

The Effects of COVID-19 & Pregnancy: A Literature Review

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Abstract

On March 11, 2020, the World Health Organization declared a pandemic of a new strain of SARS-CoV-2, now officially named COVID-19. As a future nurse in labor and delivery I decided to focus on how coronavirus affects pregnancy. Pregnancy is considered a state of immune suppression, which makes this population especially vulnerable. The purpose of this literature review is to explore the health effects coronavirus has on the mother and fetus, while at the same time research possible treatment plans. The paper will highlight coronavirus's history, pathophysiology, diagnosis, treatment, obstetric workflow, how it affects the placenta, and breastfeeding recommendations. I selected 12 different articles provided by CINAHL and PubMed to review. All articles were peer-reviewed, full text, and screened for eligibility. Limits to the study include evolving research and articles only available in 2020. Results revealed coronavirus is an RNA virus working by reverse transcriptase. This makes it difficult to develop a vaccine. Also, placenta blood vessels suffered, but fetal APGAR scores were promising (8 and 9's). Breastfeeding remains the best for fetal nutrition. Staff has been educated on proper obstetric workflow, and Dashraath et al. (2020) provided an excellent chart for reference. Overall, coronavirus and pregnancy outcomes is evolving and it is important to stay up to date on research.

History

Starting late December of 2019 in Wuhan Hubei province China a respiratory virus emerged. We now identify this virus as the coronavirus or COVID-19. The virus is 80% genetically identical to SARS-CoV, known for the SARS epidemic in 2002 (Kowalik et al., 2020). It is also genetically close to Middle East Respiratory Syndrome or MERS. MERS started in 2012, located in Saudi Arabia (Bhargava, 2020). Coronavirus belongs to a large family of different viruses. Many of these viruses cause a common cold, while others produce severe respiratory distress. Hosts for the virus are bats and birds that infect other animals such as civets, camels, and cattle (Bhargava, 2020).

Wuhan China is known for its "wet markets" where people buy fresh meat and fish (Bhargava, 2020). Here animals can be killed and sold in the same spot. These wet markets are known for selling banned species such as cobras (Bhargava, 2020). Crowded and unsanitary conditions make it easy for viruses to replicate and change their genetic makeup (Bhargava, 2020). Many speculate an individual ate an infected civet cat sold at the wet market. Shortly after, the virus spread like wildfire throughout China. It was not long before it hit other countries officially becoming a pandemic. In the United States, we have 9.96 million confirmed cases, with this number rising every day (CDC, 2020). More people recover (97%) than die (238,000) (CDC,2020).

Pathophysiology

Researchers have been busy breaking down the pathophysiology of the ever-evolving coronavirus. It is interesting to see how some become deathly ill, while others are asymptomatic. Pregnancy is considered a vulnerable state. The mother's immune system is weakened, allowing

the respiratory illness to enter more easily. Roughly one-third of infected pregnant women die from the virus (Dashraath et al., 2020). To better understand this strain of the virus, we must break down SARS-CoV-2. Understanding the pathophysiology results in possible treatment plans.

Coronavirus is known as an RNA virus working by reverse transcriptase (Kowalik et al., 2020). Therefore, it has the potential to keep changing its genetic makeup. The virus can be tested in sputum, nasal, blood, feces, sometimes urine, and semen (Kowalik et al., 2020). Coronavirus is transmitted via microdroplets from an infected individual. The virus droplets then enter a host via the nose or conjunctiva, leading to the respiratory tract (Kowalik et al., 2020). It is still being researched, but it is suggested that the virus can remain in a closed unventilated room for hours (Kowalik et al., 2020).

What is known as a double-domain glycoprotein remains on the virus's surface, which likes to bind with angiotensin-converting enzyme type 2 (ACE2) (Kowalik et al., 2020). Activating ACE2 differs between populations, which explains why the virus severity effects regions of the world differently. With many receptors in human tissues, the virus can infect different human cell subtypes. The replication starts in the nose's ciliated epithelium, which also has the highest number of receptors (Kowalik et al., 2020). This is why testing is done through a nasal swab for most accurate results.

Once the virus enters the host, there is a window of up to two weeks to start seeing symptoms. Initially, symptoms are a slight cough, mild shortness of breath, fatigue, sore throat, a low-grade fever, and a loss of taste and smell (Kowalik et al., 2020). Unique to pregnancy, women develop gestational rhinitis or a “stuffy” nose (Dashraath et al., 2020). This has to do with "estrogen-mediated hyperemia of the nasopharynx" (Dashraath et al., 2020, p. 523). One-

fifth of healthy pregnant women in late pregnancy show nasal congestion and rhinorrhea, which can mask coronavirus (Dashraath et al., 2020). Many have mild symptoms (80%) for roughly two weeks, while (5%) of others develop acute respiratory distress syndrome (ARDS) (Dashraath et al., 2020). The lungs' pneumocytes become inflamed and start secreting pro-inflammatory cytokines (Kowalik et al., 2020).

Respiratory System

In a healthy pregnancy, women experience physiologic dyspnea from increased oxygen demands and gestational anemia. This is important to note and separate from pathologic breathlessness (Dashraath et al., 2020). Also, in a normal circumstance pulmonary volume decreases because of the diaphragmatic changes throughout pregnancy. As the fetus grows, the mother's total lung capacity is reduced and causes concern for effectively clearing secretions. This is key because in COVID-19 pneumonia does not stay focal (local), it becomes diffuse. The healthcare provider will be monitoring mom for the production of a viral pneumonia. A viral pneumonia could predispose mom to hypoxia and respiratory failure (Dashraath et al., 2020).

Immune System

Pregnancy is a state of immune suppression which makes pregnant women more vulnerable to viruses. T-helper Lymphocytes create cytokines to help regulate immunity and decrease inflammation (Dashraath et al., 2020). Th1 cytokines are pro-inflammatory, while Th2 are anti-inflammatory. In pregnancy, the body shifts from a Th1 to a Th2 environment. In pregnancy, hormones change, which affects the immune system. With hormones shifting and the body favoring a Th2 environment, the body may respond to the lesser severity of COVID-19 than nonpregnant women (Dashraath et al., 2020).

Circulatory System

With evolving research, there has become a tie with the coronavirus causing thrombi and clotting, mainly in the lungs (Kowalik et al., 2020). The platelet count becomes lower while d-dimer rises (Kowalik et al., 2020). This is especially important for an expecting mother because pregnancy is already a hypercoagulable state. Klok et al. (2020) studied 184 patients in the ICU and found that 31% of them developed a thrombus. Many experienced no therapeutic effects of using low-molecular-weight heparin and unfractionated heparin (Klok et al., 2020, as cited in Kowalik, 2020). To date, the best nursing intervention to prevent the formation of thrombi is active movement and breathing exercises.

Diagnosis

When the mother and father arrive to deliver their baby, the mother must get coronavirus tested. Some facilities will also test the father. If the mother has symptoms before arriving, she must communicate this with the hospital. This ensures that staff provide a proper room and set up PPE (CDC, 2020). There are two different test types to test for coronavirus: one a viral test and second an antibody test. The viral test will be used to determine if an individual currently has the virus. The antibody test will tell the individual if they previously had coronavirus. Antibodies take approximately one to three weeks to show in the blood (CDC, 2020). Research is still being conducted on how long the antibodies will stay in the blood and protect the individual from getting sick again.

It is best to gather a specimen from the upper respiratory system for more accurate results (CDC, 2020). The healthcare provider will either perform a nasopharyngeal or oropharyngeal specimen. After the specimen is collected, it will be placed in a sterile transport tube with 2-3ml

of viral transport medium, sterile saline, or an Amies transport medium (CDC, 2020). To correctly perform the test, the healthcare provider will insert a swab with a flexible wire shaft into the nose. This leads parallel to the palate until they hit resistance or if the distance is from the ear to the nose. The provider will then rub and roll the swab, leaving the specimen in for a few seconds to collect secretions. Lastly, the provider will slowly remove the swab while rotating (CDC, 2020).

The laboratory will test the reverse transcription-polymerase chain reaction assay from the infected host (Dashraath et al., 2020). The test uses probes and primers to analyze the RNA genes. There have been instances where an individual has a false negative, and this is due to a low viral load. It takes approximately three days for the virus to cause cell effects (Dashraath et al., 2020). Therefore, if a person tests negative but has symptoms, they should take proper isolation precautions.

To aid in diagnosis but not replace a viral test is a chest radiograph. Physicians have been finding "peripheral airspace shadowing" as well as "multi-lobar, bilateral, ground-glass opacities" on a CT scan (Dashraath et al., 2020, p. 523). These images appear in normal circumstances as well as pregnancy. There are concerns for the fetus when completing a CT scan because of the ionization radiation. Rest assured, research has shown that the small amount of radiation does not increase the risk of fetal anomalies or loss (Dashraath et al., 2020). Visualization of a chest radiograph of the effects of the coronavirus is available in Appendix A.

Obstetric Workflow

All healthcare personnel working on an obstetric unit have three main goals. One, to provide continuous adequate service. Two, implement social distancing of all healthcare

personnel. Third, to provide infection control techniques. The mother is seen in three different settings: outpatient, inpatient, and the labor and delivery unit. All team members must communicate together and implement the same protocols.

In an outpatient setting, the mother will be seen for routine prenatal visits, such as scans. When the mother arrives, a team member will take her temperature and have her take a seat that is 6ft away from another individual. If not deemed essential, outpatient scans will be postponed lessening the risk of exposure (Dashraath et al., 2020). Fathers will not be able to accompany mom, but this is starting to change. Inpatient mothers will go through the same routine of being temperature screened, and depending on how long the mother will be staying may require testing for the virus (Dashraath et al., 2020).

When the mother arrives at the labor and delivery unit, she will be asked a series of questions: Do you have a fever, shortness of breath, or a cough? If the patient says no, she is considered low risk, and the team will provide routine care (Dashraath et al., 2020). Team members will still be required to deliver with a surgical gown, face mask, and face shield. If the mother states yes to the symptoms, she will be asked if she has traveled out of the country within the last 30 days, if she has been in contact with anyone who has had the virus, and if she has been recently diagnosed with coronavirus (Dashraath et al., 2020). If mom answers no to those questions, she is considered a moderate risk. Mom will be placed in a negative pressure isolated room and tested for coronavirus (Dashraath et al., 2020). Staff will be required to wear a surgical mask and shield for delivery. If mom answers yes to the travel screening and exposure risk assessment, she is considered high risk (Dashraath et al., 2020). The same rules apply to high-risk mothers, except nurses will be required to wear an N-95. C-sections and vaginal deliveries

will be performed in a negative pressure room if the mother comes back positive (Dashraath et al., 2020).

In a positive case it is advised not to delay clamping of the umbilical cord and to initially avoid skin to skin contact (Dashraath et al., 2020). Breastfeeding is not contraindicated and still encouraged. Research has shown no detectable coronavirus in breast milk. To help lessen the risk of transmission, mom must wear a face mask while breastfeeding (Dashraath et al., 2020). If separation is required, mom should start expressing milk to gather supply (Spatz, 2020). When mom is done pumping, all parts need to be thoroughly cleaned. If mom or a family member becomes ill, it is noted not to interrupt breastfeeding, causing more harm than good (Spatz, 2020). Globally only 41% of women exclusively breastfeed (Spatz, 2020). We see a rise in formula use since the pandemic, and we must educate moms on all the health benefits of breast milk (Spatz, 2020). Dashraath et al. (2020) provided a detailed chart of the obstetric workflow and recommendations provided below in Appendix B.

Placental Perfusion Compromise

It is essential to note the placenta's pathophysiology to better understand the complications that arose from coronavirus. The placenta is the main organ that transfers oxygen and nutrients between the mother and fetus. The placental membrane is very thin, only a single cell layer (Lowdermilk et al., 2016). This causes easy access to viruses and bacteria from mothers' circulation to the fetus. Part of the placenta is the chorionic plate sided with the fetus (Burton & Fowden, 2015). The basal plate is sided with maternal endometrium. Between the plates is a vital cavity known as the intervillous space. Here branches of villi or blood vessels form a lobule that helps in exchanging nutrients. One of the primary nutrients it helps exchange

is oxygen. COVID-19 suggests targeting the villi's oxygen exchanging capabilities between the mother and fetus (Burton & Fowden, 2015).

A new study conducted by Northwestern Medicine found the effects of placental compromise. The study consisted of sixteen placentas from mothers who tested positive for coronavirus (Shanes et al., 2020). Mothers delivered between March 18 and May 5, 2020. Fifteen gave birth in the third trimester while one delivered in the second due to intrauterine fetal demise. During the mother's third trimester, the placenta showed features of maternal vascular malperfusion (MVM) (Shanes et al., 2020). Other perinatal outcomes are associated but are not as likely such as miscarriages, preterm birth, preeclampsia, and stillbirth (Shanes et al., 2020).

In the labor and delivery room, the physician will initially examine the placentas for compromise (Shanes et al., 2020). Once samples are collected, a perinatal specialist will further examine the placenta and confirm the diagnosis. Placentas were analyzed by measurement, sectioning, weight, and of the cut surface. Sections examined include 2 membrane rolls, two umbilical cord samples, two maternal surface biopsies, and two full-thickness parts of the placenta (Shanes et al., 2020).

Maternal vascular malperfusion was present in 12 out of the 15 cases (Shanes et al., 2020). Other findings include villous infarctions, villous agglutination (clusters), and villous maturation. Also present was decidual arteriopathy (muscle of the blood vessels within the placenta are showing enlargement), atherosclerosis (lipid deposits), fibrinoid necrosis, and mural hypertrophy of the membrane's arterioles (Shanes et al., 2020). Interestingly, there was no inflammation noted. Overall, maternal malperfusion features cause concern for thrombi and chorangiosis (abundance of blood vessels in the chorionic villi) (Shanes et al., 2020).

Results showed five placentas that were small for gestational age and large (Shanes et al., 2020). APGAR scores at one minute were 8 and 9 following at five minutes a score of 9. Fifteen of the live-born babies were discharged from the hospital on the first and second days. All infants tested negative for coronavirus via a nasal swab (Shanes et al., 2020). While outcomes for the baby and mother have been positive, research shows we should still keep a close eye on the mother and baby's progress. Appendix C shows pictures from Northwestern's study on the placentas. To the naked eye, we cannot see the microscopic damage, but it is interesting to view their results.

Treatment

To date, there is no antiviral therapy that cures coronavirus. A vaccine is in the making but is nowhere near ready. Although there is no cure, there are some mechanisms to help alleviate symptoms. Treatment depends on the individual's severity of symptoms. Majority of the time, coronavirus is treated with adequate rest, hydration, nutrition, and electrolytes. The go-to therapies for more extreme cases are oxygen, ventilation, antibiotics, vasopressor medications, antivirals, and extracorporeal oxygenation (Provenzani & Polidori, 2020).

Combining Azithromycin and Hydroxychloroquine has shown viral load reduction (Provenzani & Polidori, 2020). Also, noted Australian researchers found Ivermectin (FDA approved anti-parasitic) a single dose can inhibit viral growth in 48 hours. To date, the most widely used drug is Remdesivir, which works by targeting RNA viruses. It has been used to help treat coronavirus, SARS, MERS, and pneumoviruses (Provenzani & Polidori, 2020). Lopinavir and Ritonavir are preferred for pregnant women to take (Liang & Acharya, 2020). Research is showing it is safe for the baby and mother. The recommended dose is two capsules, orally twice a day (Liang & Acharya, 2020). While stated above, there is no single drug that has cured the

virus; there have been effects shown with multiple antiviral therapies. Researchers are busy at work, and it will be interesting to see how soon a vaccine or drug therapy can be formulated that completely cures the virus.

Conclusion

Overall, the novel coronavirus has caused much concern for the health and well-being of our nation. We must protect our vulnerable populations, such as the elderly and mothers who are expecting. We have learned throughout this paper that coronavirus is an RNA virus working by reverse transcriptase. The result of this is the difficulty in finding a cure. Pregnancy is a state of hypercoagulability and immune suppression, which is why moms should especially take precautions. Dashraath et al. (2020) provided an excellent obstetric workflow chart that is easy for healthcare personnel to follow. We explored how the placenta's blood vessels are being impacted, although maternal and fetal outcomes thus far are promising. Breastfeeding is a concern for mothers, but research shows more harm than good if a mother does not breastfeed. In the upcoming year, I am hopeful for more answers on how coronavirus affects pregnancy. Nevertheless, for now, it is best to stay safe by following CDC guidelines.

Appendix A

FIGURE 1
Chest radiograph in COVID-19

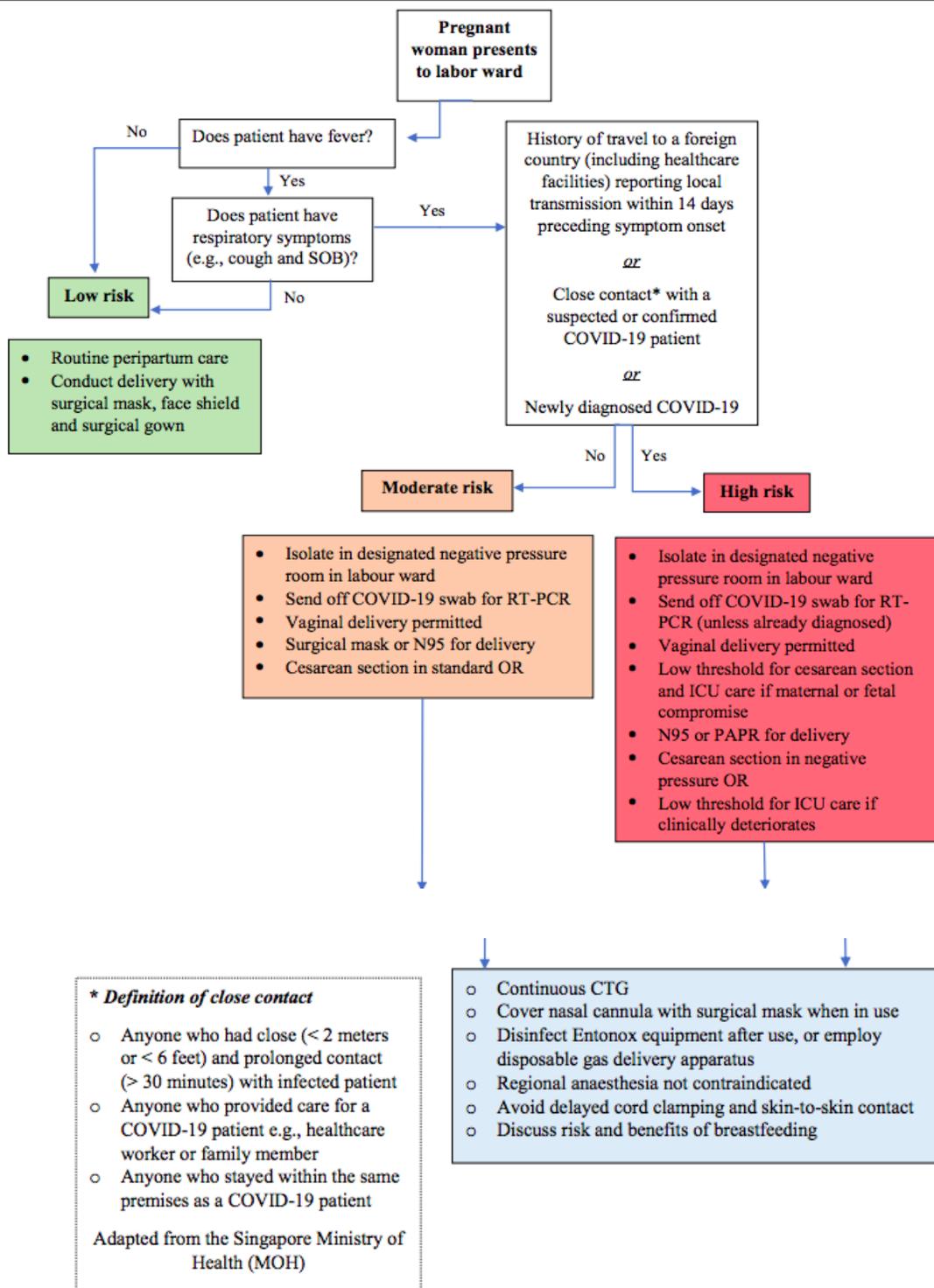


An erect plain radiograph of the chest in a nonpregnant woman from Singapore with laboratory confirmed COVID-19 demonstrates bilateral and peripherally distributed air-space opacities.

Dashraath. COVID-19 pandemic and pregnancy. Am J Obstet Gynecol 2020.

(Dashraath. COVID-19 pandemic and pregnancy. Am J Obstet Gynecol 2020)

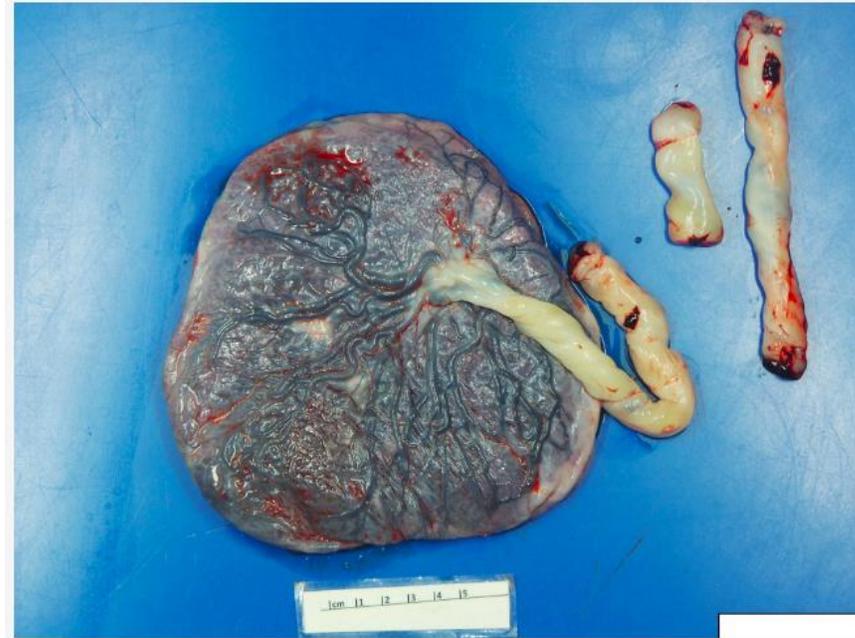
Appendix B



Schematic representation demonstrating a model for stratifying risk in obstetric patients presenting to the labor floor.

Dashraath. COVID-19 pandemic and pregnancy. *Am J Obstet Gynecol* 2020.

Appendix C



This picture shows the fetal side of the placenta. (Shanes et al., 2020).



This picture shows the maternal side of the placenta. (Shanes et al., 2020).

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