Journal of **R**eproduction & **I**nfertility
Volume 25, Issue no. 3
https://doi.org/10.18502/jri.v25i3.17018

Case Report

Check for updates

Placental Histopathological Changes and the Level of Anti-Spike Antibody After Covid-19 Vaccination During Pregnancy: A Case Series

Zohreh Heidary [1], Omid Kohandel Gargari [2], Majid Zaki-Dizaji [3], Arman Shafiee [2], Haniyeh Fathi [2], Roya Saeednejad [4], Marjan Ghaemi [1], Sedigheh Hantoushzadeh [1*]

1- Vali-E-Asr Reproductive Health Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran
2- Student Research Committee, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran
3- Human Genetics Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
4- Irman Pathobiology Laboratory, Tehran, Iran

Abstract

Background: COVID-19 infection during pregnancy could be associated with placental histopathological changes such as vascular diseases and malperfusion. There are studies showing that mRNA vaccines are not associated with significant placental pathological changes. Our objective was to evaluate the placental histopathology in pregnant women who received Sinopharm, an inactivated virus vaccine, during pregnancy.

Case Presentation: The study included placental samples collected from mothers who gave birth of living singletons through elective cesarean sections performed between March 2022 and May 2022 at Imam Khomeini Hospital Complex. The study included women who had no history of positive reverse transcription polymerase chain reaction (RT-PCR) testing for COVID-19 during pregnancy, and had received at least one dose of COVID-19 vaccine during their pregnancy. Humoral levels of anti-SARS-CoV-2 spike IgG were measured in both the mothers and neonates.

Results: The study included 20 mother-neonate pairs. The mean maternal age was 34±3.6 years, and all mothers received Sinopharm vaccine as their first and second doses. The last vaccine dose was administered during pregnancy, with 3 mothers receiving it in the first trimester, 9 in the second trimester, and 8 in the third trimester. The histopathological findings in the placental samples included decidual vasculopathy, subchorionic thrombosis, and chronic histiocytic intervillositis. All mothers and neonates, except one pair, were positive for anti-spike antibody.

Conclusion: Multiple abnormal histopathological findings were reported in placenta of vaccinated mothers. However, similar to previous studies, these placental findings are considered mild lesions and have been observed in both vaccinated and unvaccinated mothers.

** Corresponding Author:*
Sedigheh Hantoushzadeh, Vali-E-Asr Reproductive Health Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran
E-mail:
hantoushzadeh@tums.ac.ir

Received: 16, Jan. 2024
Accepted: 26, May 2024

Keywords: COVID-19, Placenta, SARS-CoV-2, Sinopharm, Vaccine.
To cite this article: Heidary Z, Kohandel Gargari O, Zaki-Dizaji M, Shafiee A, Fathi H, Saeednejad R, et al. Placental Histopathological Changes and the Level of Anti-Spike Antibody After Covid-19 Vaccination During Pregnancy: A Case Series. J Reprod Infertil. 2024; 25(3):231-237. https://doi.org/10.18502/jri.v25i3.17018.

Introduction

There is now accumulating evidence that coronavirus disease 2019 (COVID-19) infection during pregnancy leads to multiple adverse outcomes for maternal, fetal, and even neonatal health including preterm birth and stillbirth (1-4). COVID-19 could also affect placenta and it is reported that COVID-19 is associated with decidual arteriopathy, maternal and/or fetal malperfusion, and chronic histiocytic intervillositis (5-7). This association raises the question of whether vaccines have similar effects on placenta or not. Vaccines are shown to be effective at prevention of

COVID-19 in pregnant women (8). mRNA vaccines are also effective at preventing placentitis and stillbirth. Vaccination decreases the viral load, decreases vascular and tissue damages, and prevents virus dissemination from lungs to placenta and other organs (9, 10). Fortunately, studies have shown that mRNA vaccines do not cause significant histopathological changes in placental pathology (5) and stillbirth following placentitis was only observed among unvaccinated mothers (4). But there are no published studies discussing inactivated vaccines such as BBIBP-CorV (Sinopharm vaccine), while these vaccines are frequently used in Middle Eastern and Eastern Asian countries. Also, neonatal level of anti-spike antibody is reported to be correlated with maternal vaccination (mRNA vaccines) (11), but there are limited data about inactivated vaccines such as Sinopharm. In this study, placental histopathological findings and level of anti-spike antibody of 20 mothers were reported who received Sinopharm vaccine during pregnancy.

Case Presentation

This project was approved by the ethical committee of Tehran University of Medical Sciences (approval code: IR.TUMS.IKHC.REC.1400.436) and was performed in accordance with good clinical practice and the principles of Declaration of Helsinki. Written informed consent was obtained from all the participants of this study. A search was conducted in the hospital's database of women who were admitted for childbirth to identify women who had received SARS-CoV-2 Sinopharm vaccine (DrugBank Accession Number of DB15807) before delivery, and for whom the placenta was submitted for pathological evaluation. The inclusion criteria for the study were as follows:

1) All healthy singleton pregnant women who delivered healthy term newborns via normal vaginal delivery or elective cesarean section between March 2022 and May 2022 at the obstetrics ward of Imam Khomeini Hospital Complex as a university hospital; 2) cases with no history of confirmed COVID-19 either by RT-PCR, imaging findings, or physicians' diagnosis; 3) cases received at least two doses of Sinopharm vaccine, with at least one dose during pregnancy; 4) participants tested negative for COVID-19 at the time of hospitalization by RT-PCR; 5) women with no pregnancy complications, such as maternal diabetes, pre-eclampsia, thrombosis, or hypertension; and 6) women with no history of abortion.

Sample collection, fixation, staining, and histopathological assessments: Immediately after birth, placental and membrane samples fixed in 10% buffered formalin were sent to the pathology laboratory. Then, paraffin-embedded blocks were stained with hematoxylin and eosin (H&E). All placentas were examined for gross and histologic findings following guidelines outlined in Amsterdam Consensus Statement (12). All samples were assessed by 2 pathologists. During the second assessment, the pathologist was blinded to the sample identifications and the results of the initial assessment.

Serological assay: The SARS-CoV-2 specific IgG testing was performed using SARS-COV-2 anti-spike IgG levels (Pishtaz Teb Zaman Diagnostics, Iran). The maternal and neonatal serum samples were evaluated for SARS-CoV-2 anti-spike IgG levels using the enzyme linked immunosorbent assay (ELISA) technique according to the company's specifications. The kit is intended to detect the presence of SARS-CoV-2 specific antibodies, indicating recent or previous infection with the SARS-CoV-2 virus. The SARS-CoV-2 anti-spike IgG ELISA assay had a reported sensitivity of 98.16% and a specificity of 99.01%, with a cut-off value of 8 *RU/ml* (relative units *per milliliter*). Any level of antibody above the cut-off of the laboratory test was considered positive (13, 14).

Results

Pregnancy women characteristics: Out of a total of 43 pregnant women who received Sinopharm vaccine, 20 pregnant women met the inclusion criteria. The mean maternal age was 34±3.6 years. All newborns included in this study were full-term with a mean gestational age of 38.2±0.79 weeks. In this study, 8 out of 20 newborns (40%) were female, and 12 (60%) were male. The mean birthweight of the newborns was 3217.75±417.44 *gr*. All newborns had Apgar scores of 9 at 1 *min* and 10 at 3 *min*. All COVID-19 vaccines received by the mothers in this study were Sinopharm (BBIBP-CorV) vaccines. Twelve mothers had received 2 doses of vaccine, while the remaining 8 mothers had received three doses. The mothers in this study received their last dose of the Sinopharm COVID-19 vaccine at different stages of pregnancy -3 in the first trimester, 9 in the second trimester, and 8 in the third trimester. All mothers were negative for SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test

Table 1. Characteristics of included mothers and newborns

Patients number	Maternal age	Delivery time	Neonate's gender	Type of delivery	Vaccine type 1st dose	Vaccine type 2nd dose	Vaccine type 3rd dose	Number of doses	G	P	A	Time of vaccination (pregnancy)
1	36	39	Female	C/S	Sinopharm	Sinopharm	Nothing	2	1	0	0	16W6D
2	36	38	Male	C/S	Sinopharm	Sinopharm	Nothing	2	4	1	2	20W4D
3	36	40	Female	NVD	Sinopharm	Sinopharm	Nothing	2	1	0	0	19W2D
4	35	38	Male	C/S	Sinopharm	Sinopharm	Sinopharm	3	2	0	1	6W5D
5	32	39	Male	C/S	Sinopharm	Sinopharm	Sinopharm	3	2	1	0	7W3D
6	27	38	Male	C/S	Sinopharm	Sinopharm	Sinopharm	3	1	0	0	0W22D
7	35	38	Female	C/S	Sinopharm	Sinopharm	Sinopharm	3	1	0	0	8W4D
8	31	38	Male	C/S	Sinopharm	Sinopharm	Sinopharm	3	1	0	0	7W2D
9	38	38	Male	C/S	Sinopharm	Sinopharm	Nothing	2	1	0	0	21W4D
10	28	37	Female	C/S	Sinopharm	Sinopharm	Sinopharm	3	1	0	0	17W5D
11	29	38	Female	C/S	Sinopharm	Sinopharm	Nothing	2	1	0	0	11W2D
12	31	39	Male	C/S	Sinopharm	Sinopharm	Nothing	2	3	1	1	20W2D
13	32	38	Male	C/S	Sinopharm	Sinopharm	Sinopharm	3	1	0	0	12W0D
14	37	38	Female	C/S	Sinopharm	Sinopharm	Nothing	2	5	2	2	11W6D
15	31	39	Female	C/S	Sinopharm	Sinopharm	Nothing	2	2	1	0	21W2D
16	41	38	Male	C/S	Sinopharm	Sinopharm	Nothing	2	4	1	2	14W2D
17	37	38	Male	C/S	Sinopharm	Sinopharm	Nothing	2	2	1	0	8W0D
18	37	38	Male	C/S	Sinopharm	Sinopharm	Nothing	2	3	2	0	18W0D
19	36	38	Male	C/S	Sinopharm	Sinopharm	Sinopharm	3	4	1	2	29W6D
20	35	38	Female	C/S	Sinopharm	Sinopharm	Nothing	2	1	0	0	22W2D

C/S: Cesarian section, NVD: Normal vaginal delivery, Hx: History, G: Gravid, P: Para, A: Abortion

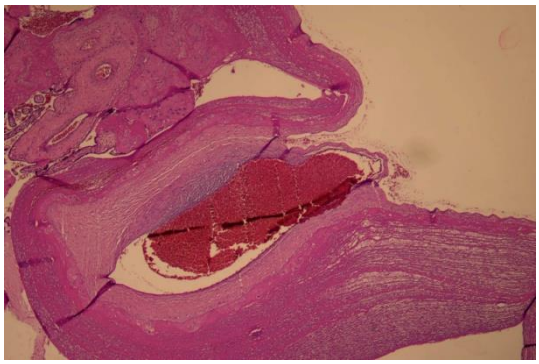

Figure 1. Histopathological examination showing massive subchorionic thrombosis in placenta

at the time of admission. Characteristics of included patients are summarized in table 1.

Histopathological and serological findings: Microscopic examination revealed histopathological changes in 5 placentas (20%). These findings consist of massive subchorionic thrombosis (MST) (1 placenta, figure 1), decidual arteriopathy (3 placentas), and chronic histiocytic intervillositis (CHI) (1). All findings are presented in table 2 and normal variations were not reported. It is important to note that none of the cases with decidual arteriopathy had a history of hypertension.

Case 13 presented with chronic histiocytic vasculitis, which was the most noteworthy histopathological finding observed in our study. She was a 32-year-old mother who delivered her first child, a healthy full-term boy, with 1-*min* and 5-*min* Apgar scores of 9 and 10, respectively. Additionally, case 13 had a body weight of 83 *kg* and a height of 166 *cm*, indicating that she was overweight. This patient also had a three-year history of multiple sclerosis (MS).

The SARS-CoV-2 spike antibody was detected in all mothers and their corresponding newborns, except for one mother-neonate pair (mother-neonate number 3). Interestingly, for all the mother-neonate pairs with positive spike antibody detection, the levels were higher in the neonatal serum compared to the maternal serum (Table 2). The mother who was tested negative for the SARS-CoV-2 spike antibody showed MST changes in her placenta.

Discussion

To our knowledge, this is the first study evaluating the placental pathology of the mothers who

Table 2. Placenta histopathological findings of included patients

Patient	Histopathological findings	Level of spike antibody	
		Maternal	Neonatal
1	None	>100	>100
2	None	54.10	79.80
3	Massive subchorionic thrombosis	2.00	3.00
4	None	>100	>100
5	None	>100	>100
6	Decidual arteriopathy	25.30	44.10
7	None	>100	>100
8	Decidual arthropathy	16.70	36.60
9	None	62.20	92.40
10	None	18.10	25.90
11	None	42.20	97.80
12	None	>100	>100
13	Chronic histiocytic intervillositis	>100	>100
14	None	>100	>100
15	None	25.20	31.90
16	None	37.20	>100
17	None	>100	>100
18	None	20.00	24.20
19	None	>100	>100
20	Decidual vasculopathy	>100	>100

Level of anti-spike is reported in RU/*ml* (Relative units *per ml*) and levels higher than 8 are considered positive

had previously received Sinopharm COVID-19 vaccine during their pregnancy. In this study, placental histopathology of 20 pregnant mothers was reported who received at least the first two doses of Sinopharm (BBIBP-CorV) COVID-19 vaccine. The key placental histopathological findings in this study were decidual arteriopathy in 3 placentas, massive subchorionic thrombosis in 1 placenta, and chronic intervillositis in 1 placenta. However, due to the limitations of our study, it is difficult to draw any statistical conclusions from these findings.

There are several reports regarding the effect of COVID-19 on placental pathology (6, 15-19). Most of these studies investigated pregnancy outcomes in addition to placental pathology and their possible correlation. These studies showed a significant histopathological change in the placenta, including avascular villi, fibrin deposition, thrombosis, meconium macrophage, malperfusion, fetal and maternal vascular defects, and villitis (6, 18, 20). However, there are reports showing no significant difference in histopathological changes between infected and non-infected placentas (19, 21). The available evidence indicates that COVID-19 vaccines, such as Sinopharm (BBIBP-CorV) and mRNA vaccines, are not only safe during pregnancy, but may also decrease the occurrence of certain adverse pregnancy outcomes (3, 7, 22-24). The majority of the available research has focused on how COVID-19 infection affects the placenta. In an evaluation of 164 mothers who were fully vaccinated with mRNA COVID-19 vaccines (at least 2 doses at >2 weeks before delivery) and 267 unvaccinated mothers, no significant differences were found in the placental findings, birthweight, or Apgar scores between the two groups (25). In a retrospective cohort study comparing a control group (with no COVID-19 history or vaccination), a group with COVID-19 infection during pregnancy, and a group with COVID-19 mRNA vaccination during pregnancy, no significant placental changes were observed in the vaccinated groups. However, increased placental vascular pathologies were detected among infected mothers (5). In another study of 84 mRNA-vaccinated mothers and 116 controls, no increased incidence of placental pathological findings was found in vaccinated mothers (7). Altogether, COVID-19 mRNA vaccination in pregnancy appears to be safe and is associated with a reduction in COVID-19-related complications (22).

Decidual arteriopathy was found in 3 mothers (15%), although this pathological finding has been shown to be related to SARS-CoV-2 infection. It is also common in both vaccinated (1.8 and 10% in two studies) and unvaccinated (5.2 and 12% in two studies) mothers (7, 25). Generally, the prevalence of placental thrombosis in pregnant women with COVID-19 is low (26) and subchorionic thrombosis was observed in both COVID-19 and control groups, without a statistically significant difference between the groups (27). The incidence of massive subchorionic thrombosis (MST) is about 0.03%–0.08%, and its etiology and pathogenesis are so far unknown (28, 29). MST association with spike antibody level cannot be determined in our study, and its absence in this case may be just a coincidence. The outcomes of MST depend on its size and location. In the case presented, the patient had a small MST without any reported prenatal or postnatal complications. Also, chronic histiocytic intervillositis was detected in one case. Chronic histiocytic intervillositis (CHI) is a microscopic abnormality that was rarely seen in placentas, occurring in less than 1% of pregnancies. CHI has been observed to occur in the placentas of newborns with perinatal complications and adverse clinical outcomes (4). The overall live birth rate in cases of CHI is 30–81%. Among these live births, most infants are premature or show fetal growth restriction (FGR). The recurrence rate of CHI in subsequent pregnancies is high (30). The occurrence of CHI with trophoblast necrosis has been reported as a risk factor for transplacental transmission of SARS-CoV-2 (31). CHI is considered as a complication that may be linked to SARS-CoV-2 infection (32, 33). No prenatal complications related to placental findings were detected in the current study. All mothers gave birth to healthy babies, and none of them were hospitalized. Therefore, in line with previous studies (23, 24), our findings demonstrated that Sinopharm vaccine is highly beneficial for pregnant women. However, due to the small sample size of our study and the absence of a control group, it cannot be determined whether the observed placental findings were associated with Sinopharm vaccination or asymptomatic SARS-CoV-2 exposure.

Altogether, the sample size and lack of a matched control group were the limitations of our study. Additionally, similar to other studies (5), SARS-CoV-2 exposure is a possible confounder, although none of our participants had confirmed

SARS-CoV-2 during pregnancy. There are limited reports about placental histopathology assessment after vaccination during pregnancy (5, 7, 22). In comparison to histologic lesions of placenta observed in term pregnancies with normal outcome, our findings are considered to be mild placental lesions (34).

Altogether, the current data suggests that vaccination with Sinopharm (BBIBP-CorV) does not appear to be associated with significant placental pathological complications, similar to observations with mRNA COVID-19 vaccines. However, the impact of vaccination on placental histopathology remains insufficiently understood, necessitating further research and studies for a more comprehensive assessment.

Conclusion

According to the findings of the present study, the Sinopharm vaccine does not appear to pose significant placental pathological risks. However, further research with larger sample sizes and control groups is needed to fully understand the impact of COVID-19 vaccination on placental health.

Acknowledgement

The authors are thankful, first and foremost, to the participants for their patience. Also, the authors express their gratitude to the hospital personnel for their help and support.

Funding: This study was supported by a grant from Tehran University of Medical Sciences [Project number: 1400-3-94-56564].

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Kumari K, Yadav R, Mittra S, Kumar A, Singh J, Bajpai PK, et al. Pregnancy consequences and vertical transmission potential of SARS-CoV-2 infection: seeking answers from a preliminary obser-vation. J Reprod Infertil. 2021;22(2):144-7.
2. Heidary Z, Kohandel Gargari O, Fathi H, Zaki-Dizaji M, Ghaemi M, Hossein Rashidi B. Maternal and neonatal complications, outcomes and possibility of vertical transmission in Iranian women with COVID-19. Arch Iran Med. 2021;24(9):713-21.
3. Kumar D, Verma S, Mysorekar IU. COVID-19 and pregnancy: clinical outcomes; mechanisms, and vaccine efficacy. Transl Res. 2023;251:84-95.
4. Schwartz DA, Mulkey SB, Roberts DJ. SARS-CoV-2 placentitis, stillbirth, and maternal COVID-19 vaccination: clinical-pathologic correlations. Am J Obstet Gynecol. 2023;228(3):261-9.
5. Boelig RC, Aghai ZH, Chaudhury S, Kazan AS, Chan JSY, Bergmann-Leitner E. Impact of COVID-19 disease and COVID-19 vaccination on maternal or fetal inflammatory response, placental pathology, and perinatal outcomes. Am J Obstet Gynecol. 2022;227(4):652-6.
6. Leal CRV, Maciel RAM, Corrêa Júnior MD. SARS-CoV-2 infection and placental pathology. Rev Bras Ginecol Obstet. 2021;43(6):474-9.
7. Shanes ED, Otero S, Mithal LB, Mupanomunda CA, Miller ES, Goldstein JA. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination in pregnancy: measures of immunity and placental histopathology. Obstet Gynecol. 2021;138(2):281-3.
8. Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. N Engl J Med. 2021;384(24):2273-82.
9. Levine-Tiefenbrun M, Yelin I, Katz R, Herzel E, Golan Z, Schreiber L, et al. Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine. Nat Med. 2021;27(5): 790-2.
10. Mohamed K, Rzymski P, Islam MS, Makuku R, Mushtaq A, Khan A, et al. COVID-19 vaccinations: the unknowns, challenges, and hopes. J Med Virol. 2022;94(4):1336-49.
11. Shook LL, Atyeo CG, Yonker LM, Fasano A, Gray KJ, Alter G, et al. Durability of anti-spike antibodies in infants after maternal COVID-19 vaccination or natural infection. JAMA. 2022;327 (11):1087-9.
12. 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 Lab Med. 2016;140(7):698-713.
13. Arab M, Noei Teymoordash S, Talayeh M, Ghavami B, Javadi A, Nouri B. Evaluation of serologic changes of IgG and IgM antibodies associated with SARS-COV-2 in cancer patients: a cohort seroprevalence study. Asian Pac J Cancer Prev. 2021;22 (6):1667-70.
14. Balou HA, Yaghubi Kalurazi T, Joukar F, Hassanipour S, Shenagari M, Khoshsorour M, et al. High seroprevalence of SARS-CoV-2 (COVID-19)-specific antibodies among healthcare workers: a cross-sectional study in Guilan, Iran. J Environ Public Health. 2021;2021:9081491.

15. Akhavan S, Borna S, Abdollahi A, Shariat M, Zamani N. Pathologic examination of the placenta and its benefits in treatment plan or follow-up of patients: a cross-sectional study. Eur J Med Res. 2022;27(1):113.
16. Singh N, Buckley T, Shertz W. Placental pathology in COVID-19: case series in a community hospital setting. Cureus. 2021;13(1):e12522.
17. Arcos Júnior GF, Francisco RPV, Kill B, Peres SV, Gibelli M, Ibidi SM, et al. Placental pathological findings in coronavirus disease 2019: perinatal outcomes. Placenta. 2022;128:23-8.
18. Al-Rawaf SA, Mousa ET, Kareem NM. Correlation between pregnancy outcome and olacental oathology in COVID-19 oregnant women. Infect Dis Obstet Gynecol. 2022;2022:8061112.
19. Gulersen M, Prasannan L, Tam Tam H, Metz CN, Rochelson B, Meirowitz N, et al. Histopathologic evaluation of placentas after diagnosis of maternal severe acute respiratory syndrome coronavirus 2 infection. Am J Obstet Gynecol MFM. 2020;2(4): 100211.
20. Motwani R, Deshmukh V, Kumar A, Kumari C, Raza K, Krishna H. Pathological involvement of placenta in COVID-19: a systematic review. Infez Med. 2022;30(2):157-67.
21. 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.
22. Prasad S, Kalafat E, Blakeway H, Townsend R, O'Brien P, Morris E, et al. Systematic review and meta-analysis of the effectiveness and perinatal outcomes of COVID-19 vaccination in pregnancy. Nat Commun. 2022;13(1):2414.
23. Jeewandara C, Jayampathi KCS, Ranasinghe T, Aberathna IS, Gunasekara B, Danasekara S, et al. Antibody responses to Sinopharm/BBIBP-CorV in pregnant mothers in Sri Lanka. PLOS Glob Public Health. 2022;2(7):e0000607.
24. Sunder A, Alqatari HM, Taha OE, Keshta MS, Bughamar FK, Darwish B. COVID-19 vaccinations in pregnancy: save mother and baby from COVID-19 pandemic. Int J Gynaecol Obstet. 2022; 160(3):864-73.
25. Smithgall MC, Murphy EA, Schatz-Siemers N, Matrai C, Tu J, Baergen RN, et al. Placental pathology in women vaccinated and unvaccinated against SARS-CoV-2. Am J Obstet Gynecol. 2022; 227(5):782-4.
26. Mohd Ariff NS, Abdul Halim Zaki I, Mohd Noordin Z, Md Hussin NS, Goh KW, Ming LC, et al. A review of the prevalence of thromboembolic complications among pregnant women infected with COVID-19. J Clin Med. 2022;11(19):5934.
27. Carbonnel M, Daclin C, Tourne M, Roux E, Le-Marchand M, Racowsky C, et al. Impact of COVID-19 on subclinical placental thrombosis and maternal thrombotic factors. J Clin Med. 2022;11 (14):4067.
28. Fung TY, To KF, Sahota DS, Chan LW, Leung TY, Lau TK. Massive subchorionic thrombohematoma: a series of 10 cases. Acta Obstet Gynecol Scand. 2010;89(10):1357-61.
29. Miyagi M, Kinjo T, Mekaru K, Nitta H, Masamoto H, Aoki Y. Massive subchorionic thrombohematoma (Breus' Mole) associated with fetal growth restriction, oligohydramnios, and intrauterine fetal death. Case Rep Obstet Gynecol. 2019;2019: 9510936.
30. Mattuizzi A, Sauvestre F, André G, Poingt M, Camberlein C, Carles D, et al. Adverse perinatal outcomes of chronic intervillositis of unknown etiology: an observational retrospective study of 122 cases. Sci Rep. 2020;10(1):12611.
31. Schwartz DA, Baldewijns M, Benachi A, Bugatti M, Collins RRJ, De Luca D, et al. Chronic histiocytic intervillositis with trophoblast necrosis is a risk factor associated with placental infection from coronavirus disease 2019 (COVID-19) and intrauterine maternal-fetal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in live-born and stillborn infants. Arch Pathol Lab Med. 2021;145(5):517-28.
32. Rebutini PZ, Zanchettin AC, Stonoga ETS, Prá DMM, de Oliveira ALP, Dezidério FDS, et al. Association between COVID-19 pregnant women symptoms severity and placental morphologic features. Front Immunol. 2021;12:685919.
33. Marton T, Hargitai B, Hunter K, Pugh M, Murray P. Massive perivillous fibrin deposition and chronic histiocytic intervillositis a complication of SARS-CoV-2 infection. Pediatr Dev Pathol. 2021; 24(5):450-4.
34. Romero R, Kim YM, Pacora P, Kim CJ, Benshalom-Tirosh N, Jaiman S, et al. The frequency and type of placental histologic lesions in term pregnancies with normal outcome. J Perinat Med. 2018;46(6):613-30.