International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Jan S et al. Int J Reprod Contracept Obstet Gynecol. 2024 Nov;13(11):3199-3202
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20243176

Original Research Article

Histopathological changes in placenta in pregnancies affected by Covid-19 infection

Sami Jan, Nowsheen Khan*, Sabreen Wani

Department of Obstetrics and Gynecology, SKIMS MCH Bemina, Jammu and Kashmir, India

Received: 28 August 2024
Revised: 08 October 2024
Accepted: 09 October 2024

***Correspondence:**
Dr. Nowsheen Khan,
E-mail: nowsheenkhan@gmail.com

ABSTRACT

Background: The 2019 coronavirus disease (COVID-19), a novel zoonotic disease, was first discovered in late December 2019 following an outbreak of severe pneumonia of unknown etiology in Wuhan, Hubei Province, China. There is increasing evidence that COVID-19 infection leaves tell-tale signs of injuries in the placenta. This study was conducted to study the histopathological changes in placenta in pregnancies affected by COVID-19 infection in any trimester.
Methods: It was a prospective observational study conducted in the Department of Gynaecology and Obstetrics SKIMS MCH for a period of one year in all pregnant patients attending our department with the history of Covid 19 infection in any trimester during this pregnancy. The placentas of patients delivered by NVD or LSCS were sent for histopathology.
Results: The women enrolled in the study were from Kashmir. The average age was 25-39 years. The average duration of pregnancy at delivery was 37-40 weeks. 37% pregnant women were affected by covid infection in their first trimester, 49% in 2nd trimester and 14% in third trimester. 29% had acute inflammatory pathology, 34% had chronic pathology, 23% had placental infarction meanwhile no placental pathology was seen in 49% patients.
Conclusions: This study concludes that Covid 19 infection does affect the placentas in pregnancies complicated by Covid infection during any trimester of their pregnancy and it does play a role in the fetal outcome as well due to the placental changes.

Keywords: Covid 19 infection, Histopathological changes, Placenta

INTRODUCTION

The 2019 coronavirus disease (COVID-19), a novel zoonotic disease, was first discovered in late December 2019 following an outbreak of severe pneumonia of unknown etiology in Wuhan, Hubei Province, China.[1] The etiological agent was successfully isolated and identified as a previously unknown beta-coronavirus, which was provisionally coined as 2019 novel coronavirus (2019-nCoV).[2]

The American College of Obstetricians and Gynecologists and the Society of Maternal-Fetal Medicine have worked with national and international leaders on recommendations for doctors working with pregnant women who might have COVID-19 or who have been diagnosed with the illness.

The normal physiologic changes of pregnancy are known to increase susceptibility to respiratory illness. Individuals who are pregnant are more likely to acquire a SARS-CoV-2 infection and develop COVID-19 than the general population; they are at increased risk for hospitalization; ventilator-assisted breathing; and other subsequent maternal, fetal, and neonatal health issues.

There is increasing evidence that COVID-19 infection leaves tell-tale signs of injuries in the placenta.

Although the incidence of infection and subsequent morbidity is increased in pregnancy, mortality does not seem to be increased. Individuals who are vaccinated against COVID-19 before childbirth can pass antibodies to their fetuses via the placenta during pregnancy and to their infants during breastfeeding.

Likewise, evidence of placental viral infection does not guarantee intrauterine vertical transmission to fetus [3]. It is assumed that there will be an active replication of the virus in the placenta. Taken together, the innate immune system, structural barrier, as well as the interaction between decidual immune cells and the invading fetal extra villous trophoblasts may play a role in the placental protective mechanisms against SARS-CoV-2 viral invasion.

Congenital infection can be challenging to characterize since pathogen detection usually requires specific methods. The placenta represents a highly specialized organ that maintains an optimal environment for fetal development. Placental evaluation after delivery provides useful information such as the identification of disease processes in the mother or infant that requires diagnoses to deliver a specific explanation for an adverse outcome related to disease.[4]

It is well recognized that analysis of the placental histopathological changes can provide valuable information, considering that a variety of pathological agents, counting infectious ones, are associated with characteristic morphological findings.[5]

Placental examination can yield invaluable information that may be essential to enhance our understanding of disease pathogenesis and to identify underlying causes of adverse pregnancy outcomes.[6]

This study was conducted to study the histopathological changes in placenta in pregnancies affected by Covid 19 infection in any trimester.

METHODS

This was a prospective observational study conducted in the Department of Gynaecology and Obstetrics SKIMS MCH, Bemina for a period of one year i.e. from January 2022 to December 2022.

Inclusion criteria

All pregnant patients with the history of Covid 19 infection in any trimester during this pregnancy.

Exclusion criteria

Pregnancies affected with diabetes and hypertension or any other co morbidity were excluded.

The study was conducted in the women fulfilling the inclusion criteria after taking proper informed written consent. Women with history of Covid 19 infection during this pregnancy were enrolled in the study. Demographic data involving maternal age, parity, gestational age, history of covid 19 exposure, gestational age, symptoms, severity, mode of treatment, hospital admission, ICU admission, medical and surgical history was noted. Clinical and lab findings were recorded. Placentas of patients delivered by NVD or LSCS were sent for histopathology.

Statistical analysis

Data was entered in Microsoft Excel Worksheet and analyzed using Standard Statistical Software 20 version.

RESULTS

A total of 100 patients with a history of Covid 19 infection during this pregnancy who came to our department during any trimester were enrolled in the study and followed till term and delivered in our department. The placentas of the patients delivered by both NVD or LSCs was sent for histopathology.

The women enrolled in the study were from Kashmir. The average age was 25-39 years. The average duration of pregnancy at delivery was 37-40 weeks. The average duration of pregnancy during covid exposure was second trimester (Table 1 and 2).

Table 1: Age distribution of study patients.

Age (years)	Number	Percentage
25-29	40	40.0
30-34	51	51.0
35-39	9	9.0
Total	100	100.00
Mean±SD (Range)= 30.45±4.38 (25-39)		

Table 2: Gestational age of study patients.

Gestational age (weeks)	Number	Percentage
≤30	8	8.0
31-35	27	27.0
36-40	65	65.0
Total	100	100
Mean±SD (Range)= 35.93±4.88 (28-40)		

The average number of patients were affected with COVID-19 Infection during their Second trimester (Table 3).

29% patients were managed conservatively at home, 47% were managed medically and 21% required hospitalization for Covid treatment and 3% required ICU admission (Table 4).

Table 3: COVID-19 exposure.

Trimester	Number	Percentage
First	37	37.0
Second	49	49.0
Third	14	14.0
Total	100	100.00
Mean±SD = 16.825±7.36		

Table 4: Mode of treatment.

Treatment	Number	Percentage
Conservative management at home	29	29
Medical management at home	47	47
Hospital admission	21	21
ICU admission	03	3
Mean±SD = 13.55±10.07		

29% had an acute inflammatory pathology, 34% had a chronic inflammatory pathology, 23% showed placental infarction on histopathology, 12% had increased perivillous fibrin, 19% had intervillous thrombosis. 26% had chorioamniotic changes and 4% had villous edema. However, 49% had no placental pathology (Table 5).

Table 5: Histopathological findings.

Histological findings	Number	Percentage
Acute inflammatory pathology	29	29.0
Chronic inflammatory pathology	34	34.0
Placental infarction	23	23.0
Increased perivillous fibrin	12	12.0
Intervillous thrombosis	19	19.0
Chorioamnionitis	26	26.0
Villous edema	04	4.0
No placental pathology	49	49.0

DISCUSSION

This study aimed to investigate the histopathological changes associated with SARS-CoV-2 infection in placentas. A higher frequency of maternal vascular malperfusion (MVM) of the placental bed was reported in placentas of pregnant women infected with SARS-CoV-2 by various studies. It is a recognized pattern of placental injury related to abnormal uterine perfusion, leading to a myriad of pathological changes such as accelerated villous maturation, increased peri villous and intervillous fibrin deposition, decidual vasculopathy, Tenney–Parker change, villous infarction, and intervillous thrombosis.[7] Some cases of maternal SARS-CoV-2 infection have been associated with placental changes, such as atheroma's in the decidua vessels, poor blood perfusion, placental vasculopathy, placental infarction foci, chorioangioma, and inflammatory infiltrates with oedema in the placental villi.[8,9] These abnormalities could be linked to the wide expression of ACE2 and TMPRSS2, the primary mediators of SARS-CoV-2 entry, and in cells of the female genital tract and the foetal-placental unit, including syncytiotrophoblasts, cytotrophoblasts, endothelial cells, and vascular smooth muscles of the primary and secondary villi.[10]

In a study conducted by Enrique et al; the histopathological analysis of the placentas revealed predominant vascular and inflammatory pathological changes.[11] The most frequent findings were placental infarction and chorioamnionitis, each accounting for 20.6% (n = 6) of cases, followed by villitis and perivillositis at 13.8% (n = 4), intervillositis at 10.3% (n = 3), and tissue laminar necrosis at 6.9% (n = 2). In this study, the analysis of extraplacental membrane samples revealed the predominant presence of fibrin deposition, necrosis, calcifications, cysts, and leukocytes. Several studies have reported similar findings associated with SARS-CoV-2 infection.[12]

The results in this study were like our study in which 23% patients had placental infarction and 19% had intervillous thrombosis.

In their study, in the extraplacental membranes, fibrin deposition was the most predominant finding (93.1%; n = 27) which was significantly higher than our study.

In the study conducted by Joshi et al; placental abnormalities were noticed in 49·16% of total 179 placentae examined.[13] Maternal vascular malperfusion (27·93%) was the most observed placental pathology followed by villous fibrin deposits (22·90%), fetal vasculopathy (16·75%), and acute inflammation (6·70%).

In our study the villous fibrin deposition was seen in 12% patients which was lesser than in their study.

In a study conducted by Tripathy et al , microcalcification of the placenta was observed in all cases (23/23) and in the majority of the control group (25/30).[14] MVM/inflammatory features including intervillositis (5/23), deciduitis (18/23), chorioamnionitis (16/23), and villitis (8/23) were also identified in varying proportions.

Sharps et al analysed 20 placentae and found that MVP is seen in 46% of cases, fetal vasculopathy is seen 35·3%, villitis in 8·7% cases, intervillositis in 5·3% of cases, and chorioamnionitis 6% of cases.[15]

CONCLUSION

This study presents an analysis of placental pathology from pregnant women infected with COVID-19. The

histopathological analysis of the placentas revealed changes that may be linked to acute infection by the novel coronavirus. This study describes the primary histological changes observed in the placentas of pregnant women with SARS-CoV-2, which align with similar findings in diverse populations, emphasizing the potential of SARS-CoV-2 to induce histological alterations, particularly with an inflammatory and vascular nature. The most common pathological findings of the placenta of COVID-19 infections are signs of maternal and fetal malperfusion.

This study concludes that Covid 19 infection does affect the placentas in pregnancies complicated by Covid infection during any trimester of their pregnancy and it does play a role in the fetal outcome as well due to the placental changes.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Mackenzie JS, Smith DW. COVID-19: A novel zoonotic disease caused by a coronavirus from China: What we know and what we don't. Microbiol Aust. 2020;41(1):45-50.
2. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. nature. 2020;579(7798):270-3.
3. Robbins JR, Bakardjiev AI. Pathogens and the placental fortress. Curr Opini Microbiol. 2012;15(1):36-43.
4. Redline RW. Classification of placental lesions. Am J Obstet. Gynecol. 2015;213(4):21-8.
5. Benirschke B, Burton GJ, Baergen RN. Pathology of the Human Placenta. 6th ed. Vol. 10. Berlin, Heidelberg: Springer; 2012:978-993.
6. Khong TY, Mooney EE, Ariel I, Balmus NC, Boyd TK, Brundler MA, et al. Sampling and definitions of placental lesions: Amsterdam placental workshop group consensus statement. Arch Pathol Laborat Medic. 2016;140(7):698-713.
7. Ernst LM. Maternal vascular malperfusion of the placental bed. APMIS. 2018;126(7):551-60.
8. Mahyuddin AP, Kanneganti A, Wong JJ, Dimri PS, Su LL, Biswas A, et al. Mechanisms and evidence of vertical transmission of infections in pregnancy including SARS-CoV-2s. Prenatal Diagn. 2020;40(13):1655-70.
9. Adhikari EH, Moreno W, Zofkie AC, MacDonald L, McIntire DD, Collins RR, et al. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus 2 infection. JAMA network open. 2020;3(11):e2029256.
10. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen 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.
11. Patiño Escarcina JE, da Silva AK, Medeiros MO, Fernandes SS, Agareno LA, et al. Histological Alterations in Placentas of Pregnant Women with SARS-CoV-2 Infection: A Single-Center Case Series. Pathogens. 2023;12(10):1197.
12. Suhren JT, Meinardus A, Hussein K, Schaumann N. Meta-analysis on COVID-19-pregnancy-related placental pathologies shows no specific pattern. Placenta. 2022;117:72-7.
13. Joshi B, Chandi A, Srinivasan R, Saini SS, Prasad GR, Puri GD, Bhalla A, Suri V, Bagga R. The placental pathology in Coronavirus disease 2019 infected mothers and its impact on pregnancy outcome. Placenta. 2022;127:1-7.
14. Tripathy S, Sreelakshmi S, Das A. Histopathological changes and clinical outcomes in placentas of COVID-19 positive mothers: a cohort study. J Clin Diagnos Res. 2024;18(2).
15. Sharps MC, Hayes DJ, Lee S, Zou Z, Brady CA, Almoghrabi Y, et al. A structured review of placental morphology and histopathological lesions associated with SARS-CoV-2 infection. Placenta. 2020;101:13-29.

Cite this article as: Jan S, Khan N, Wani S. Histopathological changes in placenta in pregnancies affected by Covid-19 infection. Int J Reprod Contracept Obstet Gynecol 2024;13:3199-202.