

Management of COVID-19 infection during pregnancy

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Introduction

“COVID-19” came into our lives in November 2019, and has since created havoc around the globe. This infection is caused by the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2), which is a single chain, enveloped RNA virus¹. The index case was reported on 17th November 2019 from Hubei province, China, and it is believed to be of animal origin². Thereafter, the outbreak of COVID-19 infection has rapidly spread worldwide causing significant morbidity and mortality, including among pregnant mothers.

This was named as “COVID-19” by the WHO (World Health Organization) on 11th February 2020 and declared as a global pandemic on 11th March 2020². More than 2.4 billion cases have been reported so far, with nearly 5 million deaths. The pandemic has affected countless more lives as relatives and friends of those who were infected. The economic and psychological impact of the many lockdowns and new health regulations is seen even today.

In Sri Lanka, more than 530,000 people have been infected and nearly 13,700 have died, including 56 maternal deaths. The impact of COVID-19 infection on pregnancy and the fetus has been evaluated

worldwide, and management guidelines have been issued by leading organizations including RCOG (Royal College of Obstetricians and Gynaecologists), ACOG (American College of Obstetricians and Gynaecologists) and FIGO (International Federation of Gynaecology and Obstetrics)^{3,4,5}. However, there is no well-established data on management of COVID-19 infection during pregnancy, since it is a new infection. Initially it was believed that pregnancy conferred a higher risk of disease morbidity and mortality, but currently, CDC (Center for Disease Control in USA) states that pregnancy has no additional risk of disease infectivity compared to the non-pregnant population⁶.

Disease transmission

COVID-19 infection is transmitted via respiratory droplets exhaled by infected patients through direct contact or through contaminated surfaces. Vertical transmission from mother to baby is a rare event and it will not depend on mode of delivery, delayed cord clamping or mode of baby feeding^{7,8}.

Symptoms and signs

Symptoms and signs of COVID-19 during pregnancy are not different from non-pregnant patients (Table 1).

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More than 75% of the patients are asymptomatic and only 15-20% of patients present with symptoms⁹. Among the symptomatic patients, majority have mild symptoms, less than 5% will have the severe disease requiring ICU admissions and less than 1% require invasive ventilatory support⁹.

Majority of the symptomatic patients presented with cough (41%), fever (40%), shortness of breath (21%) and tiredness^{10,11,12}. Less common symptoms include sore throat, headache, diarrhea, loss of taste or smell, nausea / vomiting and rhinorrhea^{10,11,2}. However, some of these symptoms are difficult to differentiate from symptoms due to normal physiological changes in pregnancy including physiological shortness of breath, nausea/vomiting and fatigue. Therefore, during the assessment of a pregnant mother more specific symptoms should be concerned.

Depending on the symptoms and signs, patients are

categorized as asymptomatic, mild disease, moderate disease, severe disease and critical disease (Table 2).

Severe disease is mostly confined to the third trimester of the pregnancy⁹. Shortness of breath / difficulty in breathing, chest pain and confusion are the alarming symptoms of severe disease. Pregnant mothers with risk factors are more vulnerable to develop severe disease¹¹. Risk factors for severe disease include obesity (BMI more than 25), age more than 35 years, Black-Asian origin, being on immunosuppressive drugs, working in healthcare or public facing occupations and presence of comorbidities like diabetes, hypertension, asthma, heart disease, chronic liver disease, chronic lung disease, chronic kidney disease, organ transplantation and malignancies¹¹. However, compared to non-pregnant women, pregnant women are more likely to be admitted to the ICU (OR 1.62) and more likely to require intubation and mechanical ventilatory support (OR 1.88)¹⁰.

Table 1. Symptoms of COVID-19 infection

Common symptoms	Cough Shortness of breath Fever Tiredness
Less common symptoms	Sore throat Headache Diarrhea Loss of taste or smell Nausea/vomiting Rhinorrhea
Serious symptoms	Shortness of breath / difficulty in breathing Chest pain Confusion

Table 2. Categorization of COVID-19 infection

Categorization	Symptoms and signs
Asymptomatic	No clinical symptoms or signs
Mild disease	Mild symptoms present No shortness of breath / dyspnoea Chest Xray – normal
Moderate disease	Evidence of viral pneumonia present Oxygen saturation 90-94% (with or without oxygen) No increase of work of breath (WOB) Respiratory rate <30/min Chest Xray involvement <50% Vital parameters stable PaO ₂ /FiO ₂ ratio >300
Severe disease	Evidence of severe viral pneumonia Oxygen saturation <90% Work of breath increased Respiratory rate >30/min Chest Xray involvement >50% Vital parameters not stable PaO ₂ /FiO ₂ ratio >300
Critical disease	Severe disease with a multi organ failure ARDS, sepsis, septic shock, complications such as pulmonary embolism and acute coronary syndrome

ARDS - Acute Respiratory Distress Syndrome

Investigations and diagnosis

RT-PCR

RT-PCR (reverse transcriptase polymerase chain reaction) test is the gold standard for diagnosis of COVID-19 infection in pregnancy¹³. The specificity of RT-PCR test is almost 100% and sensitivity is 70%¹⁴. The patients who are suspected to have COVID-19 infection based on symptoms, should undergo RT-PCR test for SARS-CoV-2 RNA using nasopharyngeal swab¹³. If the initial test result is negative but with high suspicion of the disease, RT-PCR test should be repeated.

RAT

RAT (rapid antigen test) is used as a diagnostic test for COVID-19 infection in certain conditions when urgent diagnosis is required, and it also used as a screening test. It is also performed using a nasopharyngeal swab. The main advantage of the test is that it requires only 15-30 minutes to receive the results, whereas RT-PCR takes 48-72 hours. However, it has a low sensitivity and specificity compared to RT-PCR¹⁵. Recent meta-analysis has found that sensitivity and specificity of RAT for SARS-CoV-2 virus is 56.2% and 99.5% respectively¹⁶. Positive predictive value of a positive result of RAT test is high, and it is higher than RT-PCR¹⁵.

Chest Xray

Chest Xray is particularly important in suspected cases of COVID pneumonia. Findings of chest Xray include patchy multi-focal opacities. However, chest Xray findings of COVID pneumonia can be seen only in advanced disease¹⁷. There is a clear indication of chest Xray in advanced disease, however risk/benefit ratio must be considered when it is being used in less severe cases.

CT chest

CT chest is considered the imaging method of choice in the diagnosis of COVID pneumonia¹⁸. This was widely used before the RT-PCR was freely available to diagnose COVID pneumonia. Sensitivity and specificity of CT chest are 97% and 25% respectively with positive predictive value of 65%¹⁹. Characteristic CT findings help to diagnose COVID pneumonia, including bilateral, subpleural, patchy and multi-focal opacities with ground glass appearance and peripheral consolidation^{20,21}. These features can be seen one to three weeks after the onset of infection¹⁷.

USS chest

Ultrasound scanning of chest can be used to diagnose COVID pneumonia in pregnancy¹⁸. It has high sensitivity (>90%) and specificity (>95%)²². Ultrasound findings of COVID pneumonia includes patchy distribution of interstitial artifactual signs, extended distribution of interstitial artifactual signs and small subpleural consolidation¹⁸.

MED test

MED (modified exertional desaturation) test is a bedside clinical test used to detect subclinical COVID pneumonia in patients who are not on oxygen therapy and whose oxygen saturation is more than 96%. Patients resting oxygen saturation is measured. The patient is asked to sit and stand for 1 minute and, then to rest for 30 seconds. Post exertional oxygen saturation is measured. Positive test result is indicative of subclinical COVID pneumonia.

Treatment

Asymptomatic patients and patients with mild symptoms can be managed in the home setting under the direct supervision of field health authority / MOH (Medical officer of health). Patients with moderate to

severe disease and symptomatic high risk groups should be managed in a dedicated hospital setup (preferably at a specialized COVID-19 care center), with a multidisciplinary involvement including physician, intensivist, obstetrician and neonatologist. Most of the drugs used to treat the COVID-19 infection do not have a proven safety profile in pregnancy. Key management aspects of the treatment of COVID-19 infection during pregnancy are summarized in table 3.

Oxygen therapy

Physiological changes in the pregnancy are important to maintain fetal oxygenation, and thus oxygen therapy for patients with COVID-19 in pregnancy is challenging. WHO recommends to maintain oxygen saturation between 92-95% and $\text{PaO}_2 > 70\text{mmHg}$ to minimize fetal hypoxia, and the RCOG recommendation is to maintain the oxygen saturation above 94%^{3,23}. Prone ventilation is a well-accepted way to improve oxygenation, and according to available data, it is a safe option in pregnancy²⁴.

Steroid therapy

RCOG recommends steroids (oral prednisolone 40 mg once daily or IV hydrocortisone 80 mg twice daily for 10 days or until discharge) if the patient has needed oxygen therapy³. Further, low dose dexamethasone therapy has proven benefit of reducing mortality in severe disease. It reduces mortality by 20% in the mothers who receive oxygen therapy and by 33% in the mothers who are ventilated (RECOVERY trial)²⁵. Dexamethasone is categorized as a pregnancy category C drug according to UK-MEC (medical eligibility criteria) due to its fetal side effects. However, ACOG recommends the use of dexamethasone in the management of COVID-19 infection in pregnancy when indicated, especially in ICU patients who are mechanically ventilated^{4,26}.

Antibiotics

Routine antibiotic administration is not recommended unless a superadded bacterial infection is suspected³.

LDA

LDA (low dose aspirin) is recommended to continue in patients with high risk of developing preeclampsia³. However, COVID-19 infection is associated with thrombocytopenia in some patients and in such patients, LDA should be discontinued³.

Table 3. Management of COVID-19 infection

Categorization	Management
Asymptomatic	<p>Can be managed in the home setting</p> <p>Observe for 10-14 days (supervised observation)</p> <p>Look for alarming symptoms and signs (SpO₂<96% with or without exertion, SOB, chest pain, altered mental status)</p> <p>Monitor saturation, respiratory rate, temperature</p> <p>Continue LDA (add if indicated)</p> <p>Daily MED test</p> <p>Supervised care via telecommunication / web-based communication</p>
Mild disease	<p>Can be managed in the home setting (POA>28 weeks with high risk factors should be admitted and closely monitored)</p> <p>Observe for 10-14 days (supervised observation)</p> <p>Symptomatic management for mild symptoms (antipyretics, antihistamines, bronchodilators)</p> <p>Look for alarming symptoms and signs (SpO₂<96% with or without exertion, SOB, chest pain, altered mental status) – if present need urgent admission to hospital-based care</p> <p>Monitor saturation, respiratory rate, pulse rate, temperature</p> <p>Continue LDA (add if indicated)</p> <p>Daily MED test</p> <p>Supervised care via telecommunication / web-based communication</p>
Moderate disease	<p>Need hospital-based care (need isolation)</p> <p>Close monitoring of vital signs and disease progression (may need ICU admission, early intubation and mechanical ventilation if disease progresses)</p> <p>Monitor for development of multiorgan failure</p> <p>Daily investigations (FBC, CRP, RFT, LFT, LDH)</p> <p>Oxygen therapy and monitor oxygen saturation closely</p> <p>Start triple therapy (LMWH, dexamethasone, antibiotics) and triple maneuvers (oxygen therapy, cyclical proning, strict bed rest with preoxygenation before exertion)</p> <p>MDT care including physician, intensivist and obstetrician</p>

(Continued)

Categorization	Management
Severe disease	Need ICU care Close monitoring of vital signs and disease progression Monitor for development of multiorgan failure Monitor investigations closely Monitor IL-6 level Continue triple therapy and triple maneuvers MDT care including physician, intensivist, obstetrician and neonatologist Early intubation and mechanical ventilation Consider Tocilizumab – if criteria fulfilled Consider REGEN-COV Consider termination of pregnancy if required
Critical disease	ICU care Continue mechanical ventilation Continue triple therapy and triple maneuvers Continue close monitoring of vital signs, lab investigations and disease progression Continue MDT care IV Tocilizumab (if criteria fulfilled) Termination of pregnancy if required

SOB – shortness of breath, LDA – low dose aspirin, MED test – modified exertional desaturation test, ICU – intensive care unit, FBC – full blood count, CRP – C reactive protein, RFT – renal function tests, LFT – liver function tests, LDH – lactate dehydrogenase, LMWH – low molecular weight heparin, IL-6 – interleukin 6, MDT – multi disciplinary team

Thromboprophylaxis – LMWH

COVID-19 infection is associated with increased risk of thromboembolic disease due to an excessive inflammatory reaction caused by the disease²⁷. Pregnancy itself is considered as a hypercoagulable state due to the physiological changes which occur. Theoretically, pregnant mothers have an added risk of thromboembolic disease during the infection. Therefore, all pregnant mothers who are admitted due to COVID-19 infection should be assessed by VTE risk assessment tools³. RCOG recommends to administer VTE (venous thromboembolism) prophylaxis with LMWH (low molecular weight heparin) for 10 days or until discharge, for all pregnant mothers

admitted with confirmed or suspected COVID-19 infection unless there is a contraindication³.

Tocilizumab

Tocilizumab is an Interleukin-6 inhibitor, and it is used to inhibit the inflammatory process caused by COVID-19 infection. Its safety in pregnancy and lactation is not well established. However, available observational studies have shown positive effect in reducing mechanical ventilation and death in non-pregnant women²⁸. RCOG strongly recommends the use of Tocilizumab (400-800mg single IV infusion) if the CRP value is 75mg/l or more or if the patient is admitted to ICUi-3.

REGEN-COV

REGEN-COV is a combination of monoclonal antibodies – casirivimab and imdevimab. U.S. FDA (United States Food and Drug Administration) authorizes the use of REGEN-COV as a therapy for post exposure prophylaxis of COVID-19 infection, and to prevent severe disease in high risk groups²⁹. RCOG strongly recommends the use of REGEN-COV (8g single IV infusion) in patients whose SARS-CoV-2 antibodies are negative³.

Remdesivir

Recently developed Remdesivir is a viral RNA polymerase inhibitor. Remdesivir has recently been approved by FDA for use in COVID-19 infection. However, well-established data on the use of Remdesivir in pregnancy is sparse. According to RCOG guidelines, its use is limited to patients who are not improving and those who are deteriorating³.

Azithromycin

Azithromycin is not recommended to use in pregnancy due to lack of proven benefit³.

Hydroxychloroquine

Hydroxychloroquine is not recommended to use in pregnancy due to lack of proven benefit³.

Lopinavir/Ritonavir

Lopinavir/Ritonavir is not recommended to use in pregnancy due to lack of proven benefit³.

Maternal complications

Complications of COVID-19 infection during pregnancy includes ARDS, respiratory failure, pneumonia, sepsis, septic shock, venous-thromboembolism, multiorgan failure and death. Estimated risk of COVID-19 associated maternal mortality is 2.4/100,000³⁰.

Further, increased risk of perinatal mental health disorders including maternal depression and anxiety has been identified³.

Neonatal complications

Available data do not suggest an increased risk of congenital anomalies, miscarriages or early pregnancy

loss due to COVID-19 infection^{f-1}. However, there is an increased risk of preterm delivery (6%), small for gestational age and still birth^{3,31,32,33}. Most of the preterm births are due to iatrogenic causes^{31,32,33}. Recent meta-analysis found that there is an increased risk of premature rupture of membranes and fetal hypoperfusion³⁴.

Vertical transmission

There is no conclusive evidence on transplacental transmission of the disease, and it is thought to be rare.

Delivery

Vaginal delivery or caesarean section confers no additional risk on the disease progression of COVID-19 infection. Therefore, mode of delivery during COVID-19 infection should be decided on an individualized basis depending on the obstetric indications and the severity of the disease. However, decision making should be based on MDT input including the obstetrician, physician and neonatologist. When iatrogenic preterm delivery is planned, antenatal corticosteroids for fetal lung maturation and MgSO₄ for fetal neuroprotection should be administered.

Strict aseptic precautions should be adhered by the staff members who are involved in the delivery, and minimum number of staff members with full PPE (personal protective equipment) should be utilized. Emergency obstetric, anaesthetic and neonatal facilities should be readily available. CEFT (continuous electrical fetal monitoring) is not recommended routinely but recommended for all symptomatic patients³. Fetal blood sampling and scalp electrode are not contraindicated during COVID-19 infection. Delayed cord clamping and skin to skin contact of the baby should be allowed if the condition permits.

Water birth is not contraindicated for asymptomatic patients. However it is not recommended for symptomatic patients³.

Postnatal care

Routine postnatal care should be offered to all patients with COVID-19 infection³. Both mother and baby should be managed together unless there is a maternal or neonatal indication.

Breast feeding

Breastfeeding should be encouraged since benefits of breastfeeding outweigh the potential risk of neonatal infection via breast milk. There is no proven evidence of transmitting the virus via breastmilk³⁵. There is a risk of transmitting the disease from mother to neonate via direct contact. However, this can be minimized by wearing a facemask and by good hand hygiene³⁵. In case of expressed breastmilk, a breast pump is recommended with careful cleaning of the pump before and after each use³⁵.

Summary

Majority of the pregnant mothers infected with COVID-19 infection are asymptomatic. Among the symptomatic patients, majority have mild symptoms. Both these groups can be managed in a home-based setting. However, supervised observation and effective communication should be maintained to identify alarming symptoms and signs early. Patients with moderate to severe disease should be managed at hospital-based setting and close monitoring should be done to identify disease progression, development of multi organ failure and critical disease.

Early identification of alarming symptoms and signs, early hospitalization of the patients with moderate to severe disease, early intubation and mechanical ventilation and effective MDT management are the key steps in reducing maternal morbidity and mortality associated with COVID-19 infection.

Author declarations

Conflicts of interest: No conflicts of interest.

References

1. Corona virus Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nature Microbiology*. 2020; 5(4): 536-544.
2. WHO. Rolling updates on coronavirus disease (COVID-19). 2020. Accessed via <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>
3. RCOG guideline on Coronavirus (COVID-19) infection in pregnancy. Published on 24th July 2020. Available at <https://www.rcog.org.uk/globalassets/documents/guidelines/2021-08-25-coronavirus-covid-19-infection-in-pregnancy-v14.pdf>
4. ACOG practice advisory on Novel coronavirus 2019 (COVID-19) published on November 2020. Available at <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019>
5. FIGO statement on Safe motherhood and COVID. March 2021 update. Available at <https://www.figo.org/safe-motherhood-and-covid-19-march-2021-update>
6. CDC. Investigating the impact of COVID-19 during pregnancy. Available at <https://www.cdc.gov/coronavirus/2019-ncov/downloads/cases-updates/covid-fs-Pregnancy.pdf>
7. Walker KF, O'Donoghue K, Grace N, Dorling J, Comeau JL, Thornton JG. Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis. *BJOG* 2020; 127(11): 1324-1336
8. Jimenez IM, Lopez RS, Garcia RE, Rodriguez DLTI, Montes GJ, De la Cruz CML, et al. Umbilical cord clamping and skin-to-skin contact in deliveries from women positive for SARS-CoV-2: a prospective observational study. *BJOG* 2021; 128(5):908-915
9. Vousden N, Bunch K, Morris E, et al. The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: A national cohort study using the UK Obstetric Surveillance System (UKOSS). *PLoS One* 2021;16:e0251123
10. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, Debenham L, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020; 370: m3320.
11. Knight M, Bunch K, Vousden N, Morris E, Simpson N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population-based cohort study. *BMJ* 2020; 369: m2107.
12. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei C, Hui DSC, Du B, Li L, et al.; China medical treatment expert group for

- Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *New England Journal of Medicine* 2020; 382(18):1708-1720.
13. Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, Biswas A, Choolani M, Mattar C, Su LL. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *American Journal of Obstetrics and Gynecology* 2020; 222(6): 521-531
 14. Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. *JAMA*. 2020; 323(22): 2249-2251.
 15. Revised guideline on laboratory testing strategy for COVID 19, Ministry of Health Sri Lanka. Available at http://epid.gov.lk/web/images/pdf/Circulars/Corona_virus/laboratory_testing_strategy.pdf
 16. Coronavirus disease 2019 (COVID-19): interim guidance for antigen testing for SARS-CoV-2 CDC (2021) Revised April 13, 2021. Available at <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html>
 17. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 20:425-434.
 18. Inchingolo R, Smargiassi A, Moro F, Buonsenso D, Salvi S, Giacomo PD, Scoppettuolo G, Demi L, Soldati G, MD; Testa AC. The diagnosis of pneumonia in a pregnant woman with coronavirus disease 2019 using maternal lung ultrasound, July 2020. *American Journal of Obstetrics & Gynecology*. 2020; 223(1): 9-11.
 19. Ai T, Yang Z, Hou H, Zhan C, Chen C, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: a Report of 1014 Cases. *Radiology*. 2020; 296(2): E32-40.
 20. Salehi S, Abedi A, Balakrishnan S, Gholamreza-zadeh A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *American Journal Roentgenol*. 2020; 215: 87-93.
 21. Committee opinion no. 723: Guidelines for diagnostic imaging during pregnancy and lactation. *Obstetrics and Gynecology* 2017; 130: 933-934. Available at <https://pubmed.ncbi.nlm.nih.gov/28937575/>
 22. Smargiassi A, Inchingolo R, Soldati G, Copetti R, Marchetti G, et al. The role of chest ultrasonography in the management of respiratory diseases: document II. *Multidisciplinary Respiratory Medicine*. 2013; 8(1): 55.
 23. Wu Y, Zhang C, Liu H, Duan C, Li C, Fan J, et al. Perinatal depressive and anxiety symptoms of pregnant women during the coronavirus disease 2019 outbreak in China. *American Journal of Obstetrics and Gynecology*. 2020; 223(2): 240.e1-240.e9
 24. Dennis AT, Hardy L, Leeton L. The prone position in healthy pregnant women and in women with preeclampsia – a pilot study. *BMC Pregnancy Childbirth*. 2018; 18 (1): 445
 25. RECOVERY (Randomised Evaluation of COVid-19 thERapY) trial Low-cost dexamethasone reduces death by up to one third in hospitalised patients with severe respiratory complications of COVID-19. 2020. https://www.recoverytrial.net/files/recovery_dexamethasone_statement_160620_final.pdf
 26. Saad AF, Chappell L, Saade GR, Pacheco LD. Corticosteroids in the management of pregnant patients with coronavirus disease (COVID-19). *Obstetrics and Gynecology*. 2020; 136(4): 823-826.
 27. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res*. 2020; 191: 145-147.
 28. Xu X, Han M, Li T, Sun W, Wang D, Fu B, et al. Effective treatment of severe COVID-19 patients with tocilizumab. *PNAS* 2020; 117: 10970-5.
 29. U.S. Food and drug Administration (FDA). FDA authorizes REGEN-COV monoclonal antibody therapy for post-exposure prophylaxis (prevention) for COVID-19. Available at <https://www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-regen-cov-monoclonal-antibody-therapy-post-exposure-prophylaxis-prevention-covid-19>
 30. Knight M, Bunch K. MBRRACE-UK : Saving Lives, Improving Mothers' Care. Rapid report 2021: Learning from SARS-CoV-2-related and associated maternal deaths in the UK June 2020-March 2021. Oxford, National Perinatal Epidemiology Unit, University of Oxford 2021. Available at https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/MBRRACE-UK_Maternal_Report_June_2021_-_FINAL_v10.pdf

31. Yan J, Guo J, Fan C, Juan J, Yu X, Li J, et al. Coronavirus disease 2019 (COVID-19) in pregnant women: a report based on 116 cases. *American Journal of Obstetrics and Gynecology*. 2020; 223(1): 111.e1-111.e14
32. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, et al. Outcome of Coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *American Journal of Obstetrics and Gynecology MFM*. 2020; 2(2):100107.
33. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020; 370:m3320.
34. Dubey P, Reddy SY, Manuel S, Dwivedi AK. Maternal and neonatal characteristics and outcomes among COVID-19 infected women: an updated systematic review and meta-analysis. *European Journal of Obstetrics Gynecology and Reproductive Biology*. 2020; 252:490-501.
35. Davanzo R, Moro G, Sandri F, Agosti M, Moretti C, Mosca F. Breast feeding and coronavirus disease-2019: Ad interim indications of the Italian Society of Neonatology endorsed by the Union of European Neonatal & Perinatal Societies. *Maternal and Child Nutrition*. 2020; 16(3):e13010.