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Evaluation of carotid artery Doppler measurements in late-onset fetal growth restriction: a cross-sectional study

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Ethics Committee Approval
The study was approved by the Kocaeli Derince Education and Research Ethics Committee (Date: May 26, 2022, Decision No: 2022-046). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: It has been reported that both the internal carotid artery (ICA) and the common carotid artery (CCA) are associated with hypoxia, also observed in late-onset fetal growth restriction (FGR). However, it has not yet been investigated whether these Doppler measurements differ in cases of late-onset FGR. This study evaluated the ICA and the CCA Doppler parameters in late-onset FGR fetuses and compared these measurements with those of healthy fetuses.

Methods: This cross-sectional observational study comprised 75 singleton pregnancies diagnosed with late-onset FGR between the 32nd and 37th weeks of gestation, alongside 75 healthy fetuses paired 1:1 based on obstetric history and gestational age between June 2022 and May 2023. The Delphi consensus of 2016 was used for the definition of late-onset FGR. The exclusion criteria were congenital anomalies, presence of any additional disease, maternal body mass index over 35 kg/m^2, abdominal scars hindering ultrasound visualization, use of medications such as antenatal steroids, sympathomimetics, and indomethacin that affect vascular function, drug use, smoking during pregnancy, concurrent preeclampsia, and multiple pregnancies. Upon the patients' admission to the hospital, their demographic characteristics were documented, and ultrasonographic examinations and Doppler measurements were subsequently performed. The Doppler velocimetry of the umbilical artery (UA) encompassed measurements of the systolic to diastolic ratio (S/D), pulsatility index (PI), and peak systolic velocity (PSV). The carotid artery Doppler velocimetry of the middle cerebral artery (MCA), ICA, and CCA encompassed measurements of the PI, resistance index (RI), and PSV. We assessed the diagnostic performance of Doppler measurements for late-onset FGR through receiver operating characteristic (ROC) analysis.

Results: In the late-onset FGR group, the mean UA-SD was higher (2.7 [0.6] *vs.* 2.5 [0.5], *P*=0.006), and the mean UA-PI (0.8 [0.2] *vs.* 0.9 [0.2], *P*=0.011) and mean PSV (35.6 [8.2] *vs.* 41.1 [7.1], *P*<0.001) were lower compared to the control group. In the late-onset FGR group, carotid Doppler measurements were more pronounced than UA Doppler measurements. Moreover, ICA Doppler measurements exhibited superior diagnostic performance in predicting late-onset FGR compared to other Doppler measurements (Area under the curve [AUC]=0.777, *P*<0.001 for ICA-PI; AUC=0.751, *P*<0.001 for ICA-RI; AUC=0.749, *P*<0.001 for ICA-PSV).

Conclusion: In fetuses with late-onset FGR, UA Doppler measurements showed minimal differences compared to healthy fetuses, but differences in carotid Doppler measurements, especially in the ICA, were more pronounced. Therefore, in the management of fetuses suspected of having late-onset FGR, a more detailed Doppler examination might be required.

Keywords: carotid artery, Doppler measurements, fetal growth restriction, umbilical artery

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Introduction

Fetal growth restriction (FGR), also referred to as intrauterine growth restriction, is a pathological state in which the fetus is unable to attain its innate genetic growth potential [1]. This condition affects up to 10% of pregnancies and is the second most common cause of infant morbidity and mortality after premature birth [2]. The pathogenesis of FGR can be attributed to maternal, fetal, placental, and genetic factors. However, a predominant underlying mechanism is compromised uteroplacental perfusion, leading to suboptimal fetal nutrition and subsequent FGR [3,4].

FGR is commonly classified into early-onset FGR, occurring before the 32nd week of pregnancy, and late-onset FGR, taking place after. In cases of early-onset FGR, umbilical artery (UA) blood flow serves as the clinical benchmark for detection and management [5,6]. However, this metric often presents as normal in late-onset FGR cases [7], emphasizing the necessity for a more accurate predictor of late-onset FGR. A study assessing structurally smaller fetuses with normal UA values identified decreased impedance levels in the middle cerebral artery (MCA) [8]. On the contrary, the vasodilation brought about by hypoxia leads to an increase in placental vascular resistance and a decrease in cerebral resistance, ultimately resulting in a reduction of the cerebroplacental ratio (CPR). This ratio is calculated by dividing the MCA-pulsatility index (PI) by the UA-PI [9]. Moreover, both MCA and CPR have been associated with adverse perinatal outcomes and poor neurodevelopment [10-12].

The MCA, which facilitates blood flow to the cerebrum, is the larger terminal branch of the internal carotid artery (ICA), which originates from the common carotid artery (CCA) and perfuses intracranial structures such as the brain and eyes [13]. Additionally, it has been reported that both the ICA and the CCA are associated with hypoxia [14,15], also observed in late-onset FGR [7]. Given the aforementioned rationales, we postulated that Doppler measurements of both the CCA and ICA could differ in late-onset FGR cases. This study aims to assess the Doppler parameters of the CCA and ICA in fetuses with late-onset FGR and compare these measurements with those of fetuses without growth restriction.

Materials and methods

This cross-sectional observational study was conducted on pregnancies having follow-ups at the Kocaeli Derince Education and Research Hospital Perinatology Clinic between June 2022 and May 2023. The study received approval from the Ethical Committee of Kocaeli Derince Education and Research Hospital (Approval Date/Number: May 26, 2022/046). The present study adhered to the ethical regulations and principles stipulated in the Declaration of Helsinki. Prior to their involvement in the study, informed consent was obtained from all participants. In a previous study, the FGR group was found to have a lower mean UA-PI than the control groups (1.27 [0.64] *vs.* 1.02 [0.29], *P*<0.001, respectively) [16]. Considering the differences in means mentioned in this study, a minimum sample size of 69 for each group was determined using G*Power v3.1 software, with a 5% alpha error probability and 90% power [17]. The sample size formula was as follows: $N = 2 \times [(Z_{1-\alpha/2} + Z_{1-\beta}) / ES]^2$, where the standard normal deviation for $\alpha = Z_\alpha = 1.96$, and the standard normal deviation for $\beta = Z_\beta = 1.28$. ES is the effect size, defined as $ES = |\mu_1-\mu_2|/\sigma$, where $|\mu 1 - \mu 2|$ is the absolute value of the difference in means between the two groups and σ is the standard deviation of the outcome of interest [18].

Study population

A total of 132 pregnant women complicated by late-onset FGR between the 32nd and 37th weeks of gestation were evaluated based on eligibility criteria. The inclusion criteria were patients diagnosed with late-onset FGR between the 32nd and 37th weeks of gestation according to the 2016 Delphi consensus [6]. The exclusion criteria were congenital anomalies, presence of any additional disease, maternal body mass index over 35 kg/m^2, abdominal scars hindering ultrasound visualization, use of medications such as antenatal steroids, sympathomimetics, and indomethacin that affect vascular function, drug use, smoking during pregnancy, concurrent preeclampsia, and multiple pregnancies. After this exclusion process, 75 singleton pregnancies complicated with late-onset FGR between the 32nd and 37th weeks of gestation were included in the study. The control group comprised pregnant women who delivered at term without any additional diseases and were matched 1:1 in terms of gestational age and obstetric histories such as gravida, parity, living, and abortion with late-onset FGR.

Study protocol

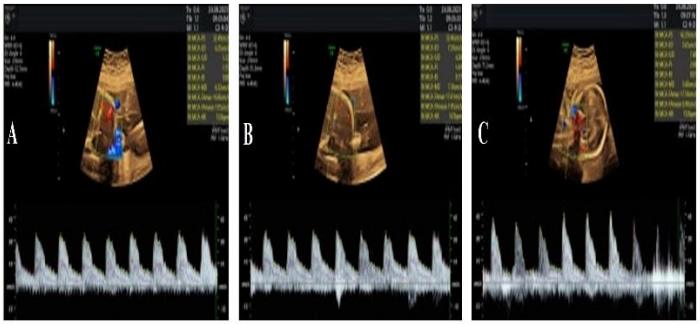
Upon the patients' admission to the hospital, their demographic characteristics such as gravida, parity, living, and abortion were documented, and subsequently, ultrasonographic examinations such as biparietal diameter, head circumference, abdominal circumference (AC), femur length, estimated fetal weight (EFW), and mean amniotic fluid index (mAFI), and Doppler measurements were performed. The Delphi consensus of 2016 was used for the definition of late-onset FGR [6]. The diagnosis of late-onset FGR was established when the AC or EFW was below the 3rd percentile at or beyond 32 weeks of gestation. In cases where the EFW or AC ranges between the 3rd and 10th percentiles, at least one abnormal Doppler finding (UA-PI > 95th percentile, CPR < 5th percentile) or AC/EFW crossing centiles by more than two quartiles on growth charts was regarded as late-onset FGR [6].

Ultrasonographic evaluation

Two experienced maternal-fetal medicine experts carried out the ultrasound evaluation. A 2–9 MHz convex transducer from the Voluson E6 (General Electric, USA) was used for the procedure. The Hadlock I formula was employed to calculate the EFW. Fetuses in the control group had an EFW between the 10th and 90th percentiles, while those in the late-onset FGR group had an EFW below the 10th percentile. The amniotic fluid index was noted. A vertical measurement of the deepest amniotic fluid pockets of four quadrants using midline and umbilicus was obtained in millimeters. The amniotic index of each pregnancy was obtained by summing the vertical measurement of amniotic pockets of the four quadrants [19]. Throughout the ultrasound examination, the thermal and mechanical indices were maintained at levels below 1.0 mW/cm^2. Gestational age was confirmed using first-trimester crown-rump length in all cases.

The Doppler velocimetry of the UA encompassed measurements of the systolic to diastolic ratio (S/D), PI, and PSV [20]. The Doppler velocimetry of the MCA (Figure 1A), ICA (Figure 1B), and CCA (Figure 1C) encompassed measurements of the PI, resistance index (RI), and PSV. These measurements were automatically determined by the sonographic device based on the following formulas: S/D ratio = systolic/diastolic ratio, RI = (systolic velocity - diastolic velocity) / systolic velocity, PI = (systolic velocity - diastolic velocity) / mean velocity, MCA-CPR = MCA-PI / UA-PI, ICA-CPR = ICA-PI / UA-PI, and CCA-CPR = CCA-PI / UA-PI. The highest systolic velocity of the waveform was defined as PSV in cm/s^2. The insonation angle was kept below 30 degrees during pulsed wave Doppler to ensure accurate measurements [21].

Figure 1: Middle cerebral artery (A), internal (B), and common (C) carotid artery flow by pulsed-wave Doppler ultrasonography examination.



Doppler positioning was at the proximal one-third of the MCA, in line with the circle of Willis, on an axial section of the fetal cranium. The ICA waveform was captured at the point where it bifurcates into the middle and anterior cerebral arteries on the axial plane [22]. The waveform for the CCA was captured at the neck region at the parasagittal plane, specifically recording from the left CCA. For each measurement, the sample gate was set to 2 mm, and no interference from nearby vessels was recorded [23]. Doppler velocimetry of the UA was conducted on the free loops of the umbilical cord, examining the spectral pattern for flow pattern. Reference ranges for UA Doppler were sourced from https://www.perinatology.com/calculators/umbilicalartery.htm Instances of absent or reverse end-diastolic flow were noted. Doppler waveform recordings were not taken during fetal breathing or movements. Waveforms were visualized on the screen, and if they appeared uniform, three consecutive waves were used for calculations [22]. For each Doppler measurement, intraobserver and interobserver variability had an intraclass correlation coefficient ranging from 0.83 to 0.95 [24].

Statistical analysis

All data were analyzed with IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). Numerical data determined to be normally distributed based on the results of Kolmogorov-Smirnov tests are given as mean and standard deviation (SD) values, while non-normally distributed variables are presented as median (25th–75th quartile) values. For comparisons between groups, the Student T-test and Mann-Whitney U test were used in line with the normality of the considered distribution. Categorical variables are given as numbers and percentages, and inter-group comparisons were conducted with Chi-square and Fisher exact tests. The receiver operating characteristic (ROC) curve analysis was applied to assess diagnostic performance. Threshold values were determined by the Youden index method. A comparison of the area under the curves (AUC) was performed with a nonparametric approach using the theory of generalized U-statistics to generate an estimated covariance matrix previously reported by DeLong et al. [25]. Significance was accepted at *P*-value <0.05 (*) for all statistical analyses.

Results

The distribution of gravida, parity, and gestational week was comparable between the late-onset FGR group and the control group (*P*=0.954, *P*=0.950, *P*=0.911, respectively). The late-onset FGR group displayed lower mean values for biometric measurements, including biparietal diameter (34.7 [1.1] vs. 33.6 [1.6], *P*<0.001), head circumference, AC, and EFW in comparison to the control group, as presented in Table 1.

Table 1: Demographic and clinical characteristics of the groups.

Variables	Control n=75	Late-onset FGR n=75	*P*-value
Gravida	1 (1–2)	1 (1–2)	0.954
Parity	0 (0–1)	0 (0–1)	0.950
Abortion	0	0	0.999
Living	0 (0-1)	0 (0-1)	0.852
Gestational week	34.7 (1.1)	34.8 (1.5)	0.911
Biparietal diameter, weeks	35.1 (1.1)	33.6 (1.6)	<0.001
Head circumference, weeks	35.3 (1.6)	34.0 (1.9)	<0.001
Abdominal circumference, weeks	35.0 (1.3)	32.0 (1.3)	<0.001
Femur length, weeks	34.9 (1.0)	32.9 (1.8)	<0.001
Estimated fetal weight, g	2451.4 (275.1)	2054.7 (286.8)	<0.001
mAFI, mm	63.5 (13.1)	61.1 (12.7)	0.257

Data are shown as mean (SD) or median (25th-75th quartile) or number and percentage (%). mAFI: mean amniotic fluid index, FGR: fetal growth restriction

In the group with late-onset FGR, the mean UA-SD was found to be higher (2.7 [0.6] *vs*. 2.5 [0.5], *P*=0.006), while the mean UA-PI (0.8 [0.2] *vs*. 0.9 [0.2], *P*=0.011) and the mean UA-PSV (35.6 [8.2] *vs*. 41.1 [7.1], *P*<0.001) were lower when compared to the control group. The Doppler measurements of MCA, ICA, and CCA showed lower PI and PSV levels in the late-onset FGR group (*P*<0.001, *P*<0.001, respectively), while the RI levels were higher (*P*<0.001). However, the differences were more pronounced in ICA Doppler measurements, as shown in Table 2.

Table 2: Comparison of Doppler measurements between the control group and late-onset fetal growth restriction groups.

Variables	Control n=75	Late-onset FGR n=75	*P*-value
Umbilical artery			
Systolic to diastolic ratio	2.5 (0.5)	2.7 (0.6)	0.006
Pulsatility index	0.9 (0.2)	0.8 (0.2)	0.011
Peak systolic velocity	41.1 (7.1)	35.6 (8.2)	<0.001
Middle cerebral artery			
Pulsatility index	4.6 (1.4)	4.2 (0.7)	0.021
Resistance index	1.3 (0.2)	1.5 (0.3)	<0.001
Peak systolic velocity	57.2 (17.5)	47.4 (10.9)	<0.001
Internal carotid artery			
Pulsatility index	5.5 (1.6)	4.0 (1.7)	<0.001
Resistance index	1.4 (0.5)	1.9 (0.5)	<0.001
Peak systolic velocity	53.4 (18.8)	38.7 (10.8)	<0.001
Common carotid artery			
Pulsatility index	4.1 (1.5)	3.6 (1.4)	0.028
Resistance index	1.2 (0.3)	1.4 (0.6)	0.037
Peak systolic velocity	41.4 (14.0)	36.6 (10.2)	0.018
Cerebroplacental ratio			
Middle cerebral artery	4.6 (4.2–6.3)	3.8 (3.4–5.4)	0.025
Internal carotid artery	6.0 (4.3–7.2)	4.1 (2.7–6.0)	0.002
Common carotid artery	4.5 (3.1–6.3)	3.3 (2.8–5.7)	0.044

Data are shown as mean (SD) or median (25th–75th quartile) or number and percentage (%). FGR: fetal growth restriction

The median MCA-CPR (3.8 *vs*. 4.6, *P*=0.025), ICA-CPR (4.1 *vs*. 6.0, *P*=0.002), and CCA-CPR (3.3 *vs*. 4.5, *P*=0.044) levels were higher in the late-onset FGR group compared to the control group (Table 2). The comprehensive analysis of the diagnostic efficacy of Doppler indices in predicting late-onset

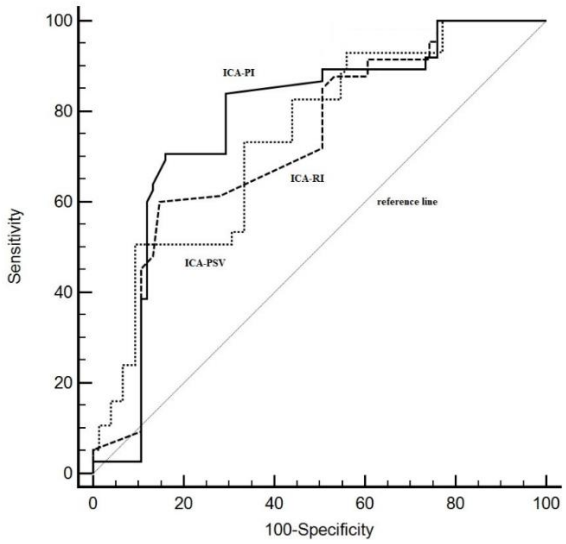
FGR is elaborated in Table 3. Accordingly, ICA Doppler measurements had superior diagnostic performance compared to other Doppler indices (AUC=0.777, *P*<0.001 for ICA-PI; AUC=0.751, *P*<0.001 for ICA-RI; AUC=0.749, *P*<0.001 for ICA-PSV). On the other hand, ICA-PI displayed a superior diagnostic performance compared to ICA-RI (difference between AUC=0.026, *P*=0.047) and ICA-PSV (difference between AUC=0.028, *P*=0.045) (Figure 2).

Table 3: Diagnostic performance of Doppler indices in predicting late-onset fetal growth restriction.

Variables	AUC (SE)	Sensitivity (%)	Specificity (%)	Cut-off value	*P*-value
Umbilical artery					
Systolic to diastolic ratio	0.615 (0.05)	77.3	34.7	>2.2	0.010
Pulsatility index	0.609 (0.05)	28.0	96.0	<1.0	0.015
Peak systolic velocity	0.692 (0.05)	58.7	93.3	≤36.0 cm/s	<0.001
Middle cerebral artery					
Pulsatility index	0.596 (0.05)	90.6	12.0	<5.0	0.025
Resistance index	0.693 (0.05)	86.7	62.7	>1.4	<0.001
Peak systolic velocity	0.650 (0.05)	80.0	64.0	≤55.0 cm/s	0.002
Internal carotid artery					
Pulsatility index	0.777 (0.04)	84.0	70.7	<3.9	<0.001
Resistance index	0.751 (0.04)	87.5	47.2	>1.5	<0.001
Peak systolic velocity	0.749 (0.04)	82.4	57.2	≤37.2 cm/s	<0.001
Common carotid artery					
Pulsatility index	0.622 (0.05)	50.7	77.3	<3.7	0.034
Resistance index	0.595 (0.05)	46.7	77.3	>1.3	0.044
Peak systolic velocity	0.608 (0.05)	69.3	62.7	≤39.5 cm/s	0.034
Cerebroplacental ratio					
Middle cerebral artery	0.605 (0.05)	38.7	85.3	≤3.9	0.036
Internal carotid artery	0.681 (0.05)	69.3	64.0	<4.7	0.001
Common carotid artery	0.586 (0.05)	77.3	49.3	<3.5	0.049

AUC: area under the curve, SE: standard error

Figure 2: Diagnostic performance of internal carotid artery Doppler indices in predicting late-onset fetal growth restriction.



ICA: internal carotid artery, PI: pulsatility index, RI: resistance index, PSV: peak systolic velocity

Discussion

To the best of our knowledge, this is the first study in the present literature that assesses the association between Doppler indices derived from four distinct arteries and late-onset FGR. The Doppler acquired from each artery revealed a significant difference in the late-onset FGR group compared to the control group. However, the ICA Doppler indices demonstrated a better diagnostic performance in predicting late-onset FGR than the Doppler indices from other arteries.

Ultrasound-based assessment of fetal weight is the most fundamental morphometric test used for FGR detection and diagnosis [26]. A reduced umbilical venous blood flow results in decreased blood flow to the liver. This leads to a reduction in AC and an increase in resistance in the UA. As the pathological condition progresses, a loss of end-diastolic flow or reverse flow is observed in the UA [27]. However, in cases of late-onset FGR, the UA Doppler might appear normal, indicating a less severe placental dysfunction [7]. The UA is straightforward to examine, while various physiological elements can alter UA Doppler indices. As the fetal heart rate decelerates, the prolonged cardiac cycle makes the diastolic flow rate approach the zero line more closely. This can lead to an increase in the S/D ratio. Besides, fetal breathing can induce similar alterations by extending the cardiac cycle and rendering the spectral curve irregular [28]. In this study, all Doppler measurements were carried out exclusively during times without any fetal heart rate abnormalities, breathing, or movement to negate the impacts of these factors.

Fetuses affected by late-onset FGR have been observed to exhibit elevated values of UA-SD and reduced UA-PSV compared to the control group. However, the diagnostic performance of these parameters in predicting FGR was lower. In a retrospective cohort study that investigated pregnancies impacted by late-onset FGR, an abnormal UA-SD ratio was reported in 23% of the infants [29]. These findings indicate that fetuses with late-onset FGR often exhibit normal UA Doppler measurements. Despite normal UA Doppler findings, MCA has been shown to be independently associated with late-onset FGR [30]. However, an advanced brain vasodilation indicative of chronic hypoxia, as indicated by an MCA-PI < 5th percentile, can be observed in 25% of late-onset FGR [31]. A previous study, which encompassed FGR, SGA, and AGA infants, indicated that the indices of UA-PI and MCA-PI were similar among the groups, while the UA-PSV levels were lower in infants diagnosed with late-onset FGR [8]. Contrary to these findings, there are studies reporting that both UA and MCA indices are associated with late-onset FGR [32,33]. Discrepancies between studies highlight the need to assess different Doppler measurements or their combinations in predicting late-onset FGR.

The MCA-CPR can significantly enhance the sensitivity of both UA and MCA alone, as heightened placental impedance in the UA typically coincides with decreased cerebral resistance in the MCA [34]. In uncomplicated pregnancies, the diastolic phase of the pulse waveform in cerebral arteries is consistently lower than that in umbilical arteries, irrespective of the gestational age. This ensures that the resistance in cerebral vessels is greater than that in the placental vessels, making the MCA-CPR exceed 1. However, in pathological pregnancies, when the blood flow distribution favors the brain, the MCA-CPR drops below 1 [35]. In the current study, the values of MCA-CPR were observed to be lower in the group with late-onset FGR than in the control group. Additionally, 7.8% of late-onset FGR fetuses had an MCA-CPR below 1. However, some studies have reported that the MCA-CPR has a low or insignificant diagnostic performance in distinguishing late-onset FGR fetuses from the SGA or the control group [8,36]. On the other hand, the link between late-onset FGR and hypoxia might cause discrepancies in Doppler readings from systemic arteries that supply the MCA [37,38]. However, we could not find any research that comprehensively evaluates both ICA and CCA Doppler indices in cases of late-onset FGR. In our study, PI and PSV levels in

both ICA and CCA Doppler measurements were observed to be lower in the late-onset FGR group, while RI levels were higher. Additionally, the levels of ICA-CPR were also lower in the late-onset FGR group. Moreover, while ICA Doppler indices had comparable diagnostic performance in differentiating late-onset FGR, they exhibited superior diagnostic performance compared to Doppler indices from other vessels. These findings suggest that changes in the ICA might offer an early indication of late-onset FGR before changes in the MCA become clinically apparent.

Limitations

This study has several significant limitations. Firstly, the Doppler indices' sequential alterations throughout the course of pregnancy, from diagnosis to delivery, were not evaluated. Secondly, distinguishing between SGA and late-onset FGR fetuses is clinically challenging, and groups with SGA were not included in this study. Therefore, this study does not depict the variances in Doppler measurements between late-onset FGR and SGA. Lastly, as this cross-sectional study evaluated pregnancies between 32 and 37 weeks of gestation, it is imperative to assess the clinical implications of these observations in terms of prognosis and management. There is a need for future large-scale prospective studies that include control groups when analyzing SGA, late-onset FGR, differences in carotid Doppler measurements, and their relationship with maternal and fetal outcomes.

Conclusion

This preliminary study highlights significant alterations in the hemodynamics of the carotid arteries in fetuses affected by late-onset FGR. Notably, Doppler indices of ICA and CCA such as PI, PSV, and CPR, exhibit a decrease, while RI displays an increase within this particular group, indicating the presence of cerebral vasodilation. Furthermore, the ICA demonstrates better diagnostic efficacy when compared to the CCA. This suggests that changes in the ICA may be more reflective of cerebral blood flow alterations, making it a more reliable measurement in fetuses with late-onset FGR. Nevertheless, larger-scale research is needed to validate these findings and to determine how to implement these results in routine clinical practice. By better understanding the cerebral hemodynamic changes associated with late-onset FGR, healthcare professionals can intervene earlier and potentially improve outcomes for the fetus.

References

1. ACOG Practice bulletin no. 134: fetal growth restriction. Obstet Gynecol. 2013;121:1122-33. doi: 10.1097/01.AOG.0000429658.85846.f9.
2. Nardozza LM, Caetano AC, Zamarian AC, Mazzola JB, Silva CP, Marcal VM, et al. Fetal growth restriction: current knowledge. Arch Gynecol Obstet. 2017;295:1061-77. doi: 10.1007/s00404-017-4341-9.
3. Malhotra A, Allison BJ, Castillo-Melendez M, Jenkin G, Polglase GRMiller SL. Neonatal Morbidities of Fetal Growth Restriction: Pathophysiology and Impact. Front Endocrinol (Lausanne). 2019;10:55. doi: 10.3389/fendo.2019.00055.
4. Brown LD, Hay WW, Jr. Impact of placental insufficiency on fetal skeletal muscle growth. Mol Cell Endocrinol. 2016;435:69-77. doi: 10.1016/j.mce.2016.03.017.
5. Dall'Asta A, Brunelli V, Prefumo F, Frusca T, Lees CC. Early onset fetal growth restriction. Matern Health Neonatol Perinatol. 2017;3:2. doi: 10.1186/s40748-016-0041-x.
6. Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol. 2016;48:333-9. doi: 10.1002/uog.15884.
7. Miller SL, Huppi PS, Mallard C. The consequences of fetal growth restriction on brain structure and neurodevelopmental outcome. J Physiol. 2016;594:807-23. doi: 10.1113/JP271402.
8. Liu H, Zhang L, Luo X, Li J, Huang SQi H. Prediction of late-onset fetal growth restriction by umbilical artery velocities at 37 weeks of gestation: a cross-sectional study. BMJ Open. 2022;12:e060620. doi: 10.1136/bmjopen-2021-060620.
9. Bahado-Singh RO, Kovanci E, Jeffres A, Oz U, Deren O, Copel J, et al. The Doppler cerebroplacental ratio and perinatal outcome in intrauterine growth restriction. Am J Obstet Gynecol. 1999;180:750-6. doi: 10.1016/s0002-9378(99)70283-8.
10. Figueras F, Cruz-Martinez R, Sanz-Cortes M, Arranz A, Illa M, Botet F, et al. Neurobehavioral outcomes in preterm, growth-restricted infants with and without prenatal advanced signs of brain-sparing. Ultrasound Obstet Gynecol. 2011;38:288-94. doi: 10.1002/uog.9041.
11. Cruz-Martinez R, Figueras F, Oros D, Padilla N, Meler E, Hernandez-Andrade E, et al. Cerebral blood perfusion and neurobehavioral performance in full-term small-for-gestational-age fetuses. Am J Obstet Gynecol. 2009;201:474 e471-7. doi: 10.1016/j.ajog.2009.05.028.
12. Şirinoğlu H, Atakır K, Özdemir S, Konal M, Mihmanlı V. Middle cerebral artery to uterine artery pulsatility index ratios in pregnancy with fetal growth restriction regarding negative perinatal outcomes. Journal of Surgery and Medicine. 2022.
13. Chandra A, Li WA, Stone CR, Geng X, Ding Y. The cerebral circulation and cerebrovascular disease I: Anatomy. Brain Circ. 2017;3:45-56. doi: 10.4103/bc.bc_10_17.
14. Lewis NC, Messinger L, Monteleone B, Ainslie PN. Effect of acute hypoxia on regional cerebral blood flow: effect of sympathetic nerve activity. J Appl Physiol (1985). 2014;116:1189-96. doi: 10.1152/japplphysiol.00114.2014.
15. Das KK, Yendigeri SM, Patil BS, Bagoji IB, Reddy RC, Bagali S, et al. Subchronic hypoxia pretreatment on brain pathophysiology in unilateral common carotid artery occluded albino rats. Indian J Pharmacol. 2018;50:185-91. doi: 10.4103/ijp.IJP_312_17.
16. Adedo AA, Arogundade RA, Okunowo AA, Idowu BM, Oduola-Owoo LT. Comparative Study of the Umbilical Artery Doppler Indices of Healthy and Growth-Restricted Foetuses in Lagos. J West Afr Coll Surg. 2022;12:63-9. doi: 10.4103/jwas.jwas_63_22.
17. Kang H. Sample size determination and power analysis using the G*Power software. J Educ Eval Health Prof. 2021;18:17. doi: 10.3352/jeehp.2021.18.17.
18. Kim HY. Statistical notes for clinical researchers: Sample size calculation 1. comparison of two independent sample means. Restor Dent Endod. 2016;41:74-8. doi: 10.5395/rde.2016.41.1.74.
19. Reddy UM, Abuhamad AZ, Levine D, Saade GR, Fetal Imaging Workshop Invited P. Fetal imaging: executive summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound Fetal Imaging workshop. Obstet Gynecol. 2014;123:1070-82. doi: 10.1097/AOG.0000000000000245.
20. McCallum WD, Williams CS, Napel S, Daigle RE. Fetal blood velocity waveforms. Am J Obstet Gynecol. 1978;132:425-9. doi: 10.1016/0002-9378(78)90779-2.
21. Bonnevier A, Marsal K, Brodszki J, Thuring A, Kallen K. Cerebroplacental ratio as predictor of adverse perinatal outcome in the third trimester. Acta Obstet Gynecol Scand. 2021;100:497-503. doi: 10.1111/aogs.14031.
22. Wladimiroff JW, Tonge HM, Stewart PA. Doppler ultrasound assessment of cerebral blood flow in the human fetus. Br J Obstet Gynaecol. 1986;93:471-5.
23. Wladimiroff JW, Noordam MJ, van den Wijngaard JA, Hop WC. Fetal internal carotid and umbilical artery blood flow velocity waveforms as a measure of fetal well-being in intrauterine growth retardation. Pediatr Res. 1988;24:609-12. doi: 10.1203/00006450-198811000-00014.
24. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med. 2016;15:155-63. doi: 10.1016/j.jcm.2016.02.012.
25. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988;44:837-45.
26. Salavati N, Smies M, Ganzevoort W, Charles AK, Erwich JJ, Plosch T, et al. The Possible Role of Placental Morphometry in the Detection of Fetal Growth Restriction. Front Physiol. 2018;9:1884. doi: 10.3389/fphys.2018.01884.
27. Krishna U, Bhalerao S. Placental insufficiency and fetal growth restriction. J Obstet Gynaecol India. 2011;61:505-11. doi: 10.1007/s13224-011-0092-x.
28. Necas M. Obstetric Doppler ultrasound: Are we performing it correctly? Australas J Ultrasound Med. 2016;19:6-12. doi: 10.1002/ajum.12002.
29. Maggio L, Dahlke JD, Mendez-Figueroa H, Albright CM, Chauhan SPWenstrom KD. Perinatal outcomes with normal compared with elevated umbilical artery systolic-to-diastolic ratios in fetal growth restriction. Obstet Gynecol. 2015;125:863-9. doi: 10.1097/AOG.0000000000000737.
30. Figueras F, Gratacos E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. Fetal Diagn Ther. 2014;36:86-98. doi: 10.1159/000357592.
31. Oros D, Figueras F, Cruz-Martinez R, Meler E, Munmany MGratacos E. Longitudinal changes in uterine, umbilical and fetal cerebral Doppler indices in late-onset small-for-gestational age fetuses. Ultrasound Obstet Gynecol. 2011;37:191-5. doi: 10.1002/uog.7738.
32. Steller JG, Gumina D, Driver C, Peek E, Galan HL, Reeves S, et al. Patterns of Brain Sparing in a Fetal Growth Restriction Cohort. J Clin Med. 2022;11. doi: 10.3390/jcm11154480.
33. Tarzamni MK, Nezami N, Sobhani N, Eshraghi N, Tarzamni MTalebi Y. Nomograms of Iranian fetal middle cerebral artery Doppler waveforms and uniformity of their pattern with other populations' nomograms. BMC Pregnancy Childbirth. 2008;8:50. doi: 10.1186/1471-2393-8-50.
34. Arbeille P, Maulik D, Fignon A, Stale H, Berson M, Bodard S, et al. Assessment of the fetal PO2 changes by cerebral and umbilical Doppler on lamb fetuses during acute hypoxia. Ultrasound Med Biol. 1995;21:861-70. doi: 10.1016/0301-5629(95)00025-m.
35. Shahinaj R, Manoku N, Kroi E, Tasha I. The value of the middle cerebral to umbilical artery Doppler ratio in the prediction of neonatal outcome in patient with preeclampsia and gestational hypertension. J Prenat Med. 2010;4:17-21.
36. Vollgraff Heidweiller-Schreurs CA, De Boer MA, Heymans MW, Schoonmade LJ, Bossuyt PMM, Mol BWJ, et al. Prognostic accuracy of cerebroplacental ratio and middle cerebral artery Doppler for adverse perinatal outcome: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2018;51:313-22. doi: 10.1002/uog.18809.
37. Canas D, Herrera EA, Garcia-Herrera C, Celentano D, Krause BJ. Fetal Growth Restriction Induces Heterogeneous Effects on Vascular Biomechanical and Functional Properties in Guinea Pigs (Cavia porcellus). Front Physiol. 2017;8:144. doi: 10.3389/fphys.2017.00144.
38. Llurba E, Baschat AA, Turan OM, Harding J, McCowan LM. Childhood cognitive development after fetal growth restriction. Ultrasound Obstet Gynecol. 2013;41:383-9. doi: 10.1002/uog.12388.