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Review Article

Pregnancy and COVID-19: an update

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ABSTRACT

COVID-19 was identified in December 2019 in China. Previous research has suggested a potential link between COVID-19 and pre-eclampsia (PE). Therefore, it is crucial to comprehensively evaluate the clinical symptoms and laboratory results of these conditions. This narrative review was conducted in light of the limited understanding of how COVID-19 affects pregnant women and its association with pre-eclampsia. It is important to note that these two conditions may share similar features that can influence the outcome of pregnancy.

Keywords: COVID-19, Pregnancy, Hypertension, COVID-19 vaccines, Pre-eclampsia

INTRODUCTION

COVID-19 is a highly contagious and potentially severe disease caused by the coronavirus. This disease primarily affects the respiratory system but can also have impacts on other organs such as the kidneys and can lead to high blood pressure. The disease is characterized by an overactive immune response, where the body produces too many proinflammatory cytokines like interleukin-2, interleukin-6, interleukin-7, and TNF-α, which can lead to severe health complications and even death. The symptoms of the disease range from mild flu to severe respiratory distress.

Individuals with weaker immune systems, such as pregnant women, cancer patients, and the elderly, are at higher risk of severe COVID-19.[1] Pregnant women, in particular, may be more susceptible to COVID-19 due to the immunological and physiological changes that occur in pregnancy. There is a concern that pregnant women having COVID-19 may be prone to severe illness, hospitalization, and even death, as well as potential risks to their unborn child. It is important for pregnant women and people in these high-risk groups to take extra precautions to protect themselves from COVID-19, such as getting vaccinated, practicing good hygiene, and social distancing.

Severe cases of COVID-19 in pregnant women can lead to a number of negative outcomes, such as fetal distress leading to cesarean section, preterm delivery, and conditions like PE (preeclampsia) and eclampsia.[2] Studies have also shown that severe COVID-19 can lead to pathological placental changes and reduced blood flow to the placenta, which can negatively impact the health of the unborn child.[3] It is believed that the virus enters the body by binding to ACE2 receptors, which are found in the placenta, and this can affect the normal development of the placenta by altering the growth of trophoblast cells and the formation of new blood vessels. This can have negative effects on the health of the fetus and may also affect blood pressure regulation.

COVID-19 can have a negative impact on pregnant women, leading to conditions such as PE and HELLP syndrome. These conditions are characterized by hypertension and proteinuria and can lead to morbidity and mortality in the fetus and mother. Studies have shown that the virus may affect the development of the placenta by altering the growth of trophoblast cells, reducing the production of proangiogenic factors, and increasing antiangiogenic factors. This may lead to placental oxidative stress and downregulation of ACE2.[2] Published

literature has shown a potential link between COVID-19 and PE, however, additional research is required to know the definitive mechanism of COVID-19 pregnancy with PE.

Given the importance of gestation, the need to understand the effects of COVID-19 on pregnant women, and the lack of a clear understanding of how the virus impacts pregnancy and PE, this review was conducted to thoroughly examine the association of PE and COVID-19.

METHODS

The aim of the study was to evaluate the link between PE and COVID-19. To gather relevant information, we searched for English articles using keywords such as COVID-19, PE, fetus, and pregnancy from various databases such as PubMed, Web of Science, and Google Scholar. The review aimed to provide an understanding of the impact of COVID-19 on pregnancy, specifically in relation to PE.

DISCUSSION

Covid-19 in pregnancy

Research shows that the majority of people who contracted the virus had a mild to moderate form of the illness. The most common symptoms reported include cough, shortness of breath, fatigue, myalgia, joint pain, headache, diarrhea, vomiting, and abdominal pain.[4]

Although there is limited information on how the immune system responds to COVID-19 during pregnancy, data from previous pandemics suggests that pregnant women may have a higher risk of infection and mortality compared to non-pregnant women. The stage of pregnancy and timing of infection may play a role in determining the immune response and outcomes. The first and third trimesters, which are characterized by increased inflammation to support implantation and labor, respectively, may put women at a higher risk of experiencing a strong immune response (cytokine storm) if infected with COVID-19 during these phases. Additionally stress during labor may cause unfavorable outcomes and increased postpartum hospital admissions.[5] PE, a common complication during pregnancy, may also exacerbate COVID-19. Studies have found a higher incidence of PE, HELLP syndrome, and eclampsia among pregnant women with COVID-19. Additionally, it can be challenging to distinguish between PE and COVID-19 as both conditions may present with similar abnormalities in laboratory tests, such as abnormal liver function and thrombocytopenia.[6,7]

WHAT IS PE?

PE is characterized by new onset of proteinuria and hypertension after 20 weeks of pregnancy. The exact cause of PE is not fully understood, but the widely accepted theory is abnormal implantation. The condition begins with abnormal infiltration of trophoblasts, which occurs before the onset of symptoms and sometimes even before the pregnancy is known. In normal implantation, trophoblasts infiltrate the decidualized endometrium, leading to the remodeling of the spiral arteries and increased placental blood flow without any change in mother's blood vessels. In PE, the failure of trophoblasts to acquire an endothelial phenotype hinders their infiltration, and as a result, the remodeling of the spiral arteries is inadequate.[8]

Other causes that may contribute to the development of PE include immune system issues, inflammation, infection, and genetic predispositions. Additionally, placental hypoxia and ischemia, which can result from a lack of oxygen and blood flow to the placenta, can cause PE. It can lead to the release of vasoactive substances into the circulation and endothelial cell dysfunction, causing PE.[9]

Demographics of PE

PE affects 5-7% of pregnant mothers and results in high maternal and fetal mortality. It is a cause of complications, hospitalizations, C-sections, and preterm delivery in USA. The incidence of hypertensive disorders in pregnancy has been increasing in developed countries. The death rate is higher among African American women compared to other racial groups.[10,11]

Categories of pre-eclampsia

There are several categories of PE: (a) early-onset PE: this type occurs before 34 weeks of pregnancy and can be severe, leading to early delivery; (b) late-onset PE: This type occurs after 34 weeks of pregnancy and is less severe than early-onset PE; (c) chronic hypertension with superimposed PE: This type occurs when a woman has pre-existing hypertension before pregnancy and develops symptoms of PE during pregnancy; (d) HELLP syndrome: a severe form of PE characterized by hemolysis, elevated liver enzymes, and low platelets; (e) eclampsia: severe PE characterized by seizures or coma; and (f) gestational hypertension: hypertension develops after 20 weeks of gesttion without signs of organ damage.

It is worth noting that these are not mutually exclusive categories, some women can have a combination of these types.The classification of hypertension and PE, as established by the ACOG in 2013, divides the condition into 4 categories: chronic hypertension, eclampsia and PE, gestational hypertension, and chronic hypertension with PE. Severe PE is characterized by specific symptoms such as high blood pressure, low platelet count, impaired liver function, renal failure, and pulmonary edema.[12]

Effect of PE on mother and fetus

PE poses to the fetus also. Maternal risks include increased blood pressure, higher mortality rates due to

cardiovascular issues, and an increased risk of stroke. On the fetal side, risks include premature birth, low amniotic fluid, growth restriction, placental detachment, and fetal death.[13]

Association of PE and COVID-19

It is important to consider the potential relationship between PE and COVID-19, as both conditions have similar symptoms and risk factors. Additionally, it is unclear if COVID-19 increases the risk of developing PE or if PE increases the risk of severe COVID-19. It is important to examine the relationship between PE and COVID-19, as the two conditions share similar symptoms and risk factors. It is important to note that the association between these two conditions may be complicated by overlapping risk factors. A multinational study found that COVID-19-positive pregnant women had higher rates of severe pregnancy complications and a higher maternal mortality rate.[14]

PE mimics

It is important to note that several disorders can present similar symptoms to PE, known as preclampsia-like syndrome. These can be vasospasm, endothelial cell dysfunction, platelet activation or destruction, and decreased perfusion. The differential diagnosis of these disorders can be challenging for healthcare providers, as they can have potentially life-threatening consequences for both the woman and her fetus. A correct diagnosis is crucial as various management options and prognoses are available. It has also been observed that severe COVID-19 in pregnant women can result in preclampsia-like syndrome.[15] It is important for health care providers to have a thorough understanding of the association between COVID-19 and PE, as well as the ability to differentiate between these disorders. This is particularly important due to the potential overlap in symptoms and the life-threatening consequences for both woman and her fetus. Angiogenic factors can be useful in differentiating between these disorders and PE, with placental-associated factors such as PlGF and sFlt-1 being highly specific for placental insufficiency, which can be detected up to 5 weeks prior to the onset of clinical PE.[16]

In summary, for the differential diagnosis of PE and PE-like syndrome in pregnant women with severe COVID-19, the measurement of angiogenic factors such as sFlt-1/PlGF and lactate dehydrogenase levels can be useful.[17] These biomarkers can help distinguish PE caused by placental insufficiency from the PE-like syndrome caused by the virus, despite the presence of common symptoms such as proteinuria, reduced platelet count, elevated liver enzymes, or hypertension.

Effect on pregnancy outcomes

This study found that there is a significant link between COVID-19 and PE, which can lead to negative results for both mothers and fetuses. The study compared the outcomes of women with COVID-19, PE, both COVID-19 and PE, and none of them and found that COVID-19 was strongly associated with PE. The study also found that this association existed irrespective of risk factors or pre-existing conditions, and both conditions were linked to high prenatal morbidity and mortality, preterm delivery, and poor maternal outcomes. The study suggested that women with PE should be considered at high risk for COVID-19.[18]

PE and COVID-19 vaccination

Based on CDC recommendations and previous studies, it has been found that receiving a coronavirus vaccine during gestation can have positive effects and is recommended during pregnancy. Studies have shown that COVID-19 vaccinations do not cause significant side effects or negative impacts on pregnancy, neonatal, or fetal outcomes.[19] A meta-analysis including pregnant women who were vaccinated and unvaccinated, found no difference in the risk of PE up to 72 hours after delivery.

CONCLUSION

In conclusion, COVID-19 and PE have similar symptoms and risk factors, making it difficult to differentiate between the two conditions. Studies have shown that pregnant women with COVID-19 have a higher risk of developing preclampsia and other severe complications, such as HELLP syndrome and eclampsia. The pathogenesis of PE remains unknown, but theories suggest that abnormal placental implantation and underlying comorbidities may play a role. The diagnosis of PE can be challenging as COVID-19 may also present with abnormal laboratory tests, such as thrombocytopenia and elevated liver enzymes. However, factors, such as PlGF and sFlt-1, can help distinguish between PE and PE-like syndrome. Additionally, COVID-19 vaccination has been found to have positive effects during pregnancy and does not cause significant side effects or adverse outcomes for the mother or fetus.

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REFERENCES

1. Sathiya R, Rajendran J, Sumathi S. COVID-19 and Preeclampsia: Overlapping Features in Pregnancy. Rambam Maimonides Med J. 2022;13(1):e0007.
2. Khalil A, Samara A, Chowdhury T, O'Brien P. Does COVID-19 cause pre-eclampsia? Ultrasound Obstet Gynecol. 2022;59(2):146-52.
3. Shanes ED, Mithal LB, Otero S, Azad HA, Miller ES, Goldstein JA. Placental Pathology in COVID-19. Am J Clin Pathol. 2020;154(1):23-32.
4. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease

2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239-42.
5. Rasmussen SA, Jamieson DJ, Macfarlane K, Cragan JD, Williams J, Henderson Z, et al. Pandemic influenza and pregnant women: summary of a meeting of experts. Am J Public Health. 2009;99(2):S248-54.
6. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr. 2021;175(8):817-26.
7. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol. 2020;5(5):428-30.
8. Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: Pathophysiology, Challenges, and Perspectives. Circ Res. 2019;124(7):1094-112.
9. Abbas AM, Ahmed OA, Shaltout AS. COVID-19 and maternal pre-eclampsia: A synopsis. Scand J Immunol. 2020;92(3):e12918.
10. Rezk M, Gamal A, Emara M. Maternal and fetal outcome in de novo preeclampsia in comparison to superimposed preeclampsia: a two-year observational study. Hypertens Pregnancy. 2015;34(2):137-44.
11. Torres J, Martinez-Portilla RJ, Espino-Y-Sosa S, Estrada-Gutierrez G, Solis-Paredes JM, Villafan-Bernal JR, et al. Comorbidity, poverty and social vulnerability as risk factors for mortality in pregnant women with confirmed SARS-CoV-2 infection: analysis of 13 062 positive pregnancies including 176 maternal deaths in Mexico. Ultrasound Obstet Gynecol. 2022;59(1):76-82.
12. Hirashima C, Ogoyama M, Abe M, Shiraishi S, Sugase T, Niki T, et al. Clinical usefulness of serum levels of soluble fms-like tyrosine kinase 1/placental growth factor ratio to rule out preeclampsia in women with new-onset lupus nephritis during pregnancy. CEN Case Rep. 2019;8(2):95-100.
13. Sathiya R, Rajendran J, Sumathi S. COVID-19 and Preeclampsia: Overlapping Features in Pregnancy. Rambam Maimonides Med J. 2022;13(1):e0007.
14. Papageorghiou AT, Deruelle P, Gunier RB, Rauch S, García-May PK, Mhatre M, et al Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study. Am J Obstet Gynecol. 2021;225(3):289.e1-289.e17.
15. Ma Y, Deng J, Liu Q, Du M, Liu M, Liu J. Effectiveness and Safety of COVID-19 Vaccine among Pregnant Women in Real-World Studies: A Systematic Review and Meta-Analysis. Vaccines (Basel). 2022;10(2):246.
16. Fu W, Sivajohan B, McClymont E, Albert A, Elwood C, Ogilvie G, et al. Systematic review of the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnant and lactating individuals and their infants. Int J Gynaecol Obstet. 2022;156(3):406-17.
17. Roberge RJ, Kim JH, Powell JB. N95 respirator use during advanced pregnancy. Am J Infect Control. 2014;42(10):1097-100.
18. Racelis S, 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.
19. 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.

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