

Review Article: A Review on the Effect of COVID-19 in Pregnant Women



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ABSTRACT

Coronavirus Disease 2019 (COVID-19) is an emerging disease with a rapid increase in cases and deaths since its first discovery in December 2019, in Wuhan, China. Limited data are available on COVID-19 effects during pregnancy; however, information on diseases associated with other highly pathogenic coronaviruses (i.e. Severe Acute Respiratory Syndrome [SARS] and the Middle East respiratory syndrome [MERS]) may provide insight into the effects of COVID-19 during pregnancy. Coronaviruses cause illnesses ranging from the common cold to severe respiratory disease and death. The data indicate an average of 5 days incubation period (range: 2-14 days). The average age range of the hospitalized patients was 49-56 years, and a third to half of them have an underlying illness. Children were rarely mentioned. Within hospitalized cases, men were more frequent (54%-73%). Fever, cough, myalgia, vomiting, and diarrhea are common symptoms. This review aims at giving an in-depth understanding of COVID-19 by comparing its effects with SARS and MERS to evaluate its severity in pregnant women. The results of varied studies show that COVID-19 affects pregnant women seriously and there is an alarming need to look into this aspect to prevent its harmful effects on the fetus.

Introduction

Scientists have recently revealed to the world their discovery of a novel disease that is an enhanced type of coronavirus. The novel COVID-19 (Coronavirus Disease 2019) has been reported as an outbreak of respiratory disease. On December 31, 2019, 27 cases of unknown etiology were registered in Hubei City of Wuhan. The Wuhan Municipal Health Commission had confirmed the identification of another seven cases of the same respiratory disease. There were some common symptoms in those cases (i.e.

dry cough, high fever, and complicated dyspnea) [1-3]. Besides, they tested positive patients infected with COVID-19 to produce radiological results of bilateral lung infiltrates by analyzing their bodies [1]. The onset of symptoms normally starts within 14 days of exposure. COVID-19 symptoms vary from mild to severe and may include shortness of breath, cough, myalgia, fever, and extreme pneumonia. The vital organs (kidney, heart, liver) might also be affected. The extent of the infection will depend on the individual's health status, and patients with pre-existing diseases such as diabetes and lung disease, as well as the elderly, are more vulnerable to rapidly-developing COVID-19.

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However, in Hubei, from 15 to about 59 cases were suspected of being contaminated with COVID-19. This coronavirus outbreak was revealed to the public on January 22, 2019, and was listed as an epidemic, sharing all details on the disease movement [2]. Nevertheless, the Center for Control Disease (CDC) announcement about finding the novel COVID-19 coronavirus prompted the World Health Organization (WHO) to declare emergency cases. It is attributed in addition to the prevalence of this novel virus in Chinese provinces, to confirm many cases globally. The province of Hubei was confirmed as the highest infected region with about 75% of cases involved [3].

Coronaviruses (CoVs) belong to the Coronavirinae subfamily of the Nidovirales order in the Coronaviridae family [4]. The CoVs are RNA viruses that are enveloped with the genome consisting of a single-stranded positive-sense RNA (+ ssRNA), ~30 kb with a 5'-cap structure, and 3'-polyA tail. The large CoV genome is related to the unique characteristics of the CoV RTC, which includes multiple RNA processing enzymes and encodes for several structural proteins (sps) and non-structural proteins (nsps). Sps that play a critical role in the transcription and synthesis of viral RNA are referred to as replicase-transcriptase proteins, while nsps, often referred to as niche-specific proteins, are non-essential for virus replication but confer selective benefits for survival and tissue invasion [5-9]. The CoVs are further broken down into four sections: A through D. Lineage B includes the extreme acute respiratory syndrome (SARS)-CoV and the novel SARS-CoV-2, while lineage C involves CoV linked to the Middle East respiratory syndrome (MERS) [5]. Until last year, the six human CoVs were known:

HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1, SARS-CoV, and MERS-CoV [10]. The newest and most virulent member of the CoV family that can infect humans is the SARS-CoV-2 or 2019-nCoV6.

Studies in pregnant women with COVID-19 have shown few maternal and neonatal complications to date but more specific evidence is needed as these studies include a limited number of people over a short period. Importantly, viral respiratory diseases, such as influenza, can propagate easily during pregnancy, suggesting that pregnant women can be more vulnerable to COVID-19 and need priority medical attention [11]. CDC and the World Health Organization (WHO) currently provide interim COVID-19 recommendations for successful counseling and education of pregnant women. Recommendations that came out after the COVID epidemic in Wuhan are also available from Chinese experts. This review tries to discuss the knowledge available on handling COVID-19, SARS, and MERS during pregnancy to protect mothers' and children's health in this crucial situation. We utilized PubMed, Embase, and Nature Research databases to collect and analyze various research studies related to virus and pregnancy.

SARS and its Effect on Pregnant Women

SARS-coronavirus (SARS CoV) causes severe, acute respiratory syndrome (SARS). News of the SARS-CoV outbreak emerged in February 2003, with the first cases observed in Guangdong Province, China [RH Xu et al., 2004]. The virus spread throughout the world to over 30 countries, resulting in more than 8000 cases and 770 deaths [12-15]. The epidemic was brought under control

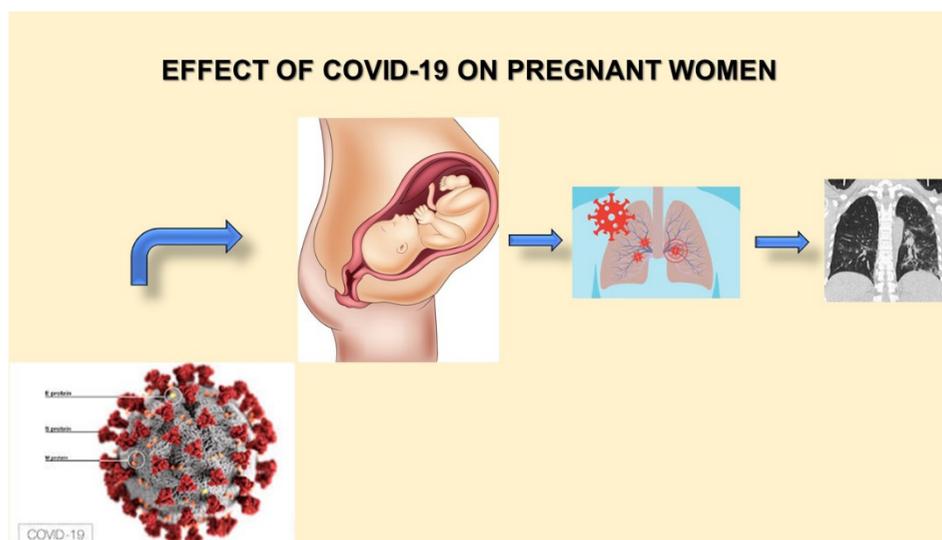


Figure 1. Graphical abstract

after public health control measures were put in place to avoid contact with infected individuals, and no cases have been seen since 2004. SARS manifests include nausea, chills, headache, malaise, and myalgia.

In some patients, diarrhea was also found. Pneumonia has almost always been seen in patients diagnosed with SARS, requiring mechanical ventilation in 10%-20% of cases. The fatality rate of the case was estimated at 9%-10%. It is thought that bats are the natural reservoir for SARS-CoV; however, some evidence supported civet cats or raccoon dogs as potential intermediate reservoirs of these diseases. SARS is transmitted by close person-to-person contact through a touch of the respiratory tract mucous membranes with respiratory droplets produced when an infected person coughs or sneezes [14]. There were also records of fecal-oral and fomites transmission. Airborne transmission may also be possible due to the inhalation of small particulate aerosols [15]. During the 2003 outbreak, transmission in health care settings was frequently seen, with superspreading (when a single patient transmits the infection to a disproportionate number of contacts) recorded [16]. The incubation period was calculated to be 4.6 days on average, with a range of 2-14 days.

Transmission tended to occur more frequently during the second week of illness when there is maximum viral excretion; there is no indication that a person with SARS is infectious before the onset of the symptoms. The largest case series of pregnant women with SARS was reported in the 2003 Hong Kong epidemic with 12 pregnant women [17]. The rate of case-fatality was 25% (three deaths). Clinical and laboratory results in the non-pregnant population were close to those observed. Pneumonia was seen in all patients on a chest x-ray or CT. Significant medical complications included four-fold adult respiratory distress syndrome, three-fold intravascular coagulopathy, three-fold renal insufficiency, two-fold secondary bacterial pneumonia, and two-fold sepsis [18].

There is approximately 90% homology between the SARS-CoV-2 genome and CoV bat viruses, bat-SL-CoVZC45, and bat-SL-CoVZXC21, while homology is approximately 96% with the bat SARS-like CoV (bat-CoV-RaTG13) genome [19]. There is consensus in the scientific community on the origin of the SARS-CoV-2 in horseshoe bats. But the 2019-nCoV bat-SL-CoVZC45 and bat-SL-CoVZXC21 are not immediate ancestors. The bat CoV can then infect another species, an intermediate host, which later transmitted the virus to humans. The isolation of a CoV with a high resemblance to SARS-CoV-2 in the Malayan pangolins candidates these species as the possible intermediate host [7, 8]. The ge-

netic sequence of CoV, found in Malayan pangolin lung samples, has a similarity of ~91% to SARS-CoV-2. The pangolin CoV also demonstrates 100%, 98.2%, 96.7%, and 90.4% amino acid similarity with the genes of SARS-CoV-2 E, M, N, and S, respectively [20, 21]. The CoVs of ancestor bat has a dissimilarity of 19 amino acids, while the CoV of pangolin has just 5 different amino acids from SARS-CoV-2 to the S protein. In particular, the pangolin-CoV receptor-binding domain of the S protein is nearly identical with that of SARS-CoV-2, with one amino acid difference.

In addition, in the experimental models, the infected pangolins exhibit clinical signs and histopathological features similar to SARS-CoV-2 and harbor the antibodies that associate with the SARS-CoV-2 protein. The genetic sequence analysis of bat CoVs, pangolin CoV, and SARS-CoV-2 appears to connect to the CoVs, indicating that bats and pangolin viruses could have exchanged genes at some stage before spilling and infecting people. Therefore, the pangolins are the most likely intermediate host while other possible intermediate host(s) cannot be ruled out [9]. COVID-19 is a global public health emergency, and during pregnancy may cause catastrophic health problems. Because of their altered physiological and immunological roles, pregnant women have a high propensity to get this infection. Previous studies have shown that during childbirth, SARS is associated with a high risk of spontaneous miscarriage, preterm birth, and restriction of intrauterine development [10]

During the SARS epidemic, many hospitals in Toronto and Hong Kong announced initiatives to decrease transmission to pregnant women, their families, community members, and health care workers. For example, at the hospital entrance, all medical personnel, patients, and visitors were screened for symptoms and should wear N95 respirators [16]. On work and delivery, the visitors were limited to one patient each, with no visitors permitted in the postpartum unit. Postpartum stays were reduced in time, with the addition of a postpartum nursing home visit. Postpartum patients were asked to observe a quarantine at home for 10 days [22]. Health care workers were forced to observe a quarantine of work in which they were told to go straight from home to work, and vice versa, to avoid group contact [23]. Suspended obstetric services considered non-essential, such as daily ultrasound and prenatal diagnosis (Table 1). Although the effect of these interventions has not been assessed, there might be some important lessons gained from these experiences during SARS that could help inform the COVID-19 approach.

MERS and its Effects on Pregnant Women

The Middle East Respiratory Syndrome (MERS) is a respiratory disease caused by MERS CoV. The disease was first reported in Saudi Arabia in 2012, spreading to other Arab peninsula countries and eventually to the outside, including the United States. The Republic of Korea's biggest outbreak outside the Arabian Peninsula happened in 2015. Nearly 2500 cases of MERS-CoV disease and more than 860 deaths were reported with continuing studies into the present [4]. MERS symptoms include extreme respiratory illness, including fatigue, cough, and shortness of breath. Some patients get diarrhea, too. The fatality rate of the event is estimated at 35%-40%. Patients who developed MERS were more likely to be older and around two-thirds of the patients were male (median age is 50 years). MERS patients were also more likely to experience an underlying illness [8].

Some patients with MERS-CoV infection were asymptomatic (identified by touch inquiries). The mean time of incubation is 5.2 days, ranges from 2 to 13 days. Similar to SARS, MERS is primarily transmitted person-to-person via close contact. The transmission was observed in health care settings and events of superspreading occurrence. However, the number of MERS-CoV cases has been dramatically reduced since 2016, thanks to public health efforts to prevent MERS-CoV transmission [16]. Information regarding MERS is limited among pregnant women (Table 1).

We received reports from several countries on 13 cases of pregnant women with MERS, including Saudi Arabia [8], Korea [2], Jordan [1], the United Arab Emirates [1], and the Philippines [1]. Two women were identified as being asymptomatic as part of a contact inquiry. Of 11 women with symptoms, signs were close to those seen in non-pregnant MERS patients [17]. Both babies born to asymptomatic women were born safely on term; among those who were symptomatic, there was one intrauterine fetal demise, one stillbirth, one baby delivered at 25 weeks, who died 4 hours after birth, two safe preterm

infants and five healthy term infants (no infant status was reported for one case) [25].

Transmission of COVID-19

2019-nCoV is a single-stranded, non-segmented, enveloped RNA virus belonging to a diverse group of zoonotic (i.e. animal- and human-capable pathogens) viruses. Seven coronaviruses that could infect humans have been identified so far. Two lethal viruses, SARS-CoV-1 and MERS CoV belong to the same viral community as 2019-nCoV. As this pathogen has a similar receptor-binding domain structure to that of SARS-CoV-1, COVID-19 and SARS are likely to have similar pathogenesis. Such viruses tend to be transmitted primarily by contact between the person and the host. The route of transmission is mainly through the infected person's respiratory droplets into the air, which is then deposited on surfaces nearby. The virus may potentially spread to the infected individual within a distance of less than 2 m (6 feet). Given that the virus can live on non-living surfaces, regular cleaning of touched surfaces is important 18-20. To date, no medications or vaccines have been approved to treat COVID-19 or to prevent it. Therefore, it is necessary to enforce preventive measures to prevent its further spread.

Symptoms of COVID-19

The onset of symptoms normally occurs within 14 days of exposure. COVID-19 symptoms vary from mild to severe, and may include shortness of breath, cough, myalgia, fever and extreme pneumonia. Injury also occurred to vital organs (kidney, heart, liver). The extent of the infection will depend on the individual's underlying health, with patients with pre-existing diseases such as diabetes and lung disease, as well as the elderly, being more vulnerable to COVID-19 rapidly developing [21].

Table 1. SARS and MERS: Effect on pregnant women

Name of the Virus	Total Cases	Total Deaths	Common Symptoms in Pregnant Women	Fatality Rate	Mode of Transmission	Incubation period	References
Severe Acute Respiratory Syndrome (SARS)	8098	774	Nausea, chills, headache, malaise, and myalgia and diarrhea	9%-10%	Fecal-oral transmission and transmission through fomites	4.6 days	Anderson et al., 2020
The Middle East Respiratory Syndrome (MERS)	2500	860	Respiratory illness, including fatigue, cough, and shortness of breath	25%	Close contact	5.2 days	Haines et al., 2003 [20]

Diagnosics of COVID-19 Among Pregnant Women

COVID-19 diagnosis is primarily based on Computed Tomography (CT) scans and the Reverse Transcription-Polymerase Chain Reaction (RT-PCR). This test is regularly used to identify viruses that are responsible for respiratory diseases. Viral isolates are used as the primary substrate in the RT-PCR technique to perform an assay that recognizes a specific virus and its gene sequence. A CT scan is considered more sensitive than RT-PCR, and a successful RT-PCR test can be confirmed [22]. A sample obtained from swabs of lungs, sweat, saliva, or stool can be used to perform RT-PCR. To get accurate results, the nucleic acid test is normally repeated with a single patient. When the virus is not detected in the throat swab sample, two tests are performed successively at an interval of 24 h. In the absence of RT-PCR, a serological test can also be used for diagnostic testing [23].

The most frequent and earliest clinical presentation of COVID-19 is fever, frequently accompanied by dry cough, myalgia, and malaise. Sore throat is the most common among the initial respiratory symptoms; however, pregnant women reported shortness and difficulty in breathing (dyspnea), and chest pain. Gastrointestinal symptoms such as diarrhea were reported in four studies [24]. Abdominal swelling and bilateral conjunctival hyperemia are among the atypical findings. In addition to the RT-PCR test, computerized Chest Tomography (CT) scan was the primary investigation mode used by the majority of the samples for diagnosing COVID-19 infection. The most common feature of COVID-19 pneumonia was patchy Ground-Glass Opacity (GGO) with or without consolidation, which resolved over time. Liu et al. further established the development of the lesion into paving patterns and consolidations. In addition to lung parenchymal alteration, one of the atypical findings was found in a 30-week pregnant woman who presented on the left side with slight pleural effusion [25].

Common laboratory findings among COVID-19 patients include lymphopenia (lymphocyte amounts smaller than average in the blood) and elevated C-reactive protein (inflammatory indicator). Other findings are impaired liver function, evidenced by increased Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST). Among other results from the laboratory, three studies recorded neutrophilia, one leukocytosis, one lower albumin levels, one elevated D-dimer, and thrombocytopenia among pregnant women.

Preventive Measures During Pregnancy

pregnant women should strictly follow preventive measures, including regular hand washing and avoiding unnecessary outdoor activities, infected individuals, crowded places, and public gatherings. They should regularly check their temperature, and notify their doctors immediately if they experience shortness of breath, cough, or fever. Also, women with a travel history or COVID-19 symptoms will be placed in solitary confinement for at least 14 days. China's National Health Commission indicated that mother neonates who are confirmed or suspected should be kept under observation and not breastfed [26]. However, no evidence for supporting the transfer of 2019-nCoV to breast milk is currently available.

Pregnant women should track their vital signs (pulse rate, breath rate, and temperature) closely. Importantly, they will tell their maternity care provider about their health status and periodically receive advice. Extracorporeal oxygenation of the membrane and inhalation of oxygen (60%–100% concentration with a flow rate of 40 L/min) should be used for hypoxia [27-30].

Management of COVID-19 During Pregnancy

Pregnant women with suspected COVID-19 should be separated for successful treatment and then moved to a hospital equipped with appropriate health services and professionally trained physicians to take good care of critically-ill obstetric patients [31-33]. Pregnant women will typically be classified as having a moderate illness (i.e. symptomatic with healthy vital signs) to provide adequate care after a full examination, extreme disease (i.e. respiration rate approximately 30/min, saturated O₂ resting approximately 93%, partial blood oxygen/oxygen concentration approximately 300 mmHg), and critical disease (i.e. organ failure shock, respiratory failure requiring mechanical ventilation or refractory hypoxemia requiring oxygenation of the extracorporeal membrane).

Case Studies Discussion About the Effect of COVID-19 in Pregnant Women

COVID-19 is a novel viral respiratory disease (Figure 1). The unknown fact is whether pregnant women are at increased risk of infection or not. Viral pneumonia is a major indirect cause of maternal death. Little is known about the effects of the acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) during childbirth. A case study was conducted to evaluate COVID-19 clinical properties during pregnancy and also in their newborn babies, and to

investigate whether SARS-CoV-2 can be transmitted vertically intrauterine. A systematic test procedure for infection with SARS-CoV-2 by oropharyngeal swab, placenta tissue, vaginal mucus, and breast mother's milk. Experiments on the oropharyngeal swab, blood from the umbilical cord, and serum of newborns were also conducted. The study conducted by Liu et al., (2020) is the most thorough virological evaluation to date, including a longer clinical observation during hospitalization in mother-infant dyads [34]. In mother-infant dyads, the clinical course and outcomes of three pregnant women who acquired late pregnancy with SARS-CoV-2 infection are described. Two were delivering caesareans in their third trimester. All patients showed a perinatal course which was uneventful and a successful outcome. No infants were reportedly infected by vertical transmission or during delivery. Thus this study concluded that both the pregnant woman and infant showed very few adverse maternal and neonatal outcomes.

Another study conducted by Schwartz et al., (2020) reveals that unlike pregnant women's coronavirus infections caused by SARS and MERS, COVID-19 did not lead to maternal death in those 38 pregnant women [35]. Importantly and similar to SARS and MERS pregnancies, no confirmed cases of intrauterine transmission of SARS-CoV-2 from COVID-19 mothers to their fetuses were reported. All neonatal specimens tested, even placentas in some cases, were negative for SARS-CoV-2 by RT-PCR. There is no evidence at this point in the global pandemic of COVID-19 infection that SARSCoV-2 is transmitted intrauterine or by the placenta from infected pregnant women to their fetuses. It is necessary to analyze additional cases to determine whether that remains true. Thus, by considering these two crucial studies on COVID-19 and pregnant, we can understand the importance of conducting extensive research studies on the effect of coronavirus on pregnant women.

Medication to COVID-19 for Pregnant Patients

The antiviral drugs are widely used to treat pregnant women with COVID-19, with atomized inhalation of interferon-ALPHA, oseltamivir, lopinavir, and ritonavir as the most frequently used four antiviral drugs. Ganciclovir and Arbidol, among other antiviral drugs, have been documented for use in two trials each [34]. Also, the use of a wide variety of antibiotics after COVID-19 was popular to treat secondary bacterial pneumonia, including beta-lactam (Abipenem and sulbactam sodium), cephalospo-

rins (cefoperazone sodium and ceftazidime), macrolides (azithromycin), and quinolones (moxifloxacin).

In addition, supportive care for pneumonia was given with methylprednisolone. The use of traditional Chinese medicines along with antiviral and antibiotic treatment was documented in two studies. In their case study, Wang et al., reported giving human serum albumin, dexamethasone, and magnesium sulfate to a 30-week pregnant woman with COVID-19 to brace her for an emergency delivery of the cesarean. After diagnosis, the health status of all pregnant women-bar two-improved. However, none of the studies commented on the effectiveness of the drug administered to pregnant women for COVID-19 management [35-38].

Implications of COVID-19 in Pregnant Women

The particular needs of pregnant women should be included in preparedness and response plans amid a rapidly evolving epidemic which could have significant effects on our public health and medical infrastructure. Clinicians at times are hesitant to treat or vaccinate pregnant women in recent outbreaks, due to concerns regarding fetal health. In the sense of a severe infectious disease threat, pregnant women mustn't decline potentially life-saving treatments unless there is a compelling reason to exclude them. As with all pregnancy treatment decisions, careful balancing of the benefits of mother and fetus safety with potential risks is needed [39, 40]. When monitoring systems for COVID-19 cases are being developed, it is important to collect and report information on pregnancy status, as well as maternal and fetal outcomes.

Severity and Susceptibility of COVID-19 During Pregnancy

Although data are scarce, there is no evidence from other serious coronavirus infections (SARS or MERS) that women who are pregnant are more vulnerable to coronavirus infection. To date, more people have been affected than women in this outbreak of a novel coronavirus infection [41]. This reported gender disparity may be attributable to discrepancies in reporting, sensitivity, exposure, or infection detection and diagnosis. No data are available to tell whether pregnancy raises the susceptibility to COVID-19. Previous evidence on SARS and MERS shows that clinical results can vary from no symptoms to serious illness and death during pregnancy. The most common symptoms of COVID-19 are fever and cough, with more than 80% of hospitalized

patients report these symptoms. Nine women diagnosed with COVID-19 during the third trimester of pregnancy had been documented in a recent study by Chen et al. Clinical presentation in this small series was close to that seen in non-pregnant adults, with fever in seven, cough in four, myalgia in three, and sore throat and malaise in two people each. Five were experiencing lymphopenia. Both had pneumonia, but no mechanical ventilation was needed and none died [42-44].

Both women were given a cesarean delivery, and Apgars was in 1 minute and 5 minutes. In the second series of 9 pregnancies with 10 infants (one set of twins) was reported by Zhu et al. The onset of symptoms in four cases was (1-6 days) before delivery, in two on delivery day, and in three cases after delivery (1-3 days). COVID-19 clinical presentation was close to that seen in non-pregnant patients [45-48]. Of the 9 births, 6 intrauterine fetal distress was noted, 7 were cesarean deliveries, and 6 preterm infants were born. Based on these limited records, and the available evidence from other respiratory pathogens such as SARS and influenza, it is not known if pregnant women with COVID-19 will suffer more serious illness [49].

Vaccination Possibility During Pregnancy

There is currently no COVID-19-prevention vaccine available. Several organizations, including the National Institutes of Health, have been working to produce a COVID-19 vaccine quickly after publishing a SARS-CoV-2 virus genetic sequence online on January 10, 2020 [50]. This vaccine has been designed upon research on SARS and MERS. However, it is not clear how soon a safe and effective vaccine can be available [51].

Conclusions

To sum up, with the minimal data published so far (March 27, 2020), it is obvious that pregnant women with COVID-19 infection have similar clinical characteristics to others. Many people experience pneumonia and are treated with radiological findings. Pregnant women with COVID-19 have been diagnosed with a wide range of antiviral drugs—mainly in China. However, to date, there is no official guideline from the World Health Organization or Center for Disease Control (dated April 1, 2020). Several of these medications are being clinically tested. Higher episodes of premature birth and cesarean delivery were reported by pregnant women with COVID-19, but it cannot be directly attributed to SARS-CoV-2. There is no information about SARS-CoV-2 vertical transmission. Pregnancy and having an immunocompromised physiological condition must

be regarded as a priority case of COVID-19 infection and must be treated in a higher-level healthcare facility. Wherever possible, pregnant women must be treated during antenatal, childbirth, or postnatal period, in isolation or negative pressure space.

The treatment of COVID-19 patients includes a comprehensive team of intensive care medicine physicians, obstetricians, anesthetists, neonatologists, microbiologists, and pathologists. Healthcare workers should use proper personal security equipment to defend themselves. Comprehensive history taking (especially for touch tracing and travel history), radiological assessment, and laboratory testing with routine monitoring of fetal health during COVID-19 should be done at every stage of pregnancy. While stated only once, the effectiveness of lung ultrasound should be evaluated as a more usable and cost-effective investigative tool. For uncomplicated COVID-19 instances, the literature did not suggest early termination or use of a cesarean section. While no vertical transmission of SARS-CoV-2 was confirmed, every effort should be made to prevent the transmission of SARS-CoV-2 or iatrogenic infection from mother to child, during and after delivery. In the postnatal stage, infants must be suspected or confirmed COVID-19 mother in an isolated manner. More evidence is required to conclude breastfeeding health at this point. The results of varied studies proved that COVID-19 affects pregnant women at a severe rate. Thus, there is an alarming need to do further research on various factors related to COVID-19 and its effects on pregnant women.

Ethical Considerations

Compliance with ethical guidelines

The study was reviewed by the Department of Pharmacy of GITAM University, India.

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Conflict of interest

The authors declared no conflict of interest.

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Reference

- [1] Rasmussen SA, Hayes EB. Public health approach to emerging infections among pregnant women. *Am J Public Health*. 2005; 95:1942-4. [DOI:10.2105/AJPH.2004.054957] [PMID] [PMCID]
- [2] Siston AM, Rasmussen SA, Honein MA, Fry AM, Seib K, Callaghan WM, et al. Pandemic 2009 influenza A (H1N1) virus illness among pregnant women in the United States. *J Am Med Assoc*. 2010; 303(15):1517-25. [DOI:10.1001/jama.2010.479] [PMID] [PMCID]
- [3] Moore CA, Staples JE, Dobyns WB, Pessoa A, Ventura CV, Da Fonseca et al. Characterizing the pattern of anomalies in congenital Zika syndrome for pediatric clinicians. *JAMA Pediatr*. 2017; 171(3):288-95. [DOI:10.1001/jamapediatrics.2016.3982] [PMID] [PMCID]
- [4] Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika virus and birth defects: Reviewing the evidence for causality. *N Engl J Med*. 2016; 374(20):1981-7. [DOI:10.1056/NEJMsr1604338] [PMID]
- [5] Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. Preliminary estimation of the basic reproduction number of novel Coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. *Int J Infect Dis*. 2020; 92:214-7. [DOI:10.1101/2020.01.23.916395]
- [6] World Health Organization (WHO). Coronavirus disease (COVID-19) outbreak. Geneva: World Health Organization; 2020.
- [7] Gorbalenya AE, Baker SC, Baric R, Groot RJ, Drosten C, Gulyaeva AA, et al. Severe acute respiratory syndrome-related coronavirus: The species and its viruses - a statement of the Coronavirus study group. *BioRxiv*. 2020; 1-15. [DOI:10.1101/2020.02.07.937862]
- [8] Hui DSC, Zumla A. Severe acute respiratory syndrome: Historical, epidemiologic, and clinical features. *Infect Dis Clin North Am*. 2019; 33(4):869-89. [DOI:10.1016/j.idc.2019.07.001] [PMID] [PMCID]
- [9] Wong G, Liu W, Liu Y, Zhou B, Bi Y, Gao GF. MERS, SARS, and Ebola: The role of super-spreaders in infectious disease. *Cell Host Microbe*. 2015; 18(4):398-401. [DOI:10.1016/j.chom.2015.09.013] [PMID] [PMCID]
- [10] Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC et al. Pregnancy and perinatal outcomes of women with Severe Acute Respiratory Syndrome. *Am J Obstet Gynecol*. 2004; 191(1):292-7. [DOI:10.1016/j.ajog.2003.11.019] [PMID] [PMCID]
- [11] Shek CC, Ng PC, Fung GP, Cheng FW, Chan PK, Peiris MJ, et al. Infants born to mothers with Severe Acute Respiratory Syndrome. *Pediatr*. 2003; 112(4):e254. [DOI:10.1542/peds.112.4.e254] [PMID]
- [12] Ng PC, Leung CW, Chiu WK, Wong SF, Hon EK. SARS in newborns and children. *Biol Neonate*. 2004; 85(4):293-8. [DOI:10.1159/000078174] [PMID]
- [13] Park MH, Kim HR, Choi DH, Sung JH, Kim JH. Emergency cesarean section in an epidemic of the middle east respiratory syndrome: A case report. *Korean J Anesthesiol*. 2016; 69(3):287-91. [DOI:10.4097/kjae.2016.69.3.287] [PMID] [PMCID]
- [14] Lam CM, Wong SF, Leung TN, Chow KM, Yu WC, Wong TY, et al. A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. *Int J Obstet Gynecol*. 2004; 111(8):771-4. [DOI:10.1111/j.1471-0528.2004.00199.x] [PMID] [PMCID]
- [15] Robertson CA, Lowther SA, Birch T, Tan C, Sorhage F, Stockman L, et al. SARS and pregnancy: A case report. *Emerg Infect Dis*. 2004; 10(2):345-8. [DOI:10.3201/eid1002.030736] [PMID] [PMCID]
- [16] Stockman LJ, Lowther SA, Coy K, Saw J, Parashar UD. SARS during pregnancy, United States. *Emerg Infect Dis*. 2004; 10(9):1689-90. [DOI:10.3201/eid1009.040244] [PMID] [PMCID]
- [17] Yudin MH, Steele DM, Sgro MD, Read SE, Kopplin P, Gough KA. Severe Acute Respiratory Syndrome in pregnancy. *Obstet Gynecol*. 2005; 105(1):124-7. [DOI:10.1097/01.AOG.0000151598.49129.de] [PMID]
- [18] Jiang X, Gao X, Zheng H, Yan M, Liang W, Shao Z, et al. Specific immunoglobulin g antibody detected in umbilical blood and amniotic fluid from a pregnant woman infected by the coronavirus associated with Severe Acute Respiratory Syndrome. *Clin Diagn Lab Immunol*. 2004; 11(6):1182-4. [DOI:10.1128/CDLI.11.6.1182-1184.2004] [PMID] [PMCID]
- [19] Lau KK, Yu WC, Chu CM, Lau ST, Sheng B, Yuen KY. Possible central nervous system infection by SARS coronavirus. *Emerg Infect Dis*. 2004; 10(2):342-4. [DOI:10.3201/eid1002.030638] [PMID] [PMCID]
- [20] Haines CJ, Chu YW, Chung TK. The effect of Severe Acute Respiratory Syndrome on a hospital obstetrics and gynaecology service. *Int J Obstet Gynecol*. 2003; 110(7):643-5. [DOI:10.1046/j.1471-0528.2003.03007.x] [PMID] [PMCID]
- [21] Owolabi T, Kwolek S. Managing obstetrical patients during Severe Acute Respiratory Syndrome outbreak. *J Obstet Gynaecol Can*. 2004; 26(1):35-41. [DOI:10.1016/S1701-2163(16)30694-6]
- [22] Bialek SR, Allen D, Alvarado-Ramy F, Arthur R, Balajee A, Bell D, et al. First confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection in the United States, updated information on the epidemiology of MERS-CoV infection, and guidance for the public, clinicians, and public health authorities - May 2014. *Morb Mortal Wkly Rep*. 2014; 63(19):431-6. <https://www.scholars.northwestern.edu/en/publications/first-confirmed-cases-of-middle-east-respiratory-syndrome-coronav-2>
- [23] Zumla A, Hui DS, Perlman S. Middle East respiratory syndrome. *The Lancet*. 2015; 386(9997):995-1007. [DOI:10.1128/microbiolspec.EI10-0020-2016] [PMID]
- [24] Donnelly CA, Malik MR, Elkholly A, Cauchemez S, Van Kerkhove MD. Worldwide reduction in MERS cases and deaths since 2016. *Emerg Infect Dis*. 2019; 25(9):1758-60. [DOI:10.3201/eid2509.190143] [PMID] [PMCID]
- [25] Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature. *J Microbiol Immunol Infect*. 2019; 52(3):501-3. [DOI:10.1016/j.jmii.2018.04.005] [PMID] [PMCID]
- [26] Alserehi H, Wali G, Alshukairi A, Alraddadi B. Impact of Middle East Respiratory Syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. *BMC Infect Dis*. 2016; 16:105. [Open Access] [DOI:10.1186/s12879-016-1437-y] [PMID] [PMCID]

- [27] Assiri A, Abedi GR, Al Masri M, Bin Saeed A, Gerber SI, Watson JT. Middle East respiratory syndrome coronavirus infection during pregnancy: A report of 5 cases from Saudi Arabia. *Clin Infect Dis*. 2016; 63(7):951-3. [DOI:10.1093/cid/ciw412] [PMID] [PMCID]
- [28] Malik A, El Masry KM, Ravi M, Sayed F. Middle East respiratory syndrome coronavirus during pregnancy, Abu Dhabi, United Arab Emirates, 2013. *Emerg Infect Dis*. 2016; 22(3):515-7. [DOI:10.3201/eid2203.151049] [PMID] [PMCID]
- [29] Payne DC, Iblan I, Alqasrawi S, Al Nsour M, Rha B, Tohme RA, et al. Stillbirth during infection with Middle East respiratory syndrome coronavirus. *J Infect Dis*. 2014; 209(12):1870-2. [DOI:10.1093/infdis/jiu068] [PMID] [PMCID]
- [30] Racelis S, de los Reyes VC, Sucaldito MN, Deveraturda I, Roca JB, Tayag E. Contact tracing the first Middle East respiratory syndrome case in the Philippines, February 2015. *Western Pac Surveill Response J*. 2015; 6(3):3-7. [DOI:10.5365/wpsar.2015.6.2.012] [PMID] [PMCID]
- [31] Jeong SY, Sung SI, Sung JH, et al. MERS-CoV Infection in a pregnant woman in Korea. *J Korean Med Sci*. 2017; 32(10):1717-1720. [DOI:10.3346/jkms.2017.32.10.1717] [PMID] [PMCID]
- [32] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. 2020; 395(10223):497-506. [Doi:10.1016/S0140-6736(20)30183-5]
- [33] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020. [DOI:10.1056/NEJMoa2001316]
- [34] Liu W, Wang Q, Zhang Q, Chen L, Chen J, Zhang B, et al. Coronavirus Disease 2019 (COVID-19) during pregnancy: A case series. *Pediatr*. 2020; 2020020373. <https://www.preprints.org/manuscript/202002.0373/v1>
- [35] Schwartz DA. An analysis of 38 pregnant women with COVID-19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: Maternal coronavirus infections and pregnancy outcomes. *Arch Pathol Lab Med*. 2020; 144(7):799-805. [DOI:10.5858/arpa.2020-0901-SA] [PMID]
- [36] Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. *The Lancet*. 2020; 395(10224):565-74. [Doi:10.1016/S0140-6736(20)30251-8]
- [37] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *The Lancet*. 2020; 395(10223):507-13. [DOI:10.1016/S0140-6736(20)30211-7]
- [38] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *J Am Med Assoc*. 2020; 323(11):1061-9. [DOI:10.1001/jama.2020.1585] [PMID] [PMCID]
- [39] Dorigatti I, Okell L, Cori A, Imai N, Baguelin M, Bhatia S, et al. Report 4: Severity of 2019-novel Coronavirus (nCoV). London: Imperial College London; 2020. <https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-02-10-COVID19-Report-4.pdf>
- [40] Shen KL, Yang YH. Diagnosis and treatment of 2019 novel coronavirus infection in children: A pressing issue. *World J Pediatr*. 2020; 16:219-21. [DOI:10.1007/s12519-020-00344-6] [PMID] [PMCID]
- [41] Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020; 382:929-36. [DOI:10.1056/NEJMoa2001191] [PMID] [PMCID]
- [42] Yu IT, Li Y, Wong TW, Tam W, Chan AT, Lee JH, et al. Evidence of airborne transmission of the Severe Acute Respiratory Syndrome virus. *N Engl J Med*. 2004; 350(17):1731-9. [DOI:10.1056/NEJMoa032867] [PMID]
- [43] Chen J. Pathogenicity and transmissibility of 2019-nCoV- A quick overview and comparison with other emerging viruses. *Microbes Infect*. 2020; 22(2):69-71. [DOI:10.1016/j.micinf.2020.01.004] [PMID] [PMCID]
- [44] Haddad LB, Jamieson DJ, Rasmussen SA. Pregnant women and the Ebola crisis. *N Engl J Med*. 2018; 379(26):2492-3. [DOI:10.1056/NEJMp1814020] [PMID]
- [45] Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. *The Lancet*. 2020; 395(10226):809-15. [DOI:10.1016/S0140-6736(20)30360-3]
- [46] Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*. 2020; 9(1):51-60. [DOI:10.21037/tp.2020.02.06] [PMID] [PMCID]
- [47] Paules CI, Marston HD, Fauci AS. Coronavirus infections— More than just the common cold. *J Am Med Assoc*. 2020; 323(8):707-8. [DOI:10.1001/jama.2020.0757] [PMID]
- [48] Pacheco LD, Saade GR, Hankins GDV. Extracorporeal Membrane Oxygenation (ECMO) during pregnancy and postpartum. *Semin Perinatol*. 2018; 42(1):21-5. [DOI:10.1053/j.semperi.2017.11.005] [PMID]
- [49] Lapinsky SE. Management of acute respiratory failure in pregnancy. *Semin Respir Crit Care Med*. 2017; 38(2):201-7. [DOI:10.1055/s-0037-1600909] [PMID]
- [50] Arabi YM, Mandourah Y, Al-Hameed F, et al. Corticosteroid therapy for critically ill patients with Middle East Respiratory Syndrome. *Am J Respir Crit Care Med*. 2018; 197(6):757-67. [DOI:10.1164/rccm.201706-1172OC] [PMID]
- [51] D'Amore R. Can coronavirus pass from mother to baby? Maybe, but experts need more research. [Internet]. 2020 [Update: 2020 Feb 07]. Available from: <https://globalnews.ca/news/6515302/coronavirus-mother-baby-transmission/>
- [52] Rasmussen SA, Kissin DM, Yeung LF, MacFarlane K, Chu SY, Turcios-Ruiz RM, et al. Preparing for influenza after 2009 H1N1: Special considerations for pregnant women and newborns. *Am J Obstet Gynecol*. 2011; 204(6):S13-S20. [DOI:10.1016/j.ajog.2011.01.048] [PMID]
- [53] Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by the novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS coronavirus. *J Virol*. 2020; 94(7):e00127-20. [DOI:10.1128/JVI.00127-20]

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