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Relationship Between Peak Systolic Velocity in Pulmonary Artery Color Doppler and Neonatal Respiratory Outcomes in Fetal Growth Restriction With Abnormal Fetoplacental Circulation: A Prospective Cohort Study

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Abstract

Objectives: Newborns with fetal growth restriction (FGR) are at a high risk of prenatal mortality and morbidity compared to infants with appropriate intrauterine growth. The importance of Doppler ultrasound as a non-invasive method for estimating the pulmonary artery pressure (PAP) in newborns and adults has been mentioned in many studies. This study investigated the relationship between peak systolic velocity in pulmonary artery color Doppler and neonatal respiratory outcomes in FGR with abnormal fetoplacental circulation.

Materials and Methods: In this prospective cohort study, 60 pregnant women with a gestational age of 32-37 weeks were studied in two groups: group I (women with fetus suspected of FGR according to ultrasound assessment) and group II (women with normal pregnancy). All women underwent Doppler ultrasound of pulmonary artery, umbilical artery, middle cerebral artery, and venous ductus. The pick systolic velocity (PSV) of the trunk of the pulmonary artery was evaluated in the fetus of all participants. After delivery, all infants were studied for respiratory outcomes at birth. Finally, variables included gestational age, fetal estimated weight based on Hadlock table, fetal amniotic fluid index, maternal parity, umbilical artery pulsatility index (PI), middle cerebral artery PI, maximum pulmonary artery velocity (PV), umbilical artery to middle cerebral artery index ratio, and the number of infants admitted to the newborn intensive care unit (NICU) due to respiratory distress were compared between two groups.

Results: Our results showed a significant association between pulmonary artery PI in FGR fetuses with abnormal fetoplacental circulation. The rate of early NICU hospitalization of infants in the group I was higher than group II due to respiratory diseases, as well as the need for oxygen and continuous positive airway pressure (CPAP).

Conclusions: Pulmonary artery color Doppler ultrasound can be effective in diagnosing FGR embryos during pregnancy and making the necessary predictions to reduce prenatal mortality and morbidity in these infants.

Keywords: Fetal growth restriction, Placental insufficiency, Pulmonary artery, Respiration, Ultrasonography, Doppler, Color.

Introduction

Fetal weight is determined based on genetic potential, fetal health, maternal capacity to deliver the nutritional requirements for fetal growth, and the placenta's ability to transfer these nutrients from the mother to the fetus. The main conditions that affect fetal development have a placental or fetal origin. The placenta plays a crucial role in pregnancy health and abortion. The primary function of the placenta is to exchange oxygen, carbon dioxide, nutrients, electrolytes, and excretion of waste products through the umbilical cord between mother and fetus. The significant events related to the placenta include changes in uterine-placental-fetal blood flow (1). Intrauterine growth restriction refers to a condition in which fetal growth is slowed or stopped during pregnancy due to placenta problems and thus the limitation of oxygenation and blood supply to the fetus. Fetal growth restriction (FGR) affects about 5% to 10% of pregnancies, and infants with FGR show a significantly higher risk of prenatal mortality and morbidity (10 to 20 times) than well-developed infants (2).

High-risk populations include women with an unhealthy lifestyle, low pre-pregnancy weight, or inappropriate weight gain during pregnancy, a history of preterm labor, and a history of previous pregnancies with FGR fetuses. Serial fundal height measurement and ultrasonic fetal biometry is one of the methods of FGR screening and diagnosis. In color Doppler ultrasound, the severity of fetal placental abnormalities can be assessed by measuring the umbilical artery pulsatility index (PI), the middle cerebral artery PI, and venous canal (1). The estimated fetal weight (EFW) is calculated using the method of Hadlock and his colleagues reported in 1985 since this method is shown to be more suitable for other criteria in different populations

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Key Messages

- Ultrasound as a method of assessing vascular index in fetuses with fetal growth restriction can be important in predicting fetal complications as a non-invasive method.
- In this study, in fetuses with fetal growth restriction, there was a significant relationship between pulmonary artery PI and neonatal hospitalization in NICU and respiratory problems and the need for CPAP, and this index can help predict neonatal respiratory status after birth.

and different times (3,4).

The uterine arteries supply a considerable amount of blood flow to the placenta. Throughout pregnancy, trophoblast invasion of spiral arteries and the 50% increase in maternal blood volume result in an increased blood flow by 10 to 20 times (4). The importance of Doppler ultrasound as a non-invasive method of estimating the pulmonary artery pressure (PAP) in newborns and adults has been shown in many studies (5-8). In the fetus, Doppler's evaluation of the main pulmonary artery helps analyses the impedance of vascular systems and changes in the relevant variables. Also, it correlates with gestational age, fetal lung maturity, and neonatal outcomes (9-12).

Different studies have been conducted to evaluate the fetal Doppler in FGR cases related to the evaluation of the umbilical artery, middle cerebral artery, and venous duct. Most Doppler evaluations in fetuses with late-onset FGR are regarding umbilical arteries, middle cerebral artery, and venous duct. There are few studies in which Doppler has measured PAP. Therefore, considering the factors that lead to FGR, on the other hand, the central and peripheral arteries of the fetus are affected by this disorder itself, and using the arterial Doppler is a non-invasive method of evaluation of the fetuses with FGR, the present study investigated the relationship between peak systolic velocity in pulmonary artery color Doppler and neonatal respiratory outcomes in FGR with abnormal fetoplacental circulation.

Materials and Methods

Study setting and Participants

In this prospective cohort study, all pregnant women with a gestational age of 32-37 weeks referred to Al-Zahra Educational and Medical Center, Tabriz, Iran from August 2021 to February 2022 were studied in two groups using the census sampling method. The group I were women with fetus suspected of FGR according to ultrasound assessment and the group II, women with normal pregnancy. All women with multiple pregnancy, congenital malformations or chromosomal abnormalities their fetuses, intrauterine fetal death, and congenital malformations due to infectious disease were excluded from the study.

All women underwent Doppler ultrasound (Philips Affiniti 50 Ultrasound, USA) of pulmonary artery, umbilical artery, middle cerebral artery, and venous ductus by a professor or fellowship of perinatology. The pick systolic velocity (PSV) of the trunk of the pulmonary artery was evaluated in the fetus of all participants by a neonatologist. After delivery, all infants were studied for respiratory outcomes at birth. Finally, variables included gestational age, fetal estimated weight based on Hadlock table, fetal amniotic fluid index (FAI), maternal parity, fetal abdominal circumference (AC), umbilical artery PI (UA PI), middle cerebral artery PI (MCA PI) of ductus venosus (DV) wave, maximum pulmonary artery velocity (PV), umbilical artery to middle cerebral artery index ratio (MCA PI/UA PI), and the number of infants admitted to the NICU due to respiratory distress were compared between two groups.

Fetus suspected of FGR defined based on the abdominal circumference <3rd percentile for the same fetal age or EFW <10th percentile for the same gestational age (according to the Hadlock table) with fetuses' UA PI above 95% for the same fetal age or ratio of the pulsed index of the middle cerebral artery to the umbilical artery index below the 5th percentile was considered for the same fetal age.

In the group I, routine treatments with betamethasone (12 mg/d) up to two doses intramuscular as well as necessary follow-up were provided.

Statistical Analysis

All of the statistical analysis was performed using the Statistical Package for the Social Sciences software (SPSS, version 21.0 for Windows; SPSS Inc., Chicago, IL). Descriptive data were reported as mean ± standard deviation (SD) and frequency. Quantitative findings will be compared between the two groups using Student's *t* test or Whitney-Mann U test. Qualitative data was assessed by Chi-Square test. Correlations between pulmonary artery Doppler indices and gestational age and fetal weight were compared using Pearson's correlation. *P* values less than 0.05 were considered statistically significant.

Results

Initially, the 82 pregnant women with a gestational age of 32-37 weeks were eligible to enter the study. Out of them, 22 women were excluded due to congenital malformations their fetuses and intrauterine fetal death. Finally, 60 women were assigned to two groups (30 in each group) and their data were analyzed (Figure 1).

The mean age of participants was 30.1 ± 5.8 and 30.8 ± 5.9 years in the group I and group II, respectively. There was no significant difference in the mean of age between two study groups. According to the results, 46.7 women in group I had a PV >95% percentile, while the majority of participants in group II had PV between percentile 5-95%, which showed a significant relationship between pulmonary artery PI and the presence of FGR in the fetus ($P < 0.001$) (Table 1). The demographic characteristics of the participants in two groups were showed in Table 1.

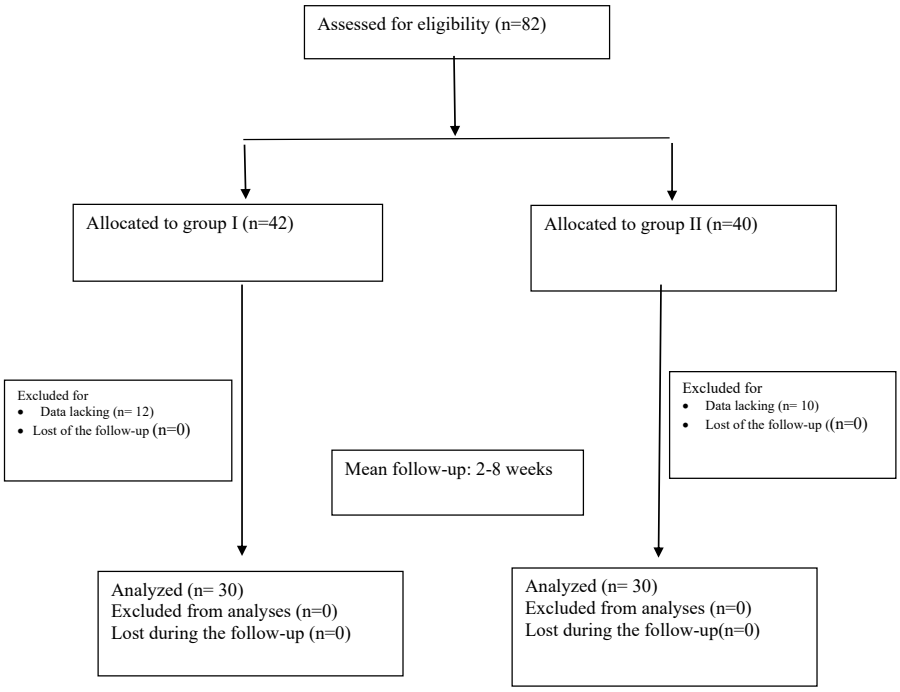

Figure 1. The study flowchart.

Since PSV of the fetal pulmonary artery was obtained in all cases between 2.5%-97.5%, this study examined PI of the pulmonary artery instead of pulmonary artery PSV. Our results showed that the PI of the pulmonary artery in group I was mainly above the 95th percentile. There was a significant relationship between the two groups regarding higher PI, while PI in group II mostly was between the 5-95th percentiles or below the 5th percentile. 22 neonates in group I (73.3%) and 8 neonates in the group II needed to be admitted to the NICU. There was a significant relationship between early hospitalization in NICU and PI of pulmonary artery >95th percentile in FGR infants with feto-placental vascular dysfunction due to respiratory problems. These infants also needed significantly more oxygen therapy, so that100.0% of infants with PI >95% required oxygen therapy. In general, 22 (73.3%) of neonates in group I and 8 (26.7%) in group II needed to oxygen therapy. Among 30 women surveyed in group 1, 2 (6.7%) had reversed end-diastolic velocity (EDV), 4 (13.3%) negative EDV, 3 (10%) normal blood velocity, and

Table 1. Demographic Characteristics of Study Participants in Two Groups (n=30/each)

Variables	Group I	Group II	*P* Value
Mother age	30.1±5.8	30.8±5.9	0.6[a]
Gestational age	33.8±1.6	33.6±1.5	0.6 [a]
Body mass index	26.4±5.1	26.2±4.8	0.8 [a]
Gravidity	2.2±1.9	1.9±1	0.4 [a]
Fetal estimated weight	1610.5±375.9	2344.5±418.7	<0.001[a]
Fetal amniotic fluid index (12)	10±3.7	14.2±3.7	<0.001[a]
Fetal abdominal circumference (4)	25±1.8	30.2±2.1	<0.001[a]
Fetal gender, No. (%)			0.7[b]
Male	21 (70%)	20 (66.7%)	
Female	9 (30%)	10 (33.3%)	
Maximum pulmonary artery velocity, No. (%)			<0.001[a]
<5%	6 (20.0)	3 (10)	
5-95%	10 (33.3)	26 (86.7)	
>95%	14 (46.7)	1 (3.3)	

[a]Independent samples *t* test.
[b] Chi-square test.

Table 2. Comparison of Study Outcomes According to PI Pulmonary Artery in Fetuses With FGR (Group I) and Fetuses Without FGR (Group II) (n=30/each)

Variables	Maximum Pulmonary Artery Velocity (PV)			*P* Value
	<5%	5-95%	>95%	
Umbilical artery PI (UA PI)				
>95%	6 (28.6)	6 (28.6)	9 (42.9)	0.737
Reverse EVD	0 (0)	1 (50.0)	1 (50.0)	
Normal	0 (0)	1 (33.3)	2 (66.7)	
Middle cerebral artery PI (MCA PI)				
>95%	6 (28.6)	6 (28.6)	9 (42.9)	
Reverse EVD	0 (0)	1 (50.0)	1 (50.0)	0.737
Negative EDV	0 (0)	2 (50.0)	2 (50.0)	
Normal	0 (0)	1 (33.3)	2 (66.7)	
Umbilical artery to middle cerebral artery index ratio (CPR)				
<5%	6 (21.4)	9 (32.1)	13 (4604)	0.736
>5%	0 (0)	1 (50.0)	1 (50.0)	
Admitted to the NICU				
Group I	2 (9.1)	6 (27.3)	14 (63.6)	0.004
Group II	4 (50.0)	4 (50.0)	0 (0)	
CPAP				
Group I	2 (11.8)	5 (29.4)	10 (58.8)	<0.001
Group II	4 (30.8)	5 (38.5)	4 (30.8)	
Need to oxygen				
Group I	2 (9.1)	6 (27.3)	14 (63.6)	0.004
Group II	4 (50.0)	4 (50.0)	0 (0)	
Need to ventilation				
Group I	0 (0)	2 (40.0)	3 (60.0)	0.470
Group II	6 (24.0)	8 (32.0)	11 (44.0)	
Neonatal Birth weight				
Group I	4 (14.8)	9 (33.3)	14 (51.9)	0.075
Group II	2 (66.7)	1 (33.3)	0 (0)	
Fetal gender				
Female	1 (11.1)	4 (44.4)	4 (44.4)	0.6
Male	5 (23.8)	6 (28.6)	10 (47.6)	

All data presented as n (%), Chi-square test.

21 (70%) EDV >95%. Also, our findings showed 70.0% of participants had umbilical artery PI > 95%, 28.6% with 5-95%, and 28.6% with PI below 5%.

In FGR infants with feto-placental vascular dysfunction and PI of the pulmonary artery >95th percentile, the need for continuous positive airway pressure (CPAP) was significantly higher. There were not significantly associated with the need for a ventilator and PI of the pulmonary artery >95th percentile in FGR infants with feto-placental vascular dysfunction (Table 2).

Discussion

PAP in infants suspected of FGR was studied using color Doppler ultrasound in the current study. Since different factors can cause FGR resulting in peripheral and central arterial disease in fetuses, the arterial Doppler ultrasound as a non-invasive method to evaluate fetuses with FGR can be helpful. Therefore, we assessed the effect of pulmonary artery color Doppler in fetuses with FGR with placental insufficiency on the neonatal respiratory outcome. There was a significant relationship between pulmonary artery PI and the presence of FGR in the fetuses with feto-placental vascular dysfunction. The early hospitalization rate of these fetuses in the NICU was higher due to respiratory distress and the need for oxygen and CPAP. Many studies have been conducted on fatal Doppler assessment in cases of FGR related to the evaluation of the umbilical artery, middle cerebral artery, and venous duct (venosus ductus). A similar study by Hidaka et al in 2017 compared ductus venosus Doppler with post-pregnancy consequences in the FGR fetuses with placental insufficiency in infants with a mean gestational age of 28 weeks and two days. Among the 18 infants, 15 survived, 2 of who were diagnosed with developmental disabilities. Their results showed that the umbilical artery pH was positively correlated with the PI value related to venosus ductus. The time interval from the first detection of the absent end-diastolic velocity in the umbilical artery (UA-AEDV) to delivery has been differently reported. Three cases had a time interval exceeding 20 days, the longest reported as 35 days (13).

Similarly, Turan et al examined the sequence of Doppler abnormalities that occurred during the interval from initial detection of FGR to delivery in 104 cases. In their study, the median intervals from the occurrence of UA-AEDV and UA-REDV to delivery were 10 and 5 days, respectively (14). Therefore, managing these growth-restricted foetuses with careful surveillance to prolong gestational age even for a short period can be helpful (7).

Müller et al studied 33 alive foetuses with UA-AREDV and compared short-term outcomes between the groups with positive (n = 23) and reverse DV flow (n = 10). The results indicated that intraventricular hemorrhage and respiratory distress syndrome were significantly higher, and the duration of ventilation was significantly longer in the group with reverse DV flow (15). Therefore, reverse DV flow has been widely studied for postnatal morbidity and impending fetal death. This study has shown that in the event of reverse current DV, rapid intervention in FGR should be performed. Ghosh and Gudmundsson studied the Doppler ultrasound of the uterine and umbilical arteries as predictors of perinatal outcome in fetuses with FGR. They evaluated 535 single pregnancies and observed abnormal uterine artery velocimetry in 33.4% and umbilical artery abnormal velocimetry in 4.28%. There was a statistically significant relationship between Doppler results of uterine and umbilical arteries and the adverse outcome of pregnancies (16). Another study compared the color Doppler of the middle cerebral artery versus umbilical artery for predicting neonatal outcomes in 150 FGR pregnancies in the third trimester. The weight of the fetus was determined via ultrasound. Before delivery, Doppler values of the umbilical and middle cerebral arteries were evaluated in FGR-diagnosed fetuses. 126 mothers had an SGA (small-for-gestational-age) neonate, while 24 women had a non-SGA neonate. No significant difference was shown between both groups regarding middle cerebral artery PI (17). Sosa-Olavarria et al used Doppler ultrasound to evaluate fetal pulmonary artery pressure in 337 pregnant women. Their results showed that the amount of the fetal main pulmonary artery Doppler acceleration time increases with decreasing the fetal main pulmonary artery pressure (FMPAP). Also, a significant negative correlation between FMPAP and gestational age were obtained. Finally, they concluded that fetal pulmonary artery pressure decreases with increased gestational age (18). Our study provided significant results on the frequency of early hospitalization due to neonatal respiratory distress in FGR with placental insufficiency compared to non-FGR infants based on PSV of pulmonary artery Doppler.

Conclusions

Pulmonary artery color Doppler ultrasound can be effective in diagnosing FGR embryos during pregnancy and making the necessary predictions to reduce prenatal mortality and morbidity in these infants.

Authors' Contribution

ShA, ZF, ShT, SY, LV, and RH designed the study and conducted the research. ShA, RH, ShT and VL monitored, evaluated, and analyzed the result of the study. Further, ShA, ZF, SY, RH, ShT and LV reviewed the article. The manuscript has been read and approved by all the authors, and each author believes that the manuscript represents honest work.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

The study proposal was approved by the ethics committee of Tabriz University of Medical Sciences, Tabriz, Iran (IR.TBZMED.REC.798). All participants' information was totally confidentially recorded and participants entered the study voluntarily and they were free to discontinue participation at any time. Written informed consent was obtained from all participants before starting the study.

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