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### Title

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### Impacts of the COVID-19 Pandemic on Maternal, Neonatal, and Childhood Outcomes

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#### Abstract

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has profoundly affected global health, presenting unprecedented challenges to pregnant women and their offspring. This paper explores the impacts of COVID-19 on maternal, neonatal, and childhood health, shedding light on both short-term and potential long-term consequences. The transmission of the virus from mother to child, though relatively low compared to other vertically transmitted diseases, remains a subject of ongoing study. Maternal COVID-19 infection during pregnancy is linked to adverse outcomes such as preterm delivery, cesarean section, preeclampsia, and gestational diabetes. Additionally, COVID-19 infection appears to influence placental pathology, raising concerns about fetal development and health in the long term. The pandemic has exacerbated maternal mental health challenges, including an increased prevalence of postpartum depression. Infants born to mothers with COVID-19 may experience lower neonatal weight, reduced head circumference, and a heightened risk of complications. Long-term health effects on children, including cardiovascular and respiratory impacts, remain areas of active investigation. Comprehensive research is vital to understand the magnitude of these risks and develop effective strategies for preventing and managing COVID-19 in pregnant women. Prioritizing the health and well-being of pregnant women and their offspring is critical in mitigating the enduring effects of the pandemic on maternal, neonatal, and childhood outcomes.

## Introduction

The COVID-19 pandemic caused by the coronavirus SARS-CoV-2 has been ravaging the world for the past few years. Despite the efforts of scientists to stop the virus, COVID-19 still

continues to be a problem to vulnerable populations, including pregnant women. The effects and symptoms of COVID-19 is well understood for the majority of the world's population, yet little is known about how COVID-19 affects pregnant women and their unknown children, both biologically and psychologically. Because COVID-19 is not fully understood yet, scientists have used older pandemics, such as the Spanish flu, as models to compare how these diseases impact pregnant women and their children. Researchers also examine how pandemics, such as COVID-19, affected minority populations with poor access to healthcare, namely Native Americans. The current state of COVID-19 research has been analyzing how environmental stressors, caused by stress, traumatic events, etc., caused by COVID-19 causes prenatal health complications. Scientists also want to explore how infants of exposed mothers develop complications both prenatally and after birth.

Although this is an important field, various limitations and barriers present themselves regarding this study. To begin, research on prenatal epigenetics is a growing field, as researchers have recently begun delving into the mechanical as well as psychological aspects of a developing infant. However, there isn't as significant research on the mechanisms of prenatal epigenetics on the development of the fetus; emerging studies connecting prenatal epigenetic exposure to the placenta is a growing topic. Further, it is difficult to understand the long-term effects of prenatal exposure to induced epigenetic disease and factors such as COVID, which would require frequent studies throughout an individual's lifetime. It is important to note that this paper is based on comparisons of prior disease exposure, however COVID functions differently biologically and bacterially from other cases (ex. Spanish Flu).

#### **Subsection 1: COVID-19 Transmission in utero**

As the pandemic proves to be influential on the well-being of pregnant women and maternal health, the question of direct transmission to infant health remains. Babies born from infected pregnant women of a virus are at risk of contracting the same virus through vertical or intrauterine transmission. The mechanism of vertical transmission from pregnant woman to fetus can be described by the following: through the hematogenous route, the virus in the maternal blood stream reaches the placenta. Once inside the placenta, the virus enters the chorionic villous tree and eventually reaches the fetal blood vessles SITE 2. Common diseases and bacterial infections that are vertically transmitted have been categorized as "TORCH" pathogens, including toxoplasma gondii, other (such as HIV), rubella, cytomegalovirus (CMV), and herpes 1 and 2. SITE 4. Vertical transmission causes an array of medical problems for the infant as well as mother, ranging from maternal pneumonia, maternal death, early pregnancy loss, and many other health implications on the born infant.

Although vertical transmission is a common occurrence for TORCH pathogens, it is less certain if SARS-COVID-2 uses this same physiological pathway for transmission to infants. In fact, many researchers believe coronaviruses do not adopt the same pathways, as the rates of vertical transmission of COVID from mother to infant are very low. Theories of placental infection have been clinically tried and various studies have proven that infants born from infected mothers of COVID rarely test positive. A study conducted by SITE 1 determined that from 100 pregnancies, 1.9 babies received the virus from their mother. SITE 1 Further, the SITE 2 ran a study on 9 pregnant women infected with COVID, and after delivery, tested 6 of those 9 women's infants for COVID. Thorough testing of amniotic fluid, breastmilk, umbilical cord blood, and neonatal throat swabs all resulted in a negative test result for the baby.

#### **Subsection 2: COVID Effects on Mother's Term**

The COVID-19 pandemic has had a significant impact on healthcare globally, and prenatal care for women is not an exception. There have been questions raised by the potential effects of COVID-19 on fetal development, including the potential increase in stillbirths. Here we will discuss the results of two studies that investigated the effects of COVID-19 on prenatal development and stillbirth.

The first study titled "Maternal and Perinatal Outcomes of Pregnant Women with COVID-19: A Systematic Review" by Iqbal S et al. aims to evaluate the maternal and perinatal outcomes of pregnant women with COVID-19. The study included 46 articles with a total of 11,432 pregnant women with COVID-19. The results showed that pregnant women with COVID-19 had a higher risk of preterm delivery, cesarean section, preeclampsia, and gestational diabetes. This creates added stressors for pregnant women. Additionally, there was a higher risk of fetal distress, low birth weight which is known to increase the risk of infant mortality, and neonatal intensive care unit (NICU) admission in newborns born to mothers with COVID-19. To conclude, mothers who were infected with COVID-19 had a higher rate of complications and a slight increase in stillbirths.

Additionally, there is growing evidence that COVID-19 can have effects on the placenta. A study published in the American Journal of Obstetrics and Gynecology in March 2021 evaluated placental pathology in women who contracted COVID-19. The study included 43 women, 28 of whom tested positive for COVID-19. Of the 28, 15 placentas were observed and compared to controls in the third trimester while one placenta was observed in the second trimester after a stillbirth. The results showed that the placentas of women with COVID-19 had a higher rate of abnormal pathology compared to the placentas of women without COVID-19. Specifically, the placentas of women with COVID-19 had a higher incidence of intervillous thrombi, necrosis in the tissue, abnormal villous maturation, and inflammation. The placenta plays a critical role in fetal development and health, and any disruption to its function can have significant consequences for the developing fetus. Placental developmental The findings from this study raise concerns about the potential long-term effects of COVID-19 on fetal development and health. It is essential to note that the long-term effects of COVID-19 on prenatal development and stillbirth is still limited. While these studies provide important insights into the potential risks, further research in the future is necessary to understand the full extent of these risks fully. Prioritizing the health of women who are pregnant is important and through prevention and biological advances, there could be better management of healthcare.

### **Subsection 3: Maternal and Offspring Health Post-birth**

#### **Maternal Mental Health Impact of COVID-19**

The COVID-19 pandemic has put unprecedented stress on individuals across the globe, with expectant and new mothers facing additional uncertainties and potential complications. Of the many groups of individuals at heightened risk of infection, pregnant women are highlighted as being prone to infection. While the scope of potential impacts of the pandemic on maternal mental health is wide and still largely unknown, recent studies indicate that postpartum depression (PPD) may be worsened with and by effects of COVID-19. PPD can lead to negative outcomes for both the mother and newborn, including difficulty with mother-child bonding and the risk of cognitive, behavioral, and emotional difficulties for the child. Defined as a major/sub-clinical depression, PPD typically affects women within one year post-delivery. In general, symptoms include irritability, anxiety, sleep difficulties, and low appetite, as well as additional, obsessive concern with the health of the child. In a systematic review conducted by Federica and colleagues, rates of PPD were reported to increase in prevalence from 32.6% to 34%, a dramatic increase in comparison to pre-pandemic numbers ranging from 6.5% to 25.8%. This data suggests that, with the added stress of the pandemic, quarantine, and other related factors, pregnant women may be at a much higher risk of suffering from PPD than during pre-pandemic times.

#### Short-term Health Effects on Children

Beyond simply considering the physical and mental health effects of COVID-19 on pregnant mothers, the short-term health effects and risks for neonates include complications with birth, as well as immediate post-delivery risks for the child. In a study that examined effects of prenatal exposure to maternal COVID-19 and perinatal care on neonatal outcome, the risk of lower neonatal weight and smaller head circumference risks were both highlighted. Side effects of lower neonatal weight can include diabetes, heart disease, high blood pressure, intellectual and developmental disabilities, metabolic syndrome, and obesity later in life. Furthermore, smaller neonatal head circumference risks developmental delays, including speech and movement, difficulties with coordination and balance, dwarfism or short stature, facial distortions, hyperactivity, intellectual delays, and seizures later in life. Beyond the risks associated with these developmental complications, maternal infection with COVID-19 during pregnancy was associated with increased maternal and neonatal complications. The aforementioned cohort study found that women with a COVID-19 diagnosis had a much higher rate of requiring a cesarean delivery as opposed to those without COVID-19 (52.8% versus 38.5%). Additional pregnancy related complications such as fetal distress and hypertensive disorders similarly increased in comparison to women without COVID-19. Rates of preterm births increased, which are additionally associated with possible health effects and risks for premature neonates. Moreover, the study found a significant correlation between the length in utero for mothers with COVID-19 to the risk of the neonate also testing positive for COVID-19.

Risk of preeclampsia and gestational diabetes mellitus may similarly be heightened by COVID-19 exposure. COVID-19, though primarily a respiratory infection, may have multiorgan and/or vascular effects. Preeclampsia, a blood pressure disorder that may develop during pregnancy, can cause endothelial damage, placental oxidative stress, and an antiangiogenic state leading to hypertension and proteinuria. In a study of 2184 pregnant women, 725 (33.2%) of which were diagnosed with COVID-19, 123 had preeclampsia, 59 of which were part of the COVID-19 positive group. In comparison to women without a diagnosis, there is a steep increase in the risk ratio of preeclampsia with versus without COVID-19. Another study examined cases of gestational diabetes mellitus, a condition where, during pregnancy, hormones for insulin resistance are produced by the placenta and prevent the body from using insulin effectively. While the study did not conclude whether or not contracting COVID-19 causes a higher risk of having gestational diabetes mellitus, it did indicate that women with gestational diabetes mellitus were particularly vulnerable to COVID-19 and additional related birth complications, such as those aforementioned.

#### Long-term Health Effects on Children

Though the long-term health effects of COVID-19 on children are still largely unknown, evidence suggests it may have potential cardiovascular and respiratory impacts. "Long COVID", the so-called lingering and long-term effects of the viral infection may cause pneumatory risks, cardiovascular risks, effect on brain function, and other symptoms in children leading into adulthood. Lasting pulmonary sequelae has been observed in many children following COVID-19 infection, with symptoms ranging from fatigue, difficulty breathing, brain fog, chest pain, trouble sleeping, cough, depression/anxiety, heart palpitations, and joint/muscle pain. Furthermore, the risks that accompany more immediate complications with birth, such as premature birth, low neonatal weight, small head circumference, etc., all carry risk for future health conditions.

## Conclusion

In summary, the COVID-19 pandemic has profound implications for the outcomes of maternal, neonatal, and childhood health. While the vertical transmission potential of the virus from mother to child remains a subject of ongoing investigation, current evidence suggests a relatively low transmission rate compared to other vertically transmitted diseases. Nevertheless, maternal COVID-19 infection during pregnancy is associated with adverse maternal outcomes, such as an elevated risk of preterm delivery, cesarean section, preeclampsia, and gestational diabetes. Furthermore, COVID-19 infection during pregnancy appears to impact placental pathology, raising concerns regarding potential long-term consequences for fetal development and health. Maternal mental health is also vulnerable, as evidenced by increased rates of postpartum depression during the pandemic. In the short term, infants born to mothers with COVID-19 may exhibit lower neonatal weight, reduced head circumference, and an increased likelihood of neonatal complications. The long-term health effects of COVID-19 on children remain largely unknown; however, emerging evidence suggests possible cardiovascular, respiratory, and developmental impacts. Further research is imperative to comprehensively comprehend the magnitude of these risks and develop effective strategies for the prevention and management of COVID-19 in pregnant women. Prioritizing the health and well-being of pregnant women and their offspring is paramount in mitigating the enduring effects of the pandemic on maternal, neonatal, and childhood outcomes.

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