DOI: 10.37990/medr.1345373 Med Records 2023;5(Suppl 1):82-6

MEDICAL RECORDS-International Medical Journal

Research Article

Evaluation of the Effect of SARS-COV-2 Infection During Pregnancy on Fetal Doppler Ultrasound Parameters: A Prospective Study

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Abstract

Aim: The fetal effects of severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) infection have been the subject of controversy since the beginning of the pandemic. We aimed to investigate the effect of SARS-COV-2 infection on fetal Doppler parameters.

Material and Methods: This prospective case-control study was conducted at İzmir Tepecik Training and Research Hospital between September 1, 2021, and June 1, 2022, on pregnant women confirmed to have SARS-CoV-2 by RT-PCR testing. Pregnant women who had mild to moderate coronavirus disease 2019 (COVID-19) infection during pregnancy were compared with a control group of pregnant women not infected with the COVID-19 virus. All Doppler and fetal biometry ultrasound assessments between 34 and 37 weeks of gestation were performed in our unit.

Results: Pregnant women infected and not infected with COVID-19 were demographically homogeneous. When the groups were compared in terms of fetal Doppler parameters, including left and right uterine artery (UtA) pulsatility index (PI), middle cerebral artery (MCA) PI, and systolic/diastolic ratio (S/D), as well as umbilical artery (UA) S/D and PI, no statistically significant difference was observed (p>0.05).

Conclusion: We consider that mild to moderate COVID-19 does not affect Doppler ultrasound parameters and fetal well-being during pregnancy.

Keywords: COVID-19, doppler ultrasound, fetal well-being

INTRODUCTION

The coronavirus disease 2019 (COVID-19) infection, which emerged at the beginning of 2020 and caused a pandemic in a short time, has been a major public health problem. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) may cause asymptomatic infection and present with various clinical conditions such as severe cough, fever, multi-organ failure, and respiratory distress (1-4). In the literature, pregnant and control groups of the same age with COVID-19 were compared and observed that pregnancy does not increase the risk of SARS-CoV-2 infection but aggravates clinical outcomes (5). Due to the immune suppression status during pregnancy, more severe complications and death rates are observed as a result of SARS-CoV and MERS-CoV infections in pregnant women (6-8).

Recent data show an increase in obstetric complications with COVID-19, such as preterm birth, fetal distress, and stillbirth (9). It was also found that the rate of hospitalization in the neonatal intensive care unit was higher in newborns born to mothers infected with SARS-

CITATION

Ozer M, Ozer PT, Oglak SC, et al. Evaluation of the Effect of SARS-COV-2 Infection During Pregnancy on Fetal Doppler Ultrasound Parameters: A Prospective Study. Med Records. 2023;5(Suppl 3):82-6. DOI:1037990/medr.1345373

Received: 18.08.2023 **Accepted:** 14.09.2023 **Published:** 09.10.2023

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CoV-2 (10). Considering the hypercoagulation and modulated immune status in pregnancy, the pulmonary and hematological effects of COVID-19 may cause adverse effects on the placental and fetal circulation (11).

Fetal Doppler parameters have been used safely for years to evaluate fetal well-being. Vascular ultrasonographic Doppler measurements such as uterine artery (UtA), umbilical artery (UA), middle cerebral artery (MCA) provide physicians with valuable information about the well-being of the fetus (12). This study aimed to evaluate the effects of COVID-19 infection on neonatal outcomes in the late preterm period, fetal biometry, and fetal Doppler measurements.

MATERIAL AND METHOD

This prospective case-control study was conducted on pregnant women infected with SARS-CoV-2 between September 1, 2021, and June 1, 2022, at Health Sciences University İzmir Tepecik Training and Research Hospital. Ethics committee approval was obtained before starting the study (decision no. 2021/8–14). Pregnant women with mild to moderate COVID-19 infection, regardless of hospitalization status, were compared with pregnant women of the same age with similar clinical characteristics followed for standard antenatal care in the control group. RT-PCR method was used to confirm the infection. Inclusion criteria were gestational age, late preterm, confirmed by head-rump length at 11-14 weeks of screening.

Women known to have multifetal pregnancies, maternal systemic diseases, need for intensive care, uterine anomaly, severe COVID-19 infection, and fetal structural anomalies were excluded. Also, even if the COVID-19 RT-PCR test result is negative, pregnant women with respiratory tract infection symptoms such as fever and cough were not included in the study. All pregnant women diagnosed with SARS-CoV-2 infection had symptoms such as fever, cough, diarrhea, and the positive PCR method obtained from nasopharyngeal swab samples was used for diagnosis.

Doppler measurements were made between 34 and 37 weeks of gestation by the same perinatologist working in the perinatology clinic of the Tepecik Training and Research Hospital, using the Samsung's HS70A with Prime Ultrasound machine CA1-7A convex probe (1.0 - 7.0 MHz) which is made Germany. UA, MCA, and UA Doppler values were recorded in the late preterm period in pregnant women who had COVID-19 infection and in control group patients. Fetal vessels used when evaluating fetal Doppler parameters; UtA, MCA, and UA (13). The recommendations provided by the International Society of Obstetric Ultrasound were followed when evaluating all Doppler parameters and measuring fetal biometry (14).

The statistical analysis was conducted using SPSS, Version 24.0 (SPSS Inc., Chicago, IL). The assumption of normality for variable distributions was assessed using the Shapiro-Wilk test. Variables with a normal distribution were presented as mean ± standard deviation, while those displaying non-normal distribution were characterized by the median and interquartile range (25th - 75th percentiles). When comparing individuals who were diagnosed with COVID-19 to those who were not, we performed an independent sample t-test or Mann-Whitney U test for continuous variables and a Chi-Square test for categorical variables. For the analysis of ultrasound parameters across different COVID-19 exposure trimesters, we employed either the one-way ANOVA or the Kruskal-Wallis test. The threshold for determining statistical significance was set at a two-tailed p-value of less than 0.05.

RESULTS

Our study included 81 pregnant women who had mild to moderate COVID-19 infections during their pregnancy and 70 patients who had no RT-PCR positivity or symptoms during their pregnancy. Table 1 shows the demographic characteristics of COVID-19 patients and the patients in the control group. The two groups were homogeneous and no statistically significant difference was recorded when demographic data were analyzed. UtA, UA, MCA Doppler measurement (pulsatility index [PI], systolic/diastolic ratio [S/D]), cerebroplacental ratio (CPR), amnion fluid index, head circumference, abdominal circumference, and femur length measurements performed in the late preterm period between 34 and 37 weeks, and there was no difference significantly between COVID-19 and control groups (Table 2).

Table 1. General characteristics of the COVID-19 group and the control group

	COVID-19 group (n= 81)	Control group (n=70)	p-value
Maternal age, years	28 (23-32)	31 (26-32)	0.286
Gravidity, n	3 (2-4)	3 (2-3)	0.153
Parity, n	2 (1-3)	2 (1-2)	0.083
Body mass index, kg/m²	27.5 (23.7-31.2)	28.04 (24.8–32.7)	0.066
Gestational week at COVID-19 infection	20 (12-25)	18.5 (17-24)	0.308
Gestational week at ultrasound examination	35.6 (35.2-37.2)	36 (36- 36.2)	0.549
Gestational week at delivery	38.3 (37.1-39.1)	38.1 (36.2-39.1)	0.536
Birth weight, g	3000 (2715-3210)	3050 (2670-3210)	0.931
Apgar score	8 (7-9)	8 (7-9)	0.250
Neonatal intensive care unit admission, n (%)	8 (9.9%)	8 (11.4%)	0.241

The patients were divided into 3 groups according to the trimester in which they had COVID-19 infection. There were 26 patients in the first trimester, 47 patients in the second trimester, and 8 patients in the third trimester. There was no significant difference between these groups in the Doppler parameters measured between 34 and 37 weeks (Table 3).

Table 2. Comparison of fetal Doppler and biometric measurements

	COVID-19 group (n= 81)	Control group (n= 70)	p-value
Umbilical artery S/D	2.76 (2.42-3.25)	2.90 (2.70-2.98)	0.433
Umblical artery PI	0.99 (0.87-1.15)	1.00 (0.90-1.10)	0.502
Middle cerebral artery S/D	6.53 (5.09-8.65)	6.11 (4.93-7.95)	0.130
Middle cerebral artery PI	1.96 (1.74-2.24)	1.90 (1.82-1.98)	0.137
Right uterine artery PI	0.93 (0.75-1.18)	0.99 (0.73-1.00)	0.266
Left uterine artery PI	0.93 (0.73-1.24)	0.96 (0.95-0.97)	0.773
Cerebroplasental ratio	2.30 (2-2.5)	2.31 (2-2.6)	0.331

S/D: Systolic/Diastolic ratio, PI: Pulsatily Index

Table 3. Doppler ultrasound parameters according to the timing of the trimester of the COVID-19 Infection

	1st trimester (n=26)	2nd trimester (n=47)	3rd trimester (n=8)	p-value
Umbilical artery S/D ratio	2.77 (2.36-3.52)	2.83 (2.47-3.21)	2.43 (2.10-2.77)	0.138
Umblical artery PI	1.01 (0.91-1.15)	1.00 (0.87-1.19)	0.86 (0.79-1.11)	0.348
Middle cerebral artery S/D	6.37 (4.49-7.83)	6.53 (5.50-9.20)	6.84 (4.91-8.13)	0.438
Middle cerebral artery PI	1.92±0.46	2.01±0.36	2.11±0.40	0.433
Right uterine artery PI	1.08 (0.86-1.39)	0.92 (0.73-1.16)	0.85 (0.60-1.17)	0.112
Left uterine artery PI	0.97 (0.76-1.25)	0.96 (0.75-1.25)	0.70 (0.57-0.93)	0.190

S/D: Systolic/Diastolic ratio, PI: Pulsatily Index

DISCUSSION

Both cohorts of pregnant women, including those with and without COVID-19 infection, demonstrated demographic homogeneity. In the course of our investigation, we meticulously analyzed several Doppler parameters, encompassing the left-right UtA PI, MCA PI, systolic/diastolic ratio (S/D), as well as UA S/D ratio and PI. Nonetheless, upon meticulous comparison of these parameters in relation to fetal Doppler profiles, no statistically significant discrepancies were ascertained.

SARS-CoV-2, which originated in Wuhan, China, spread rapidly, causing a pandemic in early January 2020 (15,16). Malperfusion and parenchymal infarction were noted in the placentas of pregnant women who had SARS-CoV-2 (17). In the angiogenic phase of placental development, there is an increase in fetal capillary volume and surface area required for fetomaternal gas exchange, and an increase in UA end-diastolic Doppler flow velocity is observed. On the contrary, in pregnancies with developmental delay with defective placentation, umbilical artery blood flow decreases abnormally, resulting in the absence of end-diastolic flow or reverse flow of UA (18,19).

Endothelial damage or hypoxemia causes low blood flow and high vascular resistance, resulting in placental insufficiency. Studies reveal that increased uterine artery flow impedance is associated with the development of preeclampsia, fetal growth restriction, and perinatal mortality. As placental dysfunction progresses, resistance in the villi causes a proportional increase in the UA Doppler indices, while a decrease in oxygen level causes a decrease in the MCA Doppler index. This effect can be easily and quickly measured non-invasively using UtA Doppler ultrasound (20). The negative effects of COVID-19 on the placenta impair uteroplacental circulation by causing pathophysiological hypoxemia, thrombosis, and villitis. In the study of Anuk et al., an increase was observed in umbilical and uterine artery PI and RI in pregnant women who had COVID-19 compared to the control group (21). In this study not found differences in UtA Doppler parameters between the two groups in this study.

MCA Doppler examination is an important tool in the diagnosis and treatment of fetal anemia and intrauterine growth restriction. Investigation of fetal central nervous system hemodynamics and in cases with intrauterine growth restriction, MCA Doppler flow shows early and late changes. When the relationship of MCA flow rate in normal and abnormal pregnancies with perinatal outcomes was evaluated, they concluded that a higher rate of abnormal flow was observed in pregnancies with intrauterine growth retardation and MCA flow rate measurement was reliable in the diagnosis of fetal distress (22). In this study, there was no difference in MCA Doppler parameters between the two groups.

CPR is especially important for the evaluation of fetal well-being in the near-term follow-up of fetuses with intrauterine growth restriction (23). The cerebroplacental ratio is an important parameter to predict adverse perinatal outcomes. No significant difference was observed when CPR was compared in the COVID-19 and control groups. A recent study reported that fetal brain and heart tissues do not express Angiotensin-Converting Enzyme-2 (ACE-2) receptors and that these organs will not be a target for the virus (24). In this study, there was no difference in CPR parameters between the two groups.

There are many publications and unanswered questions in the literature about the effect of SARS-CoV-2 infection on the fetus and placenta. In the early stages of the pandemic, transmission from mother to fetus was reported as negligible. However, in a study that included 936 newborns from mothers affected by COVID-19 according to newer and larger studies, 27 newborns reported that they were RT-PCR positive and the rate of transmission was 3.2% (25). Despite this, the actual risk of vertical transmission and its potential consequences on the fetus is currently largely unknown.

In recent studies, it has been observed that SARS-CoV-2 causes arteriopathy in the placenta, fibrinoid necrosis, and mural hypertrophy of decidual arterioles, but it was not detected in newborns (26). In this study, the placenta was not analyzed. However, like any situation that may cause placental hypoperfusion, it is thought that SARS-CoV-2 infection may be associated with conditions such as intrauterine growth restriction and stillbirth, preeclampsia (27). However, in this study, no significant difference was observed between the two groups in Doppler and biometric measurements, in which we evaluated perfusion and fetal well-being.

The strengths of the study are its prospective design, Doppler and biometric measurements made by the same perinatologist, and numerous parameters investigated. Limitations are examination of mild to moderate COVID-19 patients only, and lack of postnatal fetal and maternal follow-up.

Anxiety symptoms are an independent risk factor for adverse obstetric outcomes during pregnancy (28). Increasing anxiety in the antenatal period may cause mental adverse conditions such as increased postnatal depression, as well as negative obstetric outcomes such as premature birth and fetal growth restriction (29-31).

CONCLUSION

It has been reported that SARS-CoV-2 has negative effects on the placenta in the literature. However, as seen in recent publications, it was observed in this study that pregnant women with mild/moderate COVID infection did not reflect negatively on newborn outcomes, fetal biometry and Doppler measurements (32). It has been reported that anxiety can cause both negative effects on maternal mental health and obstetric complications during pregnancy. It has been reported that pregnancy anxiety increases during the COVID-19 pandemic and that early diagnosis and intervention by a psychiatrist can prevent stress-related pregnancy complications (33). In the literature, it is considered that there is no need for additional visits in pregnancy follow-up for mild to moderate COVID-19 patients (26). In this study, it was observed that there was no deterioration in Doppler and biometric measurements for mild and moderate COVID-19 patients compared to the controls.

Financial disclosures: *The authors declared that this study has received no financial support.*

Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *Ethical approval was obtained from the Tepecik Training and Research Hospital Ethics Committee (2021/8–14).*

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