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A systematic review on 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 on COVID-19 during pregnancy are available; however, information on diseases associated with other highly pathogenic coronaviruses (i.e., severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) may provide insight into the effects of COVID-19 during pregnancy. Coronaviruses cause illness ranging from the common cold to severe respiratory disease and death. Currently, COVID-19's primary epidemiological risk factors include travel from mainland China (especially the province of Hubei) or close contact with infected individuals within 14 days of the onset of symptoms. The data indicate a ~5-day incubation period (range-2-14 days). The average age of hospitalized patients was 49-56 years, with an underlying illness a third to half. Children were rarely mentioned. Within hospitalized cases men were more frequent (54-73 percent). Fever, cough, myalgia, vomiting and diarrhea are common symptoms. This review aims at giving a in depth understanding on COVID-19 by comparing its effect with SARS and MERS to evaluate its severity in recent times in pregnant women.

Introduction

Scientists have recently revealed to the world their discovery of a novel disease that is enhanced coronavirus type. The novel CoVID-19 coronavirus has been reported as an outbreak of respiratory disease. On 31 December 2019, 27 cases of unknown etiology were registered in Hubei city of Wuhan. The Wuhan Municipal Health Commission has confirmed that seven cases of the same respiratory disease have been identified. There were some symptoms in those cases (i.e. very dry cough, very high fever and complicated dyspnea). In addition, they tested positive for radiological results of bilateral lung infiltrates by analyzing their bodies [1]

However, in Hubei, from 15 to about 59 cases were suspected of being contaminated with CoVID-19. CoVID-19 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, CCDC's 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. China or the People's Republic of China (PRC) is a country situated in the continent of Asia at 35,8617° North and 104,1954 ° South. This includes more than 32 provinces, plus the Special Administrative Regions (i.e. Hong Kong, Inner Magnolia and Macau). By time, the number of confirmed infected cases has increased rapidly, especially in Hubei and other provinces in China. 95425 cases were confirmed globally by the 5th of March-2020, while 80410 cases were confirmed in China region [3-5]. The province of Hubei has been confirmed to be the highest infected region with about 75 percent of cases infected.

Coronaviruses (CoVs) belong to the Coronavirinae subfamily of the order Nidovirales in the Coronaviridae family. The CoVs are RNA viruses enveloped with the genome consisting of a single-stranded positive-sense RNA (+ ssRNA), ~30 kb with 5′-cap structure and 3′-poly-A 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 nsps1. 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. 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 Middle East respiratory syndrome (MERS). Till last year the six human CoVs were known and included HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1, SARS-CoV and MERS-CoV. The newest and most virulent member of the CoV family that can infect humans is the SARS-CoV-2 or 2019-nCoV. The SARS-CoV-2 shares SARS-CoV with strong sequence identity [6]. Examination of the protein sequence has reported that the amino acid similarity between SARS-CoV-2 and SARS-CoV between the preserved nsps is as high as 94.6 percent, indicating that they are closely related.

There is approximately 90 percent homology between the SARS-CoV-2 genome and CoV bat viruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21, while it is approximately 96 percent with the bat SARS-like CoV (bat-CoV-RaTG13) genome. 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 aren't immediate ancestors. The bat CoV can then infect another species, an intermediate host, which later transmitted the virus to humans. The

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isolation of a CoV with a high resemblance to SARS-CoV-2 in the Malayan pangolins connects these species as the possible intermediate host [7,8]. The genetic sequence of CoV, found in Malayan pangolin lung samples, has a similarity of ~91 per cent 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. The CoVs of ancestor bat have a dissimilarity of 19 amino acids, while the CoV of pangolin has just 5 dissimilarity of 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 difference in amino acid.

In addition, in 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-26 protein. The bat CoVs, pangolin CoV and SARS-CoV-2's genetic sequence analysis appears to connect 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 excluded [9]. COVID-19 is a global public health emergency, and during pregnancy may cause catastrophic health problems. Because of their altered physiological and immunological role, 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].

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 of time. Importantly, viral respiratory diseases, such as influenza, can grow easily during pregnancy, suggesting that pregnant women can be more vulnerable to COVID-19 and need priority medical attention [11]. The Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) currently provide interim COVID-19 recommendations for successful counselling and education of pregnant women. Recommendations that came out after the COVID epidemic in Wuhan are also available from Chinese experts. This essay discusses the knowledge available on handling COVID-19 during pregnancy to protect mothers and children's health in this crucial situation.

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 China's Guangdong Province. 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 after public health control measures were put in place to avoid contact with infected individuals, and no cases have been seen since 2004. SARS manifestos include nausea, chills, headache, malaise, and myalgia. In some patients diarrhea was found. Pneumonia has almost always been seen in patients diagnosed with SARS, requiring mechanical ventilation in 10-20 per cent 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 touch of the respiratory tract mucous membranes with respiratory droplets produced when an infected person coughs or sneezes. There were also records of fecal-oral transmission and transmission through fomites. Airborne transmission may also be possible due to inhalation of small particulate aerosols. During the 2003 outbreak, transmission in health care settings was frequently seen, with superspreading (when a single patient transmits infection to a disproportionate number of contacts) recorded. The incubation period was calculated to be 4.6 days in 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 resulted from the Hong Kong epidemic of 2003, in which 12 pregnant women were reported. The rate of case-fatality was 25 per cent (three deaths). Clinical and laboratory results in the non-pregnant population were close to those observed. Pneumonia was seen in all patients on chest x-ray or CT. Significant medical complications included four-fold adult respiratory distress syndrome, three-fold intravascular coagulopathy (DIC), three-fold renal insufficiency, two-fold secondary bacterial pneumonia, and two-fold sepsis.

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 were wearing N95 respirators [16]. On work and delivery, the visitors were limited to one per patient, with no visitors permitted in the postpartum unit. Postpartum stays were reduced in length, with the addition of a postpartum nursing home visit. Postpartum patients were asked to observe a quarantine at the home for 10 days. 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. Suspended obstetric services considered non-essential, such as daily ultrasound and prenatal diagnosis. 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

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 countries outside the Arab peninsula, including the United States. The Republic of Korea's biggest outbreak outside the Arabian Peninsula was in 2015. Nearly 2,500 cases of MERS-CoV disease and more than 860 deaths were reported with continuing studies into the present. 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 per cent. Patients who developed MERS were more likely to be older with around two-thirds of patients being male (median age is 50 years). MERS patients were also more likely to experience an underlying illness. Some patients with MERS-CoV infection were asymptomatic (identified by touch inquiries). The mean time of incubation is 5.2 days, with a duration of 2-13 days. As with SARS, MERS is primarily transmitted person-to-person via close contact, transmission was observed in health care settings, and events of superspreading occurence. However, the number of MERS-CoV cases has been dramatically reduced since 2016, despite public health efforts to prevent MERS-CoV transmission [16]. Information regarding MERS is limited among pregnant women. We reported 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 as being asymptomatic as part of a contact inquiry. Of the 11 women with symptoms, signs were close to those seen in non-pregnant MERS patients [17]. Both babies born to asymptomatic women were born safe 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).

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 corona viruses that could infect humans have been identified so far. Two lethal viruses, SARS-CoV-1 and the Middle East coronavirus respiratory syndrome (MERSCoV), 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 a 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 are then deposited on surfaces nearby. The virus may potentially spread to the infected individual within a distance of < 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].

Diagnostics of COVID-19 among pregnant women

COVID-19 diagnosis is primarily based on computed tomography (CT) scans and the polymerase chain reaction (RT-PCR) to reverse transcription. This test is regularly used to identify viruses that are responsible for respiratory diseases. Viral isolates are used as 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. In order 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 a distance of 24 h. In the absence of RT-PCR, a serological test can also be used for diagnostic testing [23].

COVID-19's most frequent and earliest clinical formulation is fever, frequently accompanied by dry cough, myalgia and malaise. Sore throat is most common among the initial respiratory symptoms; however, in pregnant women reported shortness and difficulty in breathing (dyspnea) and chest pain. Gastrointestinal symptoms such as diarrhoea 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 sample 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). Also found was impaired liver function, evidenced by increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Among other results from laboratory, three studies recorded neutrophilia; one study documented leukocytosis; one study recorded lower albumin levels; one study reported elevated D-dimer and thrombocytopenia among pregnant women.

Preventive measures during pregnancy

Preventive measures should be strictly followed by pregnant women, including regular hand washing, avoiding unnecessary outdoor activities unless an emergency occurs, and avoiding infected individuals, crowded places and public gatherings. They will regularly check their temperature, and notify their doctor immediately if they experience shortness of breath, cough, or fever. In addition, 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 percent 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: moderate illness (i.e., symptomatic with healthy vital signs) to provide adequate care after full examination; Extreme disease (i.e., respiration rate approximately 30/min, saturated O_2 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 hypoxaemia requiring oxygenation of the extracorporeal membrane).

Medication to COVID-19 for pregnant patients

The antiviral drug was most widely used to treat pregnant women with COVID-19, with atomized inhalation of interferon-ALPHA, oseltamivir, lopinavir, and ritonavir being 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 popular was the use of a wide variety of antibiotics after COVID-19 to treat secondary bacterial pneumonia, including beta-lactam (Abipenem and Sulbactam Sodium), cephalosporins (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 his case study, Wang *et al.* reported being given 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 or 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 in the midst of a rapidly evolving epidemic which could have significant effects on our public health and medical infrastructure. Clinicians have at times been 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, it is important that pregnant women are not refused 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 treatments 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 show that clinical results can vary from no symptoms to serious illness and death during pregnancy. COVID-19's most common symptoms are fever and cough, with more than 80 per cent of hospitalized patients reporting 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 nonpregnant 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 a second series of nine pregnancies with ten infants (one set of twins) reported by Zhu *et al.* the onset of symptoms was in four (1-6 days) before delivery, in two on delivery day, and in three cases after delivery (1-3 days). COVID-19's clinical presentation was close to that seen in non-pregnant patients [45-48]. Of the nine births, six intrauterine fetal distress was noted, seven were cesarean deliveries, and six 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 organisations, including the National Institutes of Health, have been working to produce a COVID-19 vaccine quickly after publishing a SARS-CoV-2 [50] virus genetic sequence online on January 10, 2020. Design of this vaccine builds upon research on SARS and MERS vaccines and benefits from it. It is not clear however how soon a safe and effective vaccine can be readily available [51,52].

Conclusions

To sum up, with the minimal data published so far (27 March 2020), it is obvious that pregnant women with COVID-19 infection have similar clinical characteristics to others. Many people experience pneumonia and is treated freely 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 guidance 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 can not be directly attributed to SARS-CoV-2. There is no known information about the SARS-CoV-2 vertical transmission. Pregnancy – being an immunocompromised physiological condition – must be regarded as a priority case of COVID-19 infection, and must be regarded in a higher-level healthcare facility. Wherever practicable, pregnant women must be treated in antenatal, childbirth, or postnatal period, in isolation or negative pressure space.

The treatment of vital 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. There needs to be more evidence to conclude breastfeeding health at this point.

References

1. Rasmussen SA, Hayes EB (2005) Public health approach to emerging infections among pregnant women. *Am J Public Health* 95: 1942-1944.

2. Siston AM, Rasmussen SA, Honein MA, Fry AM, Seib K, et al. (2010) Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *JAMA* 303: 1517-1525. [Crossref]

3. Moore CA, Staples JE, Dobyns WB, Pessoa A, Ventura CV, et al. (2017) Characterizing the pattern of anomalies in congenital Zika syndrome for pediatric clinicians. *JAMA Pediatr* 171: 288-295. [Crossref]

4. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR (2016) Zika vrus and birth defects-- Reviewing the evidence for causality. *N Engl J Med* 374: 1981-1987.

5. Zhao S, Lin Q, Ran J, Musa SS, Yang G, et al. (2020) 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* 92: 214-217. [Crossref]

6. World Health Organization. Coronavirus disease (COVID-19) outbreak. Accessed February 17, 2020. 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019.

7. Gorbalenya AE, Baker SC, Baric RS, et al. (2020) Severe acute respiratory syndrome-related coronavirus: The species and its viruses – a statement of the Coronavirus Study Group. Accessed on February 16, 2020. https://www.biorxiv.org/content/10.1101/2020.02.07.937862v1.full.pdf.

8. Hui DSC, Zumla A (2019) Severe acute respiratory syndrome: Historical, epidemiologic, and clinical features. *Infect Dis Clin North Am* 33: 869-889.

9. Wong G, Liu W, Liu Y, Zhou B, Bi Y, et al. (2015) MERS, SARS, and Ebola: The role of super-spreaders in infectious disease. *Cell Host Microbe* 18: 398-401.

10. Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, et al. (2004) Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol* 191: 292-297. [Crossref]

11. Shek CC, Ng PC, Fung GP, Cheng FWT, Chan KS, et al. (2003) Infants born to mothers with severe acute respiratory syndrome. *Pediatrics* 112: e254. [Crossref]

12. Ng PC, Leung CW, Chiu WK, Wong SF, Hon EK (2004) SARS in newborns and children. *Biol Neonate* 85: 293-298.

13. Park MH, Kim HR, Choi DH, Sung JH, Kim JH (2016) Emergency cesarean section in an epidemic of the middle east respiratory syndrome: a case report. *Korean J Anesthesiol* 69: 287-291.

14. Lam CM, Wong SF, Leung TN, Chow KM, Yu WC, et al. (2004) A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. *BJOG* 111: 771-774. [Crossref]

15. Robertson CA, Lowther SA, Birch T, Tan C, Sorhage F, et al. (2004) SARS and pregnancy: a case report. *Emerg Infect Dis* 10: 345-348. [Crossref]

16. Stockman LJ, Lowther SA, Coy K, Saw J (2004) Parashar UD. SARS during pregnancy, United States. *Emerg Infect Dis* 10: 1689-1690.

17. Yudin MH, Steele DM, Sgro MD, Read SE, Kopplin P, et al. (2005) Severe acute respiratory syndrome in pregnancy. *Obstet Gynecol* 105: 124-127.

18. Jiang X, Gao X, Zheng H, Yan M, Liang W, et al. (2004) 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* 11: 1182-1184. [Crossref]

19. Lau KK, Yu WC, Chu CM, Lau ST, Sheng B, Yuen KY (2004) Possible central nervous system infection by SARS coronavirus. *Emerg Infect Dis* 10: 342-344.

20. Haines CJ, Chu YW, Chung TK (2003) The effect of severe acute respiratory syndrome on a hospital obstetrics and gynaecology service. *BJOG* 110: 643-645.

21. Owolabi T, Kwolek S (2004) Managing obstetrical patients during severe acute respiratory syndrome outbreak. *J Obstet Gynaecol Can* 26: 35-41.

22. Bialek SR, Allen D, Alvarado-Ramy F, Arthur R, Balajee A, et al. (2014) 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. *MMWR Morb Mortal Wkly Rep* 63: 431-436. [Crossref]

23. Rasmussen SA, Watson AK, Swerdlow DL (2016) Middle east respiratory syndrome (MERS). *Microbiol Spectr*.

24. Donnelly CA, Malik MR, Elkholy A, Cauchemez S, Van Kerkhove MD (2019) Worldwide reduction in MERS cases and deaths since 2016. *Emerg Infect Dis* 25: 1758-1760.

25. Alfaraj SH, Al-Tawfiq JA, Memish ZA (2019) Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature. *J Microbiol Immunol Infect* 52: 501-503.

26. Alserehi H, Wali G, Alshukairi A, Alraddadi B (2016) Impact of Middle East Respiratory Syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. *BMC Infect Dis* 16: 105.

27. Assiri A, Abedi GR, Al Masri M, Bin Saeed A, Gerber SI, et al. (2016) Middle East respiratory syndrome coronavirus infection during pregnancy: A report of 5 cases from Saudi Arabia. *Clin Infect Dis* 63: 951-953.

28. Malik A, El Masry KM, Ravi M, Sayed F (2016) Middle East respiratory syndrome coronavirus during pregnancy, Abu Dhabi, United Arab Emirates, 2013. *Emerg Infect Dis* 22: 515-517.

29. Payne DC, Iblan I, Alqasrawi S, Al Nsour M, Rha B, et al. (2014) Stillbirth during infection with Middle East respiratory syndrome coronavirus. *J Infect Dis* 209: 1870-1872. [Crossref]

30. Racelis S, de los Reyes VC, Sucaldito MN, Deveraturda I, Roca JB, et al. (2015) Contact tracing the first Middle East respiratory syndrome case in the Philippines, February 2015. *Western Pac Surveill Response J* 6: 3-7.

31. Jeong SY, Sung SI, Sung JH, Ahn SY, Kang ES, et al. (2017) MERS-CoV Infection in a pregnant woman in Korea. *J Korean Med Sci* 32: 1717-1720. [Crossref]

32. Huang C, Wang Y, Li X, Ren L, Zhao J, et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* [Crossref]

33. Li Q, Guan X, Wu P (2020) Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med.*

34. Zhu N, Zhang D, Wang W, Li X, Yang B, et al. (2020) A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 382: 727-733. [Crossref]

35. Lu R, Zhao X, Li J (2020) Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*.

36. Chen N, Zhou M, Dong X (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*.

37. Wang D, Hu B, Hu C, Zhu F, Liu X, et al. (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 323: 1061-1069. [Crossref]

38. Dorigatti I, Okell L, Cori A, et al. (2020) Report 4: Severity of 2019-novel coronavirus (nCoV). WHO Collaborating Centre for Infectious Disease Modelling, MRC Centre for Global Infectious Disease Analysis, Imperial College London. Accessed February11, 2020. https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gidafellowships/Imperial-College-2019-nCoV-severity-10-02-2020.pdf.

39. Shen KL, Yang YH (2020) Diagnosis and treatment of 2019 novel coronavirus infection in children: a pressing issue. *World J Pediatr*.

40. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, et al. (2020) First case of 2019 novel noronavirus in the United States. *N Engl J Med* 382: 929-936. [Crossref]

41. Yu IT, Li Y, Wong TW, Tam W, Chan AT, et al. (2004) Evidence of airborne transmission of the severe acute respiratory syndrome virus. *N Engl J Med* 350: 1731-1739. [Crossref]

42. Chen J (2020) Pathogenicity and transmissibility of 2019-nCoV-A quick overview and comparison with other emerging viruses. *Microbes Infect.*

43. Haddad LB, Jamieson DJ, Rasmussen SA (2018) Pregnant women and the Ebola crisis. *N Engl J Med* 379: 2492-2493.

44. Chen H, Guo J, Wang C, et al. (2020) Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet.*

45. Zhu H, Wang L, Fang C, et al. (2020) Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*.

46. Paules CI, Marston HD, Fauci AS (2020) Coronavirus infections-More than just the common cold. *JAMA*.

47. Pacheco LD, Saade GR, Hankins GDV (2018) Extracorporeal membrane oxygenation (ECMO) during pregnancy and postpartum. *Semin Perinatol* 42: 21-25.

48. Lapinsky SE (2017) Management of acute respiratory failure in pregnancy. *Semin Respir Crit Care Med* 38: 201-207.

49. Arabi YM, Mandourah Y, Al-Hameed F, Sindi AA, Almekhlafi GA, et al. (2018) Corticosteroid therapy for critically ill patients with Middle East Respiratory Syndrome. *Am J Respir Crit Care Med* 197: 757-767. [Crossref]

50. D'Amore R (2020) Can coronavirus pass from mother to baby? Maybe, but experts need more research. Global News. Posted February 7, 2020. (Accessed February 10, 2020). https://globalnews.ca/news/6515302/coronavirus-motherbabytransmission/.

51. Rasmussen SA, Kissin DM, Yeung LF, MacFarlane K, Chu SY, et al. (2011) Preparing for influenza after 2009 H1N1: special considerations for pregnant women and newborns. *Am J Obstet Gynecol* 204: S13-S20. [Crossref]

52. Wan Y, Shang J, Graham R, Baric RS, Li F (2020) Receptor recognition by novel coronavirus

53. from Wuhan: An analysis based on decade-long structural studies of SARS. *J Virol.*