REVIEW ARTICLE

Impact of COVID-19 on the histopathological aspect of the placenta during pregnancy

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ABSTRACT

The coronavirus disease 2019 (COVID-19) is still classified as a world pandemic. This disease can affect numerous systems of the human body. Pregnant women are classified as a vulnerable group since COVID-19 can cause high morbidity and mortality. Angiotensin-converting enzyme-2 (ACE-2) acts as a COVID-19 receptor, and this receptor is also present in the placenta. The placenta plays a significant part in the fetus, especially protecting it from harmful conditions. Since only a few studies are available, COVID-19's influence on the placenta in pregnancy needs to be discussed further. The SARS-CoV-2-infected pregnant woman's placenta showed histopathological alterations. Viral particles were detected on syncytiotrophoblast and chorionic villi vascular endothelial cells. Some studies show inflammatory conditions are not prominent in SARS-CoV-2 positive infection. This, perhaps due to the placenta's immunological reaction, plays a significant role. The SARS-CoV-2 disorder tends to cause abnormalities within the placental tissue. Fetal vascular malperfusion (FVM) and maternal vascular malperfusion (MVM) are the most frequent findings from the studies included.

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Highlights:

1. Pregnant women with positive SARS-CoV-2' placenta showed histopathological alterations.
2. SARS-CoV-2 tends to cause abnormalities within the placental tissue.

INTRODUCTION

COVID-19 is a disease that attacks the breathing system. SARS-CoV-2 causes this disease, initially reported in December 2019 in Wuhan, China. This disease had been declared a global pandemic, resulting in more than six million deaths. Existing research shows the spread of this disease through respiratory droplets, especially those close to a COVID-19 patient.[1,2]

In addition to affecting the respiratory system, it is known that this disease can attack by various other techniques. Its symptoms resemble viral infections, i.e., fever, shortness of breath, cough, and runny nose. The condition is divided into mild, moderate, and severe degrees. This disease can affect all age groups, from infants to the elderly. Pregnant mothers are the vulnerable groups, which may cause high morbidity or mortality if attacked by this disease.[3]

Existing research indicates that COVID-19 infection can occur via ACE-2 receptor, which is found in various bodies, including the placenta. During pregnancy, the placenta is critical in the mother-delivery. In addition, the placenta is essential in protecting the unborn baby from harmful infections or toxins from the mother. Based on several existing studies, SARS-CoV-2-infected pregnant women's placenta showed histo-pathological alterations. SARS-CoV-2 can pass through the placenta, resulting in various adverse effects.[4–6]

Presently, there remains a requirement for numerous additional studies to thoroughly explore the effect of COVID-19 on placental function. In this review, the author's focus is directed towards the disclosing of the influence of COVID-19 on the histopathological dimension of the placenta in pregnancy.

SARS-COV-2 INFECTION IN PREGNANT WOMAN

The pregnant woman is regarded as one of the most prone clusters in the population. Changes in physiological and immunological function during pregnancy might raise the risk of severe sickness and the danger of vertical transmission to the infant or fetus. The first and second trimesters are essential for the fetus during vertical transmission because they account for most complications associated with viral infections. Even though the placental wall defends the fetus from intrauterine infections, certain viruses have been linked to congenital abnormalities or syndromes. They have an impact on the health of newborns. SARS-CoV-2 in pregnancy is expected to increase the risk of fetal and maternal health issues progressing to severe pneumonia, necessitating hospitalization in critical care units. In placental tissue, several virulent, polytrophic strains of the coronavirus have been shown to transmit and are said to harm both the fetus and the mother.[7]

Many new types of research suggest some intrauterine transmission, despite several prior studies that do not support the SARS-CoV-2 transmission vertically in humans. As a result, SARS-CoV-2 in prenatal is constantly a contentious subject since there is a lack of relevant data and because finding viral particles in the placental tissue is the most reliable technique to confirm this infection. Some reports stated there is a chance of SARS-CoV-2 transplacental infections with positive virions in amnion fluid, nasopharyngeal swabs, placental, and positive serology of neonatal. However, verifying maternal-fetal contagion validity constantly needs to be determined. Pathogens can transverse the placenta and infect the fetus in several ways, such as transvaginal ascending infection, placental, and breastfeeding transmission.[8]

ACE-2 and transmembrane protease serine-2 are primarily expressed in exact cell types of the maternal–fetal interface. Viruses enter the innate immune system of the mother and the placental trophoblastic host when the maternal-fetal interface barrier breaks. Some studies found that SARS-CoV-2 may contaminate monocytes and macrophages via the antibody-dependent enhancement pathway and macrophages and monocytes via the ACE-2 pathway. Specifically, the SARS-CoV-2' S protein attaches to the monocytes and macrophages ACE-2, allowing the cell to be invaded by the viruses.[9,10]

Jing et al. reported that there is ACE-2 expression and activity during pregnancy, and it was discovered that ACE-2 is found to be expressed in numerous parts, including the placenta. ACE-2 is mainly expressed in placental villi syncytiotrophoblast, cytotrophoblast, endothelium, and vascular smooth muscle. The ACE-2 expression in the placenta is higher than in the lung, signifying a viral infection of the placenta. ACE-2 expression was found in invasive and intravascular trophoblast and decidual cells of the maternal stroma. ACE-2 is also present in the umbilical cord's endothelium and smooth muscle.[11,12]

Another study stated that a SARS-CoV-2-infected woman who had a miscarriage at 13 weeks of pregnancy. This study recommends the opportunity of straight-up transmission via the monocytes and macrophages of the infected mother and maybe also by contaminating the fetus via the disease-ridden macrophages during pregnancy. Few studies have linked COVID-19 during pregnancy to issues, i.e., membranes' early rupture or preterm labor.[13–17]

IMPACT OF COVID-19 ON HISTOPATHOLOGICAL ASPECT OF PLACENTA

The SARS-CoV-2-infected mother's placentas show considerable histopathological alterations. Bertero et al. observed the histopathological deviations in the placenta in chronic villitis. In 66.67% of cases, there was CD8+ T cell decidual infiltration and thrombo-hemorrhagic regions with laminar fibrin precipitation inside the intervillous area. Thrombo-hemorrhagic and inflamma-tory changes were the majority, and unusual pathological abnormalities were observed. However, only chronic villitis and rapid villous maturation preserved statistical significance after limiting the study to placentas delivered before a cesarean section.[18]

Another study found that placentas in the third trimester tended to contain at least one MVM characteristic, specifically aberrant or damaged maternal blood vasculatures, and intervillous thrombi. In intrauterine fetal death patient' placenta, villous edema, and retroplacental bruises were discovered. COVID-19 placentas had a higher incidence of decidual arteriopathy and other MVM characteristics, an illustration of placental damage defined by anomalies in intervillous space oxygenation and associated with poor perinatal outcomes.[19]

Another study performed a pathological examination of a 3rd-trimester pregnant woman infected with COVID-19 and showed features of MVM, i.e., an increasing number of syncytial knots. The cases showed higher focal perilous fibrin depositions.[20] There were rises in intervillous or subchorionic fibrin in pregnant women in the acute stage of severe acute respiratory syndrome placentas, which could be linked to troubles in the mother's placenta blood flow caused by respiratory hypoxia.[21]

Khong et al. reported that the most prevalent results in the histological examination were intramural fibrin accumulation and FVM. Villous stromal-vascular karyorrhexis was seen in two instances. Additionally, intramural nonocclusive thrombi, meconium, macrophages, lesions of MVM, and perilous fibrin deposits were caught in the particular placenta. Placental tissue showed acute chorioamnionitis and acute funisitis in patients with pneumonia and acute hypoxia. Other individuals were found to have chronic villitis and obliterative vasculopathy. Increased incidence of a hypercoagulable state was also seen in COVID-19-infected mothers.[22]

Smithgall et al. also reported about MVM and FVM changes in COVID-19 cases during pregnancy. Histopathological examination found that the SARS-CoV-2-infected woman's placentas were found to have subchorionic thrombi and villous agglutination.[23] In women with COVID-19, placental pathology revealed a more considerable prevalence of FVM, indicating thrombi in fetal blood vasculatures.[24] Similar previous studies also reported that COVID-19 patients tended to demonstrate FVM evidence, such as avascular villi and mural fibrin precipitation and villitis of the unclear source.[25]

Another study that analyzed the placenta showed the presence of MVM and FVM. The finding of FVM in two cases indicated thrombus development in the fetus and caused the late villous effect. Another mother's placenta with mild respiratory symptoms had lymphohistiocytic villitis and intervillositis, with CD8-positive T-cells being the most prevalent cell population. There were also a few CD68-positive macrophages, CD4-positive T-cells, a small number of plasma cells, and no neutrophil rise. The authors used ISH to show the virus particles in the identical placenta's decidual and umbilical cords. Other authors also noticed a similar discovery of persistent villitis, which they labeled villitis of unknown etiology (VUE).[26–29]

Villous chorangiosis and acute chorioamnionitis are two additional frequent findings in several investigations. Some case reports also noted the existence of chronic and massive histiocytic intervillositis, perilous fibrin precipitation linked with virus spike glycoprotein, primarily in the trophoblast coat. In a 13-week twin pregnancy in which COVID-19 was positive, N-protein and RNA, as well as viral duplication, were discovered in the fetal kidneys, plumes, and placentas. Diffuse infarction, chronic histiocytic intervillositis, and subcortical inflammation were seen in the placental tissue.[13,30–33]

A clinical pathology study by Debelenko et al., which examined 75 placentas from mothers with confirmed COVID-19, showed cell damage characterized by cytoplasm clearing, karyorrhexis, pyknosis, lack of nuclear basophilia, and darkish nuclei with homogenized chromatin. Besides that, it can also be accompanied by an inflammatory infiltrate dominated by monocytes/macrophages, neutrophils, and some lymphocytes such as CD3, CD15, and CD68. Activation of fibroblasts and reactive vascular proliferation were visible in the villous stroma.[34]

Another recent study reported that maternal-fetal malperfusion (MFM), hypoxic placental, decidual arteriopathy, and uteroplacental inadequacy in the intervillous region were all more common in COVID-19 placentas. The COVID-19-induced inflammatory or hypercoagulable state could be to blame. The majority of prevalent pathological discoveries of the COVID-19-infected patient' placenta are signs of MFM. These conditions, however, had little effect on mother outcomes in near-delivery patients, although FVM caused fetal discomfort.[35] SARS-CoV-2-infected pregnant women's placenta and umbilical cord also show substantial pathological changes in another recent study. These data demonstrated that the virus could produce immune responses in the placenta, and the disease is probably associated with a greater likelihood of unfavorable newborn outcomes and mother ICU hospitalization.[36] Table 1 summarizes several histopathological findings of the SARS-CoV-2-infected pregnant woman's placenta.

Table 1. Impact of COVID-19 on the histopathological aspect of placenta

Author (Year)	Research Type	Finding
Al-Rawaf (2022)[36]	Case-control	Pregnant women's placenta and umbilical cord with COVID-19 show substantial pathological changes.
Bertero (2021)[18]	Case series	The most common and unusual pathological abnormalities described were inflammatory and thrombo-hemorrhagic changes.
Gao (2021)[20]	Cohort	Features of MVM were presented in the 3rd trimester of COVID-19-infected pregnant women.
Garg (2022)[35]	Case-control	Signs of MFM are the majority type of pathological discoveries.
Patberg (2021)[25]	Cohort	Patients were found to have an increased risk of placental histopathologic abnormalities.
Prabhu (2020)[24]	Cohort	According to placental pathology, women with COVID-19 had a higher prevalence of FVM, indicating thrombi in fetal vasculature.
Shanes (2020)[19]	Case-control	Placentas in the 3rd trimester tended to exhibit at least an MVM characteristic.
Smithgall (2020)[23]	Case-control	SARS-CoV-2-infected 3rd-trimester women's placentas tended to display indications of MFM.

CONCLUSION

SARS-CoV-2-infected pregnant women may have substantial histopathological abnormalities in the placental. The majority of monsters are MFM and villitis with unclear causes. Careful research of the relationship between microscopic abnormalities and the obstetric outcome is required to better aid physicians in delivering obstetric therapy for their patients during the COVID-19 pandemic.

DISCLOSURES

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Conflict of interest

There is no conflict of interest for the author.

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Author Contribution

The author contributed to all aspects of this study, including preparation, article searching, drafting, and manuscript approval for publication.

REFERENCES

1. World Health Organization. WHO Coronavirus (COVID-19) dashboard [Internet]. WHO. 2020. Available from: https://covid19.who.int/
2. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020;382 (13): 1199-207. doi: 10.1056/NEJMoa2001316. Epub 2020 Jan 29. PMID: 31995857; PMCID: PMC 7121484.
3. Brandt JS, Hill J, Reddy A, et al. Epidemiology of coronavirus disease 2019 in pregnancy: risk factors and associations with adverse maternal and neonatal outcomes. Am J Obstet Gynecol. 2021; 224(4):389.e1-389.e9. doi: 10.1016/j.ajog.2020.09.043. Epub 2020 Sep 25. PMID: 32986989; PMCID: PMC7518835.
4. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020;181(2):271-80.e8. doi: 10.1016/j.cell.2020.02.052. Epub 2020 Mar 5. PMID: 32142651; PMCID: PMC7102627.
5. Hosier H, Farhadian SF, Morotti RA, et al. SARS-CoV-2 infection of the placenta. J Clin Invest. 2020;130(9):4947-53. doi: 10.1172/JCI139569. PMID: 32573498; PMCID: PMC7456249.
6. Zhao X, Jiang Y, Zhao Y, et al. Analysis of the susceptibility to COVID-19 in pregnancy and recommendations on potential drug screening. Eur J Clin Microbiol Infect Dis. 2020;39(7):1209-20. doi: 10.1007/s10096-020-03897-6. Epub 2020 Apr 23. PMID: 32328850; PMCID: PMC7178925.
7. Aplin JD, Myers JE, Timms K, et al. Tracking placental development in health and disease. Nat

Rev Endocrinol. 2020;16(9):479-494. doi: 10.1038/s41574-020-0372-6. Epub 2020 Jun 29. PMID: 32601352.
8. Wang J, Dong W. COVID-19: the possibility, ways, mechanisms, and interruptions of mother-to-child transmission. Arch Gynecol Obstet. 2023; 307(6):1687-96. doi: 10.1007/s00404-022-06639-5. Epub 2022 Jun 4. PMID: 35665849; PMCID: PMC9166277.
9. Karthik K, Senthilkumar TMA, Udhayavel S, et al. Role of antibody-dependent enhancement (ADE) in the virulence of SARS-CoV-2 and its mitigation strategies for the development of vaccines and immunotherapies to counter COVID-19. Hum Vaccin Immunother. 2020;16(12):3055-60. doi: 10.1080/21645515.2020.1796425. Epub 2020 Aug 26. PMID: 32845733; PMCID: PMC7484565.
10. Shaath H, Vishnubalaji R, Elkord E, et al. Single-Cell transcriptome analysis highlights a role for neutrophils and inflammatory macrophages in the pathogenesis of severe COVID-19. Cells. 2020; 9(11):2374. doi: 10.3390/cells9112374. PMID: 33138195; PMCID: PMC7693119.
11. Zeng L, Xia S, Yuan W, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. JAMA Pediatr. 2020;174(7):722-5. doi: 10.1001/jamapediatrics.2020.0878. PMID: 32215598; PMCID: PMC7099530.
12. Jing Y, Run-Qian L, Hao-Ran W, et al. Potential influence of COVID-19/ACE2 on the female reproductive system. Mol Hum Reprod. 2020; 26(6):367-73. doi: 10.1093/molehr/gaaa030. PMID: 32365180; PMCID: PMC7239105.
13. Valdespino-Vázquez MY, Helguera-Repetto CA, León-Juárez M, et al. Fetal and placental infection with SARS-CoV-2 in early pregnancy. J Med Virol. 2021;93(7):4480-7. doi: 10.1002/jmv.26965. Epub 2021 Apr 6. PMID: 33764543; PMCID: PMC8250563.
14. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet. 2020;395(10226):809-15. doi: 10.1016/S0140-6736(20)30360-3. Epub 2020 Feb 12. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. PMID: 32151335; PMCID: PMC7159281.
15. He M, Skaria P, Kreutz K, et al. Histopathology of Third Trimester Placenta from SARS-CoV-2-Positive Women. Fetal Pediatr Pathol. 2022;41(3): 403-12. doi: 10.1080/15513815.2020.1828517. Epub 2020 Oct 12. PMID: 33040615.
16. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, et al. Vertical transmission of coronavirus disease 19 (COVID-19) from infected pregnant mothers to neonates: A review. Fetal Pediatr Pathol. 2020; 39(3):246-50. doi: 10.1080/15513815.2020.1747120. Epub 2020 Apr 2. PMID: 32238084; PMC ID: PMC7157948.
17. Mullins E, Evans D, Viner RM, et al. Coronavirus in pregnancy and delivery: rapid review. Ultrasound Obstet Gynecol. 2020;55(5):586-592. doi: 10.1002/uog.22014. PMID: 32180292.
18. Bertero L, Borella F, Botta G, et al. Placenta histopathology in SARS-CoV-2 infection: analysis of a consecutive series and comparison with control cohorts. Virchows Arch. 2021;479(4):715-28. doi: 10.1007/s00428-021-03097-3. Epub 2021 May 1. PMID: 33934229; PMCID: PMC8088311.
19. Shanes ED, Mithal LB, Otero S, et al. Placental Pathology in COVID-19. Am J Clin Pathol. 2020; 154(1):23-32. doi: 10.1093/ajcp/aqaa089. PMID: 32441303; PMCID: PMC7279066.
20. Gao L, Ren J, Xu L, et al. Placental pathology of the third trimester pregnant women from COVID-19. Diagn Pathol. 2021;16(1):8. doi: 10.1186/s13000-021-01067-6. PMID: 33441152; PMCID: PMC7806280.
21. Ng WF, Wong SF, Lam A, et al. The placentas of patients with severe acute respiratory syndrome: a pathophysiological evaluation. Pathology. 2006; 38(3):210-8. doi: 10.1080/00313020600696280. PMID: 16753741; PMCID: PMC7131423.
22. Khong TY, Mooney EE, Ariel I, et al. Sampling and definitions of placental lesions: Amsterdam placental workshop group consensus statement. Arch Pathol Lab Med. 2016;140(7):698-713. doi: 10.5858/arpa.2015-0225-CC. Epub 2016 May 25. PMID: 27223167.
23. Smithgall MC, Liu-Jarin X, Hamele-Bena D, et al. Third-trimester placentas of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive women: histomorphology, including viral immunohistochemistry and in-situ hybridization. Histopathology. 2020;77(6):994-9. doi: 10.1111/his.14215. Epub 2020 Sep 26. PMID: 32692408; PMCID: PMC7405484.
24. Prabhu M, Cagino K, Matthews KC, et al. Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: a prospective cohort study. BJOG. 2020;127(12):1548-56. doi: 10.1111/1471-0528.16403. Epub 2020 Aug 13. PMID: 32633022; PMCID: PMC7361728.
25. Patberg ET, Adams T, Rekawek P, et al. Coronavirus disease 2019 infection and placental histopathology in women delivering at term. Am J Obstet Gynecol. 2021;224(4):382.e1-382.e18. doi: 10.1016/j.ajog.2020.10.020. Epub 2020 Oct 19.

Erratum in: Am J Obstet Gynecol. 2023 Jan;228(1) :128. PMID: 33091406; PMCID: PMC7571377.
26. Marinho PS, da Cunha AJLA, Chimelli L, et al. Case Report: SARS-CoV-2 mother-to-child transmission and fetal death associated with severe placental thromboembolism. Front Med (Lausanne). 2021;8:677001. doi: 10.3389/fmed.2021.677001. PMID: 34485327; PMCID: PMC8415358.
27. Menter T, Mertz KD, Jiang S, et al. Placental pathology findings during and after SARS-CoV-2 infection: Features of villitis and malperfusion. Pathobiology. 2021;88(1):69-77. doi: 10.1159/000511324. Epub 2020 Sep 18. PMID: 32950981; PMCID: PMC7573905.
28. Ozer E, Cagliyan E, Yuzuguldu RI, et al. Villitis of unknown etiology in the placenta of a pregnancy complicated by COVID-19. Turk Patoloji Derg. 2021;37(2):167-71. English. doi: 10.5146/tjpath.2020.01506. PMID: 32897537.
29. Roberts J, Cheng JD, Moore E, et al. Extensive perivillous fibrin and intervillous histiocytosis in a SARS-CoV-2 infected placenta from an uninfected newborn: A case report including immunohistochemical profiling. Pediatr Dev Pathol. 2021;24(6) :581-4. doi: 10.1177/10935266211025122. Epub 2021 Jun 28. PMID: 34176361.
30. Pulinx B, Kieffer D, Michiels I, et al. Vertical transmission of SARS-CoV-2 infection and preterm birth. Eur J Clin Microbiol Infect Dis. 2020; 39(12):2441-5. doi: 10.1007/s10096-020-03964-y. Epub 2020 Jul 13. PMID: 32661809; PMCID: PMC7357443.
31. Marton T, Hargitai B, Hunter K, et al. Massive perivillous fibrin deposition and chronic histiocytic intervillositis a complication of SARS-CoV-2 infection. Pediatr Dev Pathol. 2021;24(5): 450-4. doi: 10.1177/10935266211020723. Epub 2021 Jun 3. PMID: 34082613.
32. Morotti D, Cadamuro M, Rigoli E, et al. Molecular pathology analysis of SARS-CoV-2 in syncytiotrophoblast and hofbauer cells in placenta from a pregnant woman and fetus with COVID-19. pathogens. 2021;10(4):479. doi: 10.3390/pathogens10040479. PMID: 33920814; PMCID: PMC8071113.
33. Hanna N, Lin X, Thomas K, et al. Underestimation of SARS-CoV-2 infection in placental samples. Am J Obstet Gynecol. 2021;225(5):572-5.e1. doi: 10.1016/j.ajog.2021.07.010. Epub 2021 Jul 21. PMID: 34297970; PMCID: PMC8294065.
34. Debelenko L, Katsyv I, Chong AM, et al. Trophoblast damage with acute and chronic intervillositis: disruption of the placental barrier by severe acute respiratory syndrome coronavirus 2. Hum Pathol. 2021;109:69-79. doi: 10.1016/j.humpath.2020.12.004. Epub 2020 Dec 13. PMID: 33321162; PMCID: PMC7733682.
35. Garg R, Agarwal R, Yadav D, et al. Histopathological Changes in Placenta of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2) Infection and Maternal and Perinatal Outcome in COVID-19. J Obstet Gynaecol India. 2023;73(1): 44-50. doi: 10.1007/s13224-022-01666-3. Epub 2022 Sep 22. PMID: 36185774; PMCID: PMC9510235.
36. Al-Rawaf SA, Mousa ET, Kareem NM. Correlation between Pregnancy Outcome and Placental Pathology in COVID-19 Pregnant Women. Infect Dis Obstet Gynecol. 2022;2022:8061112. doi: 10.1155/2022/8061112. PMID: 36046178; PMCID: PMC9420637.