnant women with such a background should be careful about SARS-CoV-2 infection. In particular, when a pregnant woman is infected with SARS-CoV-2 in the latter half of pregnancy, it is considered that the infected pregnant woman is likely to become severely affected by COVID-19. There is no medical evidence that the COVID-19 mRNA vaccine (BNT162b2, mRNA-1273) has adverse effects on pregnancy, fetal, breast milk and genital organs. Therefore, the World Health Organization (WHO) recommends that women who are pregnant, breastfeeding, or planning to become pregnant should be vaccinated with the COVID-19 vaccine. Oral medication prescribed for mild cases of COVID-19: Molnupiravir is not approved for pregnant women. In addition, cocktail antibody medications for pregnant women are also conditional prescriptions. In this mini-review, we would like to discuss the treatment method of COVID-19 in pregnant women with the latest findings.

**KEYWORDS:** SARS-CoV-2, COVID-19, pregnancy, COVID-19 vaccination

The United States (US) and many parts of the world have now lost control of the coronavirus disease 2019 (COVID-19) pandemic owing to the respiratory spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and to inconsistent adherence to effective public health measures, including wearing masks and maintaining social distancing. The COVID-19 has caused over two-million deaths worldwide, with over 412,000 deaths reported in the US. To date (January 2022), at least 160,873 pregnant women in the US have been infected and 263 have died [1-3]. Vaccination is a powerful method of disease prevention that is relevant to people of all ages and in all countries, as the Covid-19 pandemic illustrates. Vaccination can

improve people's chances of survival, protect communities from new and reemerging health threats, and enhance societal productivity. However, much more is needed than the vaccine itself to meet the promise of COVID-19 vaccination for pregnant women. The latest information on preventive strategies against COVID-19 for pregnant and puerperal women is described herein.

In *The Lancet*, Guillaume Favre and colleagues present that coronaviruses have the potential to cause severe maternal or perinatal adverse outcomes, or both [4-5]. Unfortunately the current lack of data on the consequences of a SARS-CoV-2 infection during pregnancy.

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Coronavirus causes fever and upper respiratory tract symptoms and six types infect humans, including the causative virus of diseases such as infectious disease with SARS-CoV [2]. The extent of the human-to-human transmission of SARS-CoV-2 currently remains unclear. In the later stages of pregnancy, increased tidal volume reduces expiratory reserve volume (ERV), residual volume (RV), and functional residual capacity (FRC) by approximately 20% due to the elevation of the diaphragm by the increasingly large uterus [7] (Figure 1). Dead spaces in the periphery of the trachea and lungs decrease. Furthermore, since immune tolerance increases during pregnancy, pregnant women are more susceptible to severe respiratory infections, such as influenza, SRAS-CoV, and MERS-CoV [4,8,9].

Blood and culture tests in addition to X-rays need to be conducted on pregnant and puerperal women with fever. If necessary, plain chest computed tomography (CT) is recommended. The cause of fever during labor is more likely to be a urinary tract or intrauterine infection than the onset of pneumonia. Furthermore, since the administration of powerful antimicrobial agents is the first-line treatment choice for fulminant group A streptococcal infections, a differential diagnosis is important. When pneumonia is detected on X-rays or by a blood test, community-acquired pneumonia, influenza, and adenovirus infection may also be identified.

Since limited information is currently available on COVID-19, it is necessary to review what is known about coronaviruses (including SARS-CoV and MERS-CoV). Pregnant women develop more severe symptoms and require more intensive care than non-pregnant women. Pregnant women infected with coronavirus are also at a higher risk of premature birth and fetal growth failure. Similar to other respiratory infections, such as influenza, maternal respiratory infections do not directly infect the fetus. Coronavirus infection in early pregnancy is currently not considered to be a direct risk factor for fetal malformations, even infections with SARS-CoV-2 [4,8,9].

On February 2, 2020, the Thai Ministry of Health announced that a doctor administered a combination of the anti-influenza drug oseltamivir (Tamiflu) with lopinavir/ritonavir (Kaletra®), an anti-viral agent used to treat human immunodeficiency virus (HIV) and human hepatitis type C virus (HCV), to a Chinese woman (71 years old) infected with SARS-CoV-2, and marked improvements were subsequently observed in her symptoms (Chinese clinical trial registry identifier: ChiCTR2000029308) [10]. Another clinical institution reported that four patients with

mild or severe COVID-19 pneumonia were cured or showed significant improvements in respiratory symptoms after being treated with lopinavir/ritonavir (Kaletra®), arbidol, and ShufengJiedu Capsule (SFJDC, a traditional Chinese medicine) and supportive care [10]. If a pregnant woman becomes infected with coronavirus, health care providers need to provide adequate fluid replacement and antibiotics when needed in order to prevent secondary bacterial infections.

Puerperal women diagnosed with coronavirus infection and the attenuation of fever are considered to have viral disease and are recommended to refrain from breastfeeding. Healthcare professionals consider the infection to be sustained until 3 days after the attenuation of fever, and need to ensure that all rooms are isolated, hand-washed, and wiped with sodium hypochlorite (0.1%). Breastfeeding may be resumed from the 4<sup>th</sup> day [10]. However, this schedule may change based on future information.

The efficacy of antiviral treatments including lopinavir/ritonavir (Chinese clinical trial registry identifier: ChiCTR2000029308), arbidol, and SFJDC warrants further verification in future studies. Effective prevention and control will be challenging due to sustained transmission and require the full cooperation of the public health sector, federal and local governments, the private sector, and every citizen.

#### **Rules for COVID-19 vaccination for pregnant women**

The COVID-19 pandemic began in 2020, and vaccine development took place in an extremely short time of about half a year. However, sufficient clinical data on efficacy and safety of the vaccine have not been fully elucidated. In Israel, where a large-scale COVID-19 vaccination has commenced, the number of new SARS-CoV-2 infections and the number of severely ill COVID-19 cases have dropped significantly. The frequency of allergic symptoms, including anaphylaxis, after vaccination with COVID-19 vaccine (BNT162b2) developed by Pfizer and BioNTech is estimated to be 0.0011% [11]<sup>11</sup>. In clinical trials of the COVID-19 vaccine, intense pain and redness at the injection site have been reported for several days. However, no fatal adverse events have been reported in clinical trials of the COVID-19 vaccine.

Unfortunately, sufficient medical findings have not been reported in COVID-19 vaccinated pregnant women. As a result, medical information about COVID-19 vaccination against pregnant women varies among countries. The US Advisory Committee on Immunization Practices (ACIP) as CDC Advisory Board on Vaccination announced that pregnant

women should not be excluded from COVID-19 vaccination [12]. In Israel, pregnant women are actively targeted for vaccination. However, COVID-19 vaccination in pregnant women is not recommended in the UK and Canada due to insufficient clinical data on the adverse effects. Studies on the effects of COVID-19 mRNA vaccination (BNT162b2) on animal reproduction have not yet been completed. To date, information on the medium- and long-term side reactions brought about by COVID-19 vaccination in the general population remains scarce.

At present, the ACIP, The American College of Obstetricians and Gynecologists (ACOG), and The Society for Maternal-Fetal Medicine (SMFM) recommend the following:

1. As of February 2021, the mid- to long-term adverse reactions of COVID-19 vaccination in pregnant women and the safety of the fetus and offspring have not been established worldwide.
2. Pregnant women are still subjects for COVID-19 vaccination in light of the current spread of COVID-19 infection. Should pregnant women wish to be injected with COVID-19 vaccination, prior to injection of the vaccine doctors must explain that long-term adverse reactions to COVID-19 vaccination have not been identified and that safety for fetuses and offspring has not been established. Consent of the pregnant woman must be obtained prior to injection of the vaccine, then follow-up the patient in the hospital for 30 min must take place. Until the organogenesis period (up to 12 weeks gestation), pregnant women will not be injected with COVID-19 vaccination. Pregnant women must receive COVID-19 vaccination at obstetrics and gynecology medical facilities where maternal and infant management can be managed, and it is necessary to confirm the fetal heartbeat by ultrasonography before and after COVID-19 vaccination.
3. COVID-19 vaccination is considered for pregnant women as healthcare workers at high risk of SARS-CoV-2 infection, and women with underlying diseases such as obesity and diabetes at risk of aggravation.
4. To prevent SARS-CoV-2 transmission at home, pregnant women's partners should consider COVID-19 vaccination.
5. Women with planned pregnancy are advised to receive COVID-19 vaccination before getting pregnant. (The COVID-19 vaccine is not a live

vaccine, so long-term contraception is not required after vaccination.)

### Conclusion

Pregnant women can be infected with SARS-CoV-2 throughout pregnancy, regardless of age. Late pregnancy, 31 years and older and after 25 weeks, is at risk of aggravation of COVID-19. Therefore, COVID-19 vaccination is recommended for pregnant women's families. Pregnant women are required to take basic actions such as wearing a mask, washing their hands, and staying out of the crowd to prevent SARS-CoV-2 infection.

### Conflicts of interest

None of the authors have any conflicts of interest to report.

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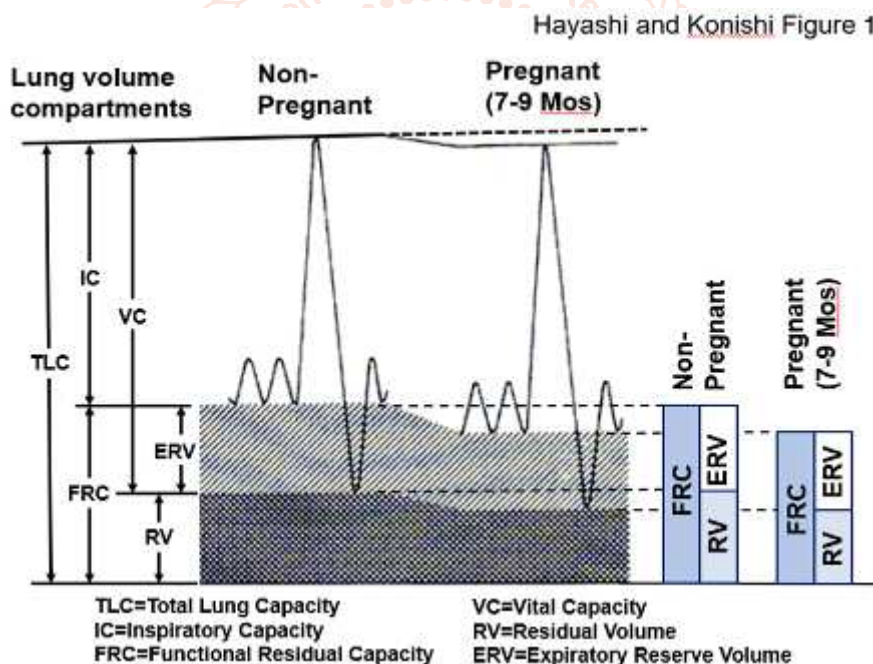
### Author Contributions

T.H. performed most of the preparation for and coordinated the manuscript, and I.K. provided information on clinical medicine and oversaw the manuscript.

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**Figure 1 Effects of pregnancy on pulmonary function. Residual volume (RV) and functional residual capacity (FRC) gradually decrease, while vital capacity (VC) and total lung capacity (TLC) remain the same. In the later stages of pregnancy, an increased tidal volume reduces the expiratory reserve volume (ERV), residual volume (RV), and functional residual capacity (FRC) by approximately 20% due to the elevation of the diaphragm by an increasingly large uterus.(Elkus R, Popovich J: Respiratory physiology in pregnancy. Clin Chest Med 13:558, 1992)**