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RESEARCH ARTICLE

Long-term Obstetric and Neonatal Outcome of SARS-CoV-2 Infection During First, Second and Third Trimesters of Pregnancy: Results of 532 Patients and 532 Healthy Controls in a Single Tertiary Center

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ABSTRACT

Objective: After clinical recovery from the SARS-CoV-2 infection, many issues about the long-term effects of the SARS-CoV-2 infection on the body are still to be clarified. The aim of this study is to investigate the obstetric and neonatal outcomes of patients who recovered from SARS-CoV-2 infection during pregnancy.

Materials and Methods: This retrospective cohort study was conducted in a single tertiary hospital with separate SARS-CoV-2 infection (+) and (-) units. Each parameter of 532 confirmed SARS-CoV-2 infected pregnant patients who recovered from the disease and subsequently delivered, and 532 controls between March 2020 and December 2021 were compared. Results were also analyzed according to the trimesters in which SARS-CoV-2 infections were diagnosed.

Results: Mean gestational age at delivery was found to be lower and preterm birth rates were found to be higher significantly in patients who recovered from SARS-CoV-2 during pregnancy compared to those of the controls (p=0.05). Rates of congenital anomalies, in utero fetal demise and comorbidities were not statistically different except for asthma and preeclampsia. APGAR scores and neonatal intensive care unit admission were not significantly different (p>0.05). The clinical severity, lung ultrasound scores, the requirement for oxygen support, and admission rates to the intensive care unit were observed to progressively rise as the pregnancy advanced during the onset of the disease.

Conclusion: The patients who recovered from SARS-CoV-2 infection during pregnancy are at higher risk of preterm delivery and preeclampsia. These effects are not related to the clinical severity of the infection. Risks of SGA and congenital anomalies are not increased.

Keywords: COVID-19, long term adverse effects, obstetrics, pre-eclampsia, pregnancy outcome, SARS-CoV-2

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INTRODUCTION

SARS-CoV-2 infection was accepted as pandemic by the World Health Organization (WHO) on March 11, 2020 and although has lost its severity continues to infect people worldwide.[1] It has been reported that close to 774 million people in the world have been infected with SARS-CoV-2 since the beginning of the pandemics.[2]

SARS-CoV-2 infection has a broad-spectrum clinical picture from asymptomatic to severe systemic disease. The lungs, liver, hematopoietic, and cardiovascular systems are the most commonly affected organs and have also been associated with increased rates of anxiety and depression in pregnant women.[3,4] Moreover, the severity of systemic disease may not necessarily coincide with the clinical signs; and little is known about the effects of the infection on fetus.[3,5,6]

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After clinical recovery from the SARS-CoV-2 infection, many issues about the long-term effects of the SARS-CoV-2 infection on the body are still to be clarified. Further studies on the changes in immunity, blood coagulability, cardiovascular system and ongoing pregnancy might be needed.

There has been no universally agreed algorithm on clinical management of SARS-CoV-2 infection in pregnancy and hence the data about those remains very heterogeneous by means of treatment and timing of the delivery.[3] In our clinic, the same team managed these patients according to both severity of the disease and the gestational week at the time of diagnosis. The primary goal was the continuation of the pregnancy during the infection until recovery or unless otherwise delivery is indicated. Premature delivery was only considered in the cases of severe uncompensated disease to relieve the burden of fetus or fetal distress or demise. This mode of management allowed us to observe SARS-CoV-2 infection patients in all trimesters of pregnancy and to compare the results with their age-matched controls.

In this study, it was aimed to investigate the obstetric and neonatal outcomes of patients recovered from SARS-CoV-2 infection during pregnancy.

MATERIALS and METHODS

This retrospective case control study was conducted in a tertiary hospital with separate SARS-CoV-2 infection (+) and (-) units. The study was approved by the Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (No: E-46059653-020, Date: 16.02.2022) and the Ministry of Health COVID-19 Scientific Research Evaluation Commission and the study protocol adhered to the principles outlined in the Declaration of Helsinki.

Five hundred and thirty-two SARS-CoV-2 infection (+) pregnant patients who recovered from the disease and subsequently delivered at our hospital between March 2020 and December 2021 were included in the study. Women delivered within the 14-days isolation period after recovery were excluded. The diagnoses of SARS-CoV-2 infection based on reverse transcription polymerase chain reaction (PCR) testing of nasopharyngeal swabs and their gestational weeks at testing were recorded. For each vaginal or cesarean birth of patients in the study group, the first consecutive vaginal or cesarean birth at the same age (±2 years) with no history of SARS-CoV-2 infection was selected for the control group. By this way, it was aimed to overcome the possible effect of the mode of delivery on the neonatal outcome of the patients. None of the patients in study and the control groups were vaccinated against SARS-CoV-2 virus.

The data on demographics and clinical characteristics of mothers, obstetric outcomes, and neonatal outcomes were collected retrospectively.

The clinical severity of SARS-CoV-2 infection was classified according to the WHO.[3] Lung ultrasound was performed on all patients during SARS-CoV-2 infection and the scores were recorded as described by Soldati et al.[7]

Pregnant women with 6 to 13+6 weeks of gestation were defined as 1st trimester, those with 14 to 27+6 weeks as 2nd trimester, and those above 28 weeks as 3rd trimester. Birth weights below 3rd and 10th percentiles were accepted as small for gestational age (SGA) separately.

In the first 12 hours after birth, all neonates of the study group were tested for SARS-CoV-2 infection using a nasopharyngeal swab reverse transcription PCR as a local protocol. They were also monitored for SARS-CoV-2 infection symptoms during their hospital stay.

The primary outcome measure was the effects of SARS-CoV-2 infection during pregnancy on long-term pregnancy outcomes. Secondary outcome measure was the pregnancy outcomes with respect to the trimesters that SARS-CoV-2 infection was diagnosed.

Statistical Analysis

Data were analyzed with SPSS Statistics version 22.0 (IBM Corporation, Armonk, NY) software. Shapiro-Wilk test, skewness, and kurtosis values were used to verify the data's assumed normality. Descriptive statistics were given as mean±standard deviation, median (interquartile range) according to normality assumption for continuous variables. Categorical variables were analyzed with Pearson Chi-Square and Fischer's Exact test where appropriate and continuous variables were analyzed with T-test, Mann-Whitney U and ANOVA tests in accordance with the normality assumption. p value <0.05 was considered as statistically significant.

RESULTS

Demographics and clinical data of the patients in the SARS-CoV-2 infection and the control groups were given in Table 1 and Table 2. Two patients had history of malignancy. One patient in the SARS-CoV-2 infection group had enucleation of eye because of malignant melanoma and one patient in the control group had gamma knife excision of vestibular schwannoma. Hypothyroidism was found in 44 (8.3%) patients in SARS-CoV-2 group and 31 (5.9 %) in the control group and all 75 patients were on thyroid replacement and euthyroid during the study.

Table 1. Demographic and clinical characteristics of the groups

	SARS-CoV-2 (n=532)		No infection (n=532)		p
	n	%	n	%	
Age (year)	28.60±5.36		28.65±5.33		0.876
BMI (kg/m^2)	26.12±3.63		26.30±4.10		0.434
Parity (median)	1 (2)		1 (1)		0.519
Comorbidity	114	21.4	98	18.4	0.218
Preeclampsia[a]	23	4.3	3	0.6	<0.001*
Hypothyrodism	44	8.3	31	5.9	0.081
Hyperthyroidism	-	-	1	0.2	0.498
Asthma	20	3.8	8	1.5	0.032*
Pregestational diabetes	5	0.9	3	0.6	0.486
Gestational diabetes	16	3.0	21	3.9	0.386
HBsAg positivity	7	1.4	13	2.5	0.184
Chronic hypertension	5	0.9	4	0.8	0.751
Rheumatoid diseases*	5	0.9	4	0.8	0.751
History of cancer	1	0.2	1	0.2	0.995
Epilepsy	-	-	3	0.6	0.081
Mode of birth					
Cesarean section	297	55.8	297	55.8	
Vaginal birth	235	44.2	235	44.2	
Type of anesthesia for cesarean section					<0.001*
General anesthesia	166	55.8	211	71.2	
Regional anesthesia	131	44.2	86	28.8	

Continuous variables are showed as mean±standard deviation or median depending on distribution characteristics. Binary variables are showed as count. *: Rheumatoid diseases: Sjögren's syndrome, rheumatoid arthritis, Behçet's disease, Familial Mediterranean Fever (FMF). a: Odds ratio: 7.893, (95% confidence interval:2.355-26.449). When the pregnant women with history of preeclampsia were excluded from the analysis, still there was a significant difference between groups with regard to preeclampsia as an indication of birth (p=0.018). BMI: Body mass index; HBsAg: Hepatitis B surface antigen

Demographic and clinical characteristics and obstetric outcomes of the pregnant women who had SARS-CoV-2 infection with respect to trimesters were summarized in Table 3 and Table 4. The mode of birth and type of anesthesia are presented in Table 5. All neonates of these mothers were PCR (-) for SARS-CoV-2. Of 532 SARS-CoV-2 infected patients, 75 (14.1%) were in 1st trimester, 239 were (44.9%) in 2nd trimester and 218 (41%) were in 3rd trimester of their pregnancy. Preeclampsia and preterm birth cases according to the clinical severity and the lung ultrasound scores (LUS) of the SARS-CoV-2 infection were given at Table 6.

Indications of birth of the all three trimester groups of patients recovered from SARS-CoV-2 infection were spontaneous uterine contractions in 44 (58.6%), previous cesarean section in 11 (14.7%), preeclampsia in 6 (8%), oligohydramnios in 2 (2.7%) and post term pregnancy in 2 (2.7%) in the first trimester group; spontaneous uterine contractions in 130 (54.4%), previous cesarean section in 49 (20.5%), oligohydramnios in 10 (4.2%), preeclampsia in 9 (3.8%), macrosomia in 5 (2.1%), and post term pregnancy in 4 (1.7%) in the second trimester group; third trimester due to spontaneous uterine contractions in 120 (55%), previous cesarean section in 42 (19.3%), oligohydramnios in 8 (3.7%), preeclampsia in 8 (3.7%), macrosomia in 2 (0.9%), post term pregnancy in 3 (1.4%) and maternal health issues in 3 (1.4%) in the third trimester group. No difference was found between all three trimester groups by means of indications of birth (p=0.486).

In the SARS-CoV-2 group, there was one neonatal death who was 26 weeks preterm and lost due to prematurity, and there was an *in utero* fetal death of a preeclamptic mother that occurred after the acute SARS-CoV-2 infection. There was no fetal or neonatal loss in the controls. Both *in utero* death

Table 2. Fetal parametres and neonatal outcomes

Fetal parametres and neonatal outcomes	SARS-CoV-2 (n=532)		No infection (n=532)		p
	n	%	n	%	
Fetal birth weight (gr)	3223.33±514.50		3304±504.97		0.010*
Gestational age at delivery (weeks)	38.62±1.95		39.01±1.49		<0.001*
Preterm birth	73	13.7	37	6.9	0.002*
Early preterm birth (<34 weeks)[b]	9	2.3	1	0.2	0.012*
Late preterm birth (34–37 week)[b]	64	12	36	6.8	0.004*
Small for gestational age <%10	77	14.5	90	16.9	0.311
Small for gestational age <%3	18	3.4	27	5.1	0.337
APGAR 5th Minute <7	6	1.1	7	1.3	0.767
NICU admission	75	14.1	91	17.1	0.183
Neonatal complications	76	14.3	92	17.3	0.183
Prematurity	29	5.5	1	0.2	<0.001*
Transient tachypnea of the newborn	23	4.3	26	4.9	0.636
Hyperbilirubinemia	22	4.1	53	9.9	<0.001*
Sepsis	1	0.2	5	0.9	0.099
Congenital anomaly	1	0.2	4	0.8	0.175
Inability to establish feeding	–	–	3	0.6	0.081
Neonatal mortality	1	0.2	–	–	0.498
In utero fetal death	1	0.2	–	–	0.498

Continuous variables are showed as mean±standard deviation or median depending on distribution characteristics. Binary variables are showed as count. *: Statistically significant. [b]: Odds ratio: 2.306, (95% confidence interval: 1.497–3.551) for all preterm births. APGAR: Aktivity, Pulse, Grimace, Appearance, Respiration; NICU: Neonatal intensive care unit.

and neonatal death cases were infected in their first trimester of pregnancy. Five neonates had congenital anomalies: one (hypospadias) in the SARS-CoV-2 group and four (one hypospadias, one patent ductus arteriosus, one anal atresia and one sacral dimple) in the controls (Table 2).

DISCUSSION

In this study, in order to investigate the long-term effects of SARS-CoV-2 infection during pregnancy on obstetrics and neonatal outcomes, unvaccinated patients who had not aborted or delivered during the infection or in their isolation period (14 days) were investigated. Mean gestational age at delivery was found to be lower and preterm birth rates were found to be significantly higher in patients recovered from SARS-CoV-2 during pregnancy compared to those of the controls. These rates did not differ in respect to which trimester the patients infected with SARS-CoV-2. Moreover, comparison of the trimesters revealed that infection in the 1st trimester results a modest but significant lesser birth weight than those of 2nd and 3rd trimesters (Table 2). On the other hand, SGA rates were not found to differ between SARS-CoV-2 recovered patients and the controls significantly which suggests that the observed lesser birth weights might be a result of increased rate of preterm birth of the SARS-CoV-2 recovered patients (Table 2). Comorbidities of the SARS-CoV-2 recovered and the control groups were not statistically different except for asthma and preeclampsia (Table 1).

In neonatal outcome, no difference was found between the groups by means of APGAR scores, neonatal intensive care unit admission, transient tachypnea of the newborn, sepsis and congenital anomalies. Hyperbilirubinemia rate was found to be lower in the SARS-CoV-2 group. On the other hand, in the SARS-CoV-2 group, there was one neonatal death who was 26 weeks preterm and lost due to prematurity; and there was an in utero fetal death of a preeclamptic mother that occurred after the acute SARS-CoV-2 infection. There was no fetal or neonatal loss in the controls. Both in utero death and neonatal death cases were infected in their first trimester of pregnancy (Table 2).

Table 3. Demographic and clinical characteristics of patients recovered from SARS-CoV-2 infection in ongoing pregnancy according to trimesters of pregnancy according to the time of (+) PCR test

	1st trimester (n=75)		2nd trimester (n=239)		3rd trimester (n=218)		p
	n	%	n	%	n	%	
Age (years)	27.65±4.9		28.8±5.4		28.71±5.36		0.253
BMI (kg/m^2)	25.46±3		26.13±3.32		26.33±4.11		0.202
Parity	1 (2)		1 (2)		1 (2)		0.523
Gestational age at birth	37.92±2.61		38.3±2		38.47±1.59		0.103
Preeclampsia*	6	8.0	9	3.8	8	3.7	0.240
Other Comorbidities	11	14.7	52	21.7	51	23.5	0.273
Maternal hospitalization	45	60	187	77.9	167	77	0.005*
Clinical severity of SARS CoV-2							<0.001*
Asymptomatic-mild	65	86.7	139	58.2	134	61.5	
Moderate	9	12	77	32.1	61	28.1	
Severe-critical	1	1.3	23	9.6	23	10.6	
Lung ultrasound scores							<0.001*
0–1	60	80	116	48.5	115	52.7	
2	14	18.7	94	39.3	85	39	
3	1	1.3	29	12.1	18	8.2	
ICU admission	–	–	3	1.3	1	0.5	0.447
Need for oxygen support during SARS CoV-2 infection with nasal cannula	–	–	27	11.3	28	12.9	0.006*
Noninvasive mechanical ventilation	–	–	5	2.1	4	1.8	0.463
Invasive mechanical ventilation	–	–	–	–	1	0.5	0.483
Preterm birth (total)	14	18.7	36	15.1	23	10.6	0.152
Preterm birth (34–37 weeks)	12	16.0	29	12.1	22	10.1	0.368
Preterm birth (<34 weeks)	2	2.7	7	2.9	1	0.5	0.131

Categorical variables were analyzed with Pearson Chi-Square test. Continuous variables are showed as mean±standard deviation or median depending on distribution characteristics. Binary variables are showed as count. *: Statistically significant. BMI: Body mass index, ICU: Intensive care unit

Acute effects of SARS-CoV-2 infection have been investigated worldwide and concluded that it worsens obstetric and neonatal outcomes. In addition, as the pregnancy advances the risk gets even higher like in the presence of comorbidities and pregnancy complications. Vaccination for SARS-CoV-2 infection is critical for minimizing risks to maternal and neonatal health for all variants of the virus.[8–10] However, yet little is known to fully elucidate the long-term effects of the infection on pregnancy.

In a study conducted by Anuk et al.,[11] doppler velocimetry values of 30 SARS-CoV-2 recovered patients with no comorbidity were compared with 40 healthy controls. Patients were PCR (+) singleton pregnancies between 23 – 40 weeks and the interval between the diagnosis of SARS-CoV-2 and doppler examinations were approximately three weeks. They found that both pulsatility and resistance indices of both uterine and umbilical arteries of SARS-CoV-2 recovered patients were higher than those of the controls. On the other hand, no meaningful result was found about middle cerebral artery measurements.

In a large retrospective study conducted by Hughes et al.,[12] results of 17 hospitals were investigated. Four hundred and two SARS-CoV-2 PCR (+) patients < 28 weeks pregnant at the time of diagnosis and recovered from the disease while pregnancy was ongoing were compared with 11705 controls. They found that the rates of preterm birth and hypertensive disorders of pregnancy were increased but no association between SARS-CoV-2 and other comorbidities was found including SGA. In the present study, preeclampsia rate was observed as 4.3% and 0.6% in the SARS-CoV-2 recovered patients during pregnancy and the controls respectively (p<0.001). Comparison of the trimesters of SARS-CoV-2 in-

Table 4. Indications of cesarean section

Indications of birth	SARS-CoV-2 (n=532)		No infection (n=532)		p
	n	%	n	%	
Spontaneous labor	294	55.2	304	57.1	0.465
Previous uterine surgery	102	19.2	101	19	0.873
Fetal distress	39	7.3	40	7.5	0.882
Abnormal fetal presentation	35	6.6	26	4.9	0.251
Preeclampsia[a]	23	4.3	3	0.6	<0.001*
Oligohydramnios	20	3.8	12	2.3	0.159
Postterm pregnancy	9	1.7	21	4	0.025*
Macrosomia	7	1.3	16	3	0.055
Maternal health issues (Asthma, DM, HT)	3	0.6	8	1.5	0.126

[a]: Odds ratio: 7.893, (95% confidence interval: 2.355-26.449). When the pregnant women with history of preeclampsia were excluded from the analysis, still there was a significant difference between groups with regard to preeclampsia as an indication of birth (p=0.018). *: Statistically significant. DM: Diabetes mellitus; HT: Hypertension

Table 5. Mode of birth and type of anesthesia

	n	%	n	%	n	%	p
Mode of delivery							0.298
Vaginal birth	37	49.3	110	46	88	40.4	
Cesarean section	38	50.7	129	54	130	59.6	
Types of anesthesia							0.061
General anesthesia	20	52.6	82	63.6	64	49.2	
Regional anesthesia	18	47.4	47	36.4	66	50.8	

Categorical variables were analyzed with Pearson Chi-Square test. Continuous variables are showed as mean±standard deviation or median depending on distribution characteristics. Binary variables are showed as count

Table 6. Preeclampsia and preterm birth according to the clinical severity and lung ultrasound

	Clinical severity of SARS CoV-2								
	Asymptomatic-mild		Moderate		Severe		Total		p
	n	%	n	%	n	%	n	%	
Preeclampsia	17	5.0	5	3.4	1	2.1	23	4.3	0.533
Preterm birth	44	13.0	22	15.0	7	14.9	73	13.7	0.824
	LUS								
	0–1		2		3		Total		p
	n	%	n	%	n	%	n	%	
Preeclampsia	13	4.5	8	4.1	2	4.2	23	4.3	0.984
Preterm birth	41	14.1	26	13.5	6	12.5	73	13.7	0.949

Categorical variables were analyzed with Pearson Chi-Square test. Binary variables are showed as count. LUS: Lung ultrasound score

fection patients revealed a modest increase in 1st trimester (8.0%) compared to the 2nd (3.8%) and the 3rd trimesters (3.7%) but did not reach the level of significance (p=0.240).

Studies on histopathological specimens suggest that SARS-CoV-2 infection may involve the placenta and pathology of the infection on placenta might persist after recovery. Boyraz et al.[13] examined placentas of 67 SARS-CoV-2 recovered deliveries and compared with a control group of 126 previously published cohort of placentas pathologically examined for the sole indication of maternal group B streptococcal (GBS) colonization. They found a higher prevalence of vascular malformations in the SARS-CoV-2 recovered group compared to controls. They also analyzed inflammatory, infectious and other thrombotic findings but found no difference. As there was no histopathologic finding about viral infection or placentitis in the SARS-CoV-2 recovered group, they concluded that there was no persistent infection and SARS-CoV-2 infection might have long lasting effects on placental perfusion.[13] On the other hand, viral infection of placenta is also considered to cause syncytiotrophoblast stress resulting preeclampsia.[14]

Clinical severity, lung ultrasound scores, need for oxygen support and intensive care unit admission rates of SARS-CoV-2 infected patients were found to increase gradually as the pregnancy advanced. These findings are consistent with the literature.[13] When cesarean section was indicated, regional anesthesia seems to be more readily preferred in the SARS-CoV-2 recovered patients compared to the controls.

Preeclampsia is a systemic inflammatory disease and its etiology is not fully understood yet. Inflammatory mediators in blood circulation and endothelial injury are thought to be responsible for the end-organ damage and hence the clinical picture. This might be aggravated by the increased concentration of cytokines in blood circulation during SARS-CoV-2 infection. Events during the placentation and syncytiotrophoblast stress are also suggested to initiate the cascade resulting in preeclampsia.[13]

According to the results of this study, SARS-CoV-2 infection during pregnancy is associated with increased risk of preeclampsia (Table 1). On the other hand, in respect to the trimester at the onset of the infection, a higher rate of preeclampsia was seen in the 1st trimester group compared to the 2nd and 3rd trimesters [n1=6 (8.0%), n2=9 (3.8%) and n3=8 (3.7%), respectively] but did not reach the level of statistical significance (p=0.240, Table 2). On the other hand, rate of preeclampsia seems unrelated to the clinical severity of the SARS-CoV-2 infection (Table 6).

The high rate of preeclampsia has been found as related with the past SARS-CoV-2 infection in pregnancies in the present study; however, the mechanism of this finding remained unsolved in this study and in the literature.[15] The exact mechanism of preeclampsia might be enlightened by future studies and the studies including the placentas of these patients and controls might explain the process.

All the women were managed by the same team which allowed a standard management of the patients and hence a homogenous data set to investigate. The data were not only analyzed according to the PCR positivity for SARS-CoV-2, but also clinical severity and the trimesters in which the SARS-CoV-2 infection was diagnosed. The study was conducted before the Omicron wave but analysis of all cases for the variants of the SARS-CoV-2 was not carried out so, the effect(s) of the different viral mutations (if any) remains unknown. Another limitation of this study is the lack of a multivariable analysis of the data.

CONCLUSION

The findings from our study can still be utilized in future treatment plans even though the pandemic has come to an end. The patients who recovered from SARS-CoV-2 infection during pregnancy may be at higher risk of preterm delivery and preeclampsia. These effects are not related to the clinical severity of the infection. Risks of SGA or congenital anomalies are not increased.

Disclosures

Ethics Committee Approval: The study was approved by the Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (No: E-46059653-020, Date: 16/02/2022).

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REFERENCES

1. Cucinotta D, Vanelli M. WHO Declares COVID-19 a pandemic. Acta Biomed 2020;91:157–60.
2. World Health Organization. WHO COVID-19 Dashboard. Available at: https://covid19.who.int/. Accessed Nov 2, 2024.
3. World Health Organization. Clinical Management of COVID-19: Living Guideline, 13 January 2023. Geneva: World Health Organization; 2023 (WHO/2019-nCoV/clinical/2023.1).
4. Bestel A, Kahve AC, Aldikactioglu Talmac A, Yalcin Bahat P, Aytufan Z, Polat İ, et al. Comparison of the anxiety and depression levels of pregnant women with COVID-19 and healthy pregnant women. East J Med 2022;27:155–63. [CrossRef]
5. Yassa M, Yirmibes C, Cavusoglu G, Eksi H, Dogu C, Usta C, et al. Outcomes of universal SARS-CoV-2 testing program in pregnant women admitted to hospital and the adjuvant role of lung ultrasound in screening: a prospective cohort study. J Matern Fetal Neonatal Med 2020;33:3820–26. [CrossRef]
6. Yong SJ. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. Infect Dis (Lond) 2021;53:737–54. [CrossRef]
7. Soldati G, Smargiassi A, Inchingolo R, Buonsenso D, Perrone T, Briganti DF, et al. Proposal for international standardization of the use of lung ultrasound for patients with COVID-19: a simple, quantitative, reproducible method. J Ultrasound Med 2020;39:1413–9. [CrossRef]
8. Tug N, Yassa M, Köle E, Sakin Ö, Çakır Köle M, Karateke A, et al. Pregnancy worsens the morbidity of COVID-19 and this effect becomes more prominent as pregnancy advances Turk J Obstet Gynecol 2020;17:149–54. [CrossRef]
9. Yassa M, Birol P, Yirmibes C, Usta C, Haydar A, Yassa A, et al. Near-term pregnant women's attitude toward, concern about and knowledge of the COVID-19 pandemic. J Matern Fetal Neonatal Med 2020;33:3827–34. [CrossRef]
10. Birol Ilter P, Prasad S, Mutlu MA, Tekin AB, O'Brien P, von Dadelszen P, et al. Maternal and perinatal outcomes of SARS-CoV-2 infection in unvaccinated pregnancies during Delta and Omicron waves. Ultrasound Obstet Gynecol 2022;60:96–102. [CrossRef]
11. Anuk AT, Tanacan A, Yetiskin FDY, Buyuk GN, Senel SA, Keskin HL, et al. Doppler assessment of the fetus in pregnant women recovered from COVID-19. J Obstet Gynaecol Res 2021;47:1757–62. [CrossRef]
12. Hughes BL, Sandoval GJ, Metz TD, Clifton RG, Grobman WA, Saade GR, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. First- or second-trimester SARS-CoV-2 infection and subsequent pregnancy outcomes. Am J Obstet Gynecol 2023; 228:226.e1–9.
13. Boyraz B, James K, Hornick JL, Roberts DJ. Placental pathology from COVID-19-recovered (nonacute) patients. Hum Pathol 2022:125;18–22. [CrossRef]
14. Redman CWG, Staff AC, Roberts JM. Syncytiotrophoblast stress in preeclampsia: the convergence point for multiple pathways. Am J Obstet Gynecol 2022;226:907–27. [CrossRef]
15. Sayad B, Mohseni Afshar Z, Mansouri F, Salimi M, Miladi R, Rahimi S, et al. Pregnancy, preeclampsia, and COVID-19: susceptibility and mechanisms: a review study. Int J Fertil Steril 2022;16:64–9.