Evaluation of Foetal Doppler After Maternal Covid-19 Disease: How Does Foetal Aortic Isthmus Doppler Change?

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ABSTRACT

Objective: We aim to evaluate the foetal aortic isthmus Doppler data after maternal COVID-19 disease.

Material and Methods: Twenty six pregnant patient who recovered from COVID-19 and 43mhealthy patient were included in this prospective case–control study. The study group consisted of those who had COVID-19 disease and completed the quarantine period.

Results: Doppler ultrasound evaluations were performed at the similar gestational week. We observed significantly high pulsatility indices (PI) of umbilical and aortic isthmus in study group than the control group (p=0,02, p=0,02). There was no significant change in cerebroplacental ratio (CPR) between the two groups (p>0.05).

Conclusion: COVID-19 may affect placental function in pregnant women and could deterioration on foetal circulation and Doppler parameters. In particular, changes in aortic isthmus doppler flow indicating foetal circulation and cerebral oxygenation help to reflect the foetal effects of COVID-19.

Keywords: COVID-19 virus, Doppler ultrasound, pregnancy outcomes.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was first observed in China, and subsequently spread to numerous countries across the globe. COVID-19 patients may have mild symptoms that spontaneously resolve. However, some patients experience various fatal complications, including acute respiratory distress syndrome, sepsis (1–3).

The studies demonstrate that pregnant women with COVID-19 are more likely than non-pregnant women to be hospitalized, require ventilation, and be received to an intensive care unit (ICU) (4–6). The studies also show that exposure to COVID-19 during the perinatal period is associated with a high prevalence of harmful maternal outcomes and adverse neonatal effects, including preterm birth, intrauterine growth retardation, and admission to the NICU (7–9).

Doppler ultrasound examinations are pivotal for predicting adverse pregnancy outcomes, such as foetal growth retardation (FGR), preeclampsia, and foetal anaemia (10, 11). Doppler data on the uterine artery, umbilical artery, and cerebral artery of COVID-19 patients have been evaluated in studies that assessed the effects of the Doppler parameters (12, 13).

The aortic isthmus (AoI) study began with animal experiments (foetal lambs) evaluating placental resistance (14). Studies show that while the blood flow in the AoI is antegrade, the oxygen content in the carotid artery remains relatively constant. However, a decrease in the level of carotid oxygenation was observed when the flow became retrograde (14).

The AoI is a vascular area located between the right and left foetal circulations. AoI Doppler velocimetry has recently been introduced as a tool for detecting hemodynamic balance in foetuses (14). The aim of this study is to evaluate the foetal aortic isthmus Doppler data after maternal COVID-19 disease.

MATERIAL and METHODS

The prospective study was conducted at our clinic between February 2021, and May 2021. Approval for the study was obtained from Ankara City Hospital Ethics Committee with the decision number E2-21-378.

There were 26 patients who have recovered from COVID-19 in the study group and 43 patient in the control group. COVID-19 was diagnosed with a polymerase chain reaction (PCR) test. They had completed quarantine period after being discharged from the hospital. Patient with maternal chronic diseases, twin pregnancies were excluded. Patient with symptoms associated with COVID-19 were excluded in control group.

The gestational week was calculated using first-trimester crown-rump length. Pregnant women in the study group were examined 6-8 weeks after recovery. All Doppler measurements were performed between 28 and 40 weeks of gestation with 2–5 MHz convex ultrasound transducer Voluson E8 and E10 (GE Healthcare, Milwaukee, Wisconsin USA). Doppler measurements of the middle cerebral artery (MCA) and the free-floating loop of the umbilical artery (UA) were performed using the methods described in an earlier study (15).

Pulsatility indices (PI) of the MCA and the UA were obtained, and the cerebroplacental ratio (CPR) was calculated as MCA PI / UA PI. AoI Doppler parameters were assessed in the longitudinal aortic arch (LAA) view. In the LAA view, the range gate was placed a few millimeters distal to the origin of the left subclavian artery, as described in an earlier study (16). The AoI flow velocity waveform had a typical shape shown in **Figure 1**. The PI values were measured, with the indices were calculated from three or more consecutive waveforms obtained during minimal foetal activity.

Statistical analysis was enforced using IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were given as mean ± standard deviation for numerical data with normal distribution or median and minimum- maximum values for numerical data which do not follow a normal distribution. The normality of the variables was tested with both Shapiro – Wilk and Kolmogorov – Smirnov tests. Groups were compared with The Student's t-test and Mann-Whitney U test. Comparison of variables was performed by Pearson Chi-square test and Fisher's exact test for categorical variables. Differences with P-values <0.05 were considered statistically significant.

RESULTS

The maternal demographic data of the study and control groups were similar (**Table 1**), and birth week and birth weight were similar across both groups (p>0.05). However, the 1st and 5th minute Apgar scores were significantly lower in the study group (p<0.001, p=0.01). Obstetric complications were evaluated, including preterm delivery, FGR, and oligohydramnios. Rate of preterm delivery was higher in the study group (p<0.001). There was no difference between the groups in terms of FGR and oligohydramnios (p=0.38, p=0.38 respectively). Although the NICU requirement was higher in the study group, these result was not statistically significant (p=0.06). In **Table 2** outlined the symptoms of COVID-19. At the time of diagnosis of COVID-19, the average gestational week was 13 (5-30). Seven (26%) of the COVID-19 patients were hospitalized and were treated with drugs. The Doppler assessment results are presented in **Table 3**. Doppler ultrasound evaluations were performed at the similar gestational week and the PI of the umbilical and AoI was significantly higher in study group than among the control group (p=0.02, p=0.02). No significant differences were evaluated in the CPR between the groups (p>0.05).

Table 1. Baseline data and characteristics of the groups

	Control (n=43)	Recovered from COVID-19 (n=26)	P-Values
Maternal age	29 (7)	29 (7,5)	0,76
Gravida	2 (2)	2 (2)	0,75
Parity	1 (1,2)	1 (2)	0,47
Gestational age at ultrasound assessment (week)	36 (4)	35 (3,5)	0,16
Preterm delivery rate (n,%)	-	3 (11,5%)	**<0,001**
Fetal growth retardation (n,%)	-	1 (3%)	0,38
Oligohydramnios (n,%)	-	1 (3%)	0,38
Gestational age at birth (week)	38 (2)	39 (4,8)	0,34
Birth weight (g)	3265 (465)	3225 (685)	0,78
APGAR 1st minute	9 (0)	8 (1)	**<0,001**
APGAR 5st minute	10 (1)	9 (1,2)	**0,01**
Hospitalization in NICU	1 (2,3%)	4 (15,4%)	0,06

Table 2. Clinical characteristics of COVID-19

Variables	Values
Gestational age at diagnosis (week)	13 (5-30)
Admission to hospital (n,%)	7 (26%)
COVİD-19 therapy (n,%)	7 (26%)
Low molecular weight heparin (n,%)	7 (26%)
Lopinavir-ritonavir (n,%)	1 (3%)

Data given as median (interquartile range), max-min value, number, percentile (n,%)

Table 3. Fetal Doppler assessment.

	Control (n=43)	Recovered from COVID-19 (n=26)	P-Values
UA PI	0,8±0,1	1±0,4	**0,02**
MCA PI	1,6±0,4	1,7±0,4	0,19
CPR	2,0±0,5	1,9±0,8	0,17
CPR percentile	47,4±31	36,3±34	0,13
AoI PI	2,2±0,1	2,3±0,1	**0,02**

Data given as mean ± SD. UA: umbilical artery, PI: pulsatility index, MCA: middle cerebral artery, CPR: cerebroplacental ratio, and AoI: aortic isthmus
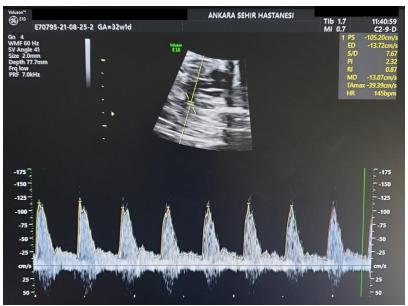

Figure 1. Doppler waveform of aortic isthmus

DISCUSSION

We found high umbilical and AoI PI values in the patient who had recovered from COVID-19 when compared to the control group. In addition, the study group recorded a high preterm delivery rate and low APGAR scores.

Doppler parameters, especially FGR and preeclampsia are used to evaluate foetal well-being in high-risk pregnancies (10). On the other hand, our knowledge about the Doppler ultrasound in pregnancies with COVID-19 is limited. Goncu et al.(12) investigated Doppler parameters (uterine artery, UA, MCA, ductus venous, CPR, and cerebral-placental-uterine ratio) in pregnant women confirmed as having COVID-19. Goncu et al. observed no differences in any Doppler parameters (12). Unlike the previous study, Anuk et al. evaluated the Doppler parameters of pregnant patient who recovered from COVID-19 and they found that the PI values of the umbilical and uterine arteries are significantly higher than in the control group (13). Similarly, we detected greater PI values in the UA in the study group. This may be related to resistance in foetal blood flow resulting from damage to the placenta caused by COVID-19. Studies have reported foetal vascular malperfusion with multiple thromboses in placentas from COVID-19 patients (17-20).

AoI Doppler velocimetry is a new way for assessing foetal hemodynamic status, and many studies have been conducted to assess its potential for predicting adverse outcomes in FGR (21, 22). The AoI is a vascular area located between the left subclavian artery and the ductus arteriosus. Because of this anatomical feature, an increase in PI values in the AoI, and even a reverse current, can be detected with increasing

systemic resistance (16). It was determined that anormal AoI Doppler indices in FGR was a finding between hypoxemia due to placental insufficiency and cardiac decompensation (22). Choudhary et al. found that increased AoI PI values have high specificity for predicting of adverse perinatal outcomes for early FGR (23). Sharma et al. evaluated 30 pregnant women with small for gestational age (SGA) foetuses and found the AoI PI values to be significantly higher in the SGA group than in the control group. They observed that AoI assessment seems to provide beneficial information for monitoring small foetuses (24). There are studies in which the sensitivity and clinical benefit of AoI Doppler PI values in FGR could not be found, especially for late-onset FGR (25, 26). No previous study has evaluated AoI Doppler data on patients with COVID-19. In pregnant women who develop COVID-19, as in pregnancies with FGR, placental dysfunction may affect foetal circulation and increase foetal systemic vasculary resistance. The significantly higher AoI PI values in our study may be related to this condition. In addition, most of the patients in our study group were pregnant women who had COVID-19 in their early gestational weeks. A study by the World Association of Perinatal Medicine (WAPM) showed that COVID-19 infection in the first trimester is strongly associated with the occurrence of adverse foetal events when compared to infection during other trimesters (27). Global study data shows that 12.9% of women with COVID-19 infection had a preterm birth, 15.2% needed NICU, and 1.06% had stillbirths (28). Similarly, in our study, the preterm birth rate was 11.5%, which is higher than the rate for the control group.

Furthermore, the NICU requirement was 15.4%, which was not different from that of the control group. This may be related to the small sample size in our patients.

Our study has strengths and weaknesses. The limitation of our study is the small number of the patient. Also, the discussion section was weak due to the lack of similar studies in the literature. Prospective evaluation is the strength of our study.

CONCLUSION

COVID-19 causes adverse foetal effects, which have been observed in different studies (27,29,30). However, many unknowns remain about the foetal consequences of COVID-19. Further Doppler studies are needed to clarify on the effect of maternal COVID-19 infection on the fetus. AoI Doppler velocimetry provides useful information for monitoring the foetuses of pregnant women with COVID-19 during the early weeks of pregnancy

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