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Doppler Evaluation of the Fetal Pulmonary Artery Pressure

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Abstract
Background: Evaluation of fetal pulmonary artery pressure (FMPAP) is important for assessing fetal cardiovascular function. **Methods:** A prospective study was conducted on 60 pregnant women between 22 and 40 weeks of gestation. Pulmonary Doppler examinations were performed at two time points during the second and third trimesters. Various Doppler variables, including the systolic/diastolic (S/D) ratio, pulsatility index (PI), resistance index (RI), peak systolic velocity (PSV), and At/Et ratio, were measured. **Results:** The mean values of the Doppler variables were determined. Significant differences were observed between the two examination time points, with higher values during the second visit. Negative correlations were found between these variables and both gestational age and fetal weight. Additionally, positive correlations were identified between the Doppler variables and neonatal intensive care unit (NICU) admission. Furthermore, the Doppler variables were significant predictors of both gestational age and fetal weight. **Conclusions:** Doppler velocimetry has been shown to be useful for detecting not just fetal pulmonary maturity, but also the FMPAP, and we expect that future research will demonstrate that estimations of the MFPAP may be able to predict whether or not the newborn will develop pulmonary hypertension.

Keywords: Doppler; Evaluation; Fetal Pulmonary Artery Pressure.

1. Introduction

Understanding the developing circulatory system and detecting possible anomalies requires the evaluation of fetal cardiovascular function. The measurement of fetal main pulmonary artery pressure (FMPAP) has attracted great interest among the different indicators that provide insight into fetal cardiovascular health [1].

FMPAP indicates the state of the pulmonary circulation's hemodynamics, providing vital information on the fetal pulmonary vascular resistance and cardiac function. Understanding the link between FMPAP and gestational age (GA) might provide light on the proper development of the cardiovascular system during pregnancy [2].

By carrying oxygenated blood from the right ventricle to the developing lungs, the major pulmonary artery performs a vital function in fetal circulation. Doppler ultrasonography, a noninvasive imaging method, permits the evaluation of FMPAP by monitoring blood flow velocities inside the major pulmonary artery. It is feasible to calculate pressure gradients and FMPAP by studying Doppler waveforms [3].

The objective of this study is to evaluate FMPAP and its correlation with GA.

2. Methods

This prospective study involved a total of 60 pregnant women, with fetuses ranging in age from 22 to 40 weeks. Participants were recruited from the Benha University Hospitals Obstetrics and Gynecology outpatient clinic. All subjects supplied written informed consent, and the Benha Faculty of Medicine's Local Ethics Committee for Human Subjects Research accepted the study's methodology.

Inclusion criteria were normal pregnant women without any health problems and women with singleton pregnancies and accurate gestational age (determined by a certain last menstrual period or first-trimester ultrasound).

Exclusion criteria were major structural abnormalities or known fetal chromosomal, prior antenatal corticosteroid administration and fetal structural anomalies discovered after delivery.

The following methods were employed for each pregnant woman: A) Detailed history: A comprehensive assessment of personal, present, past, and family medical history was conducted. B) Complete general examination: A thorough physical examination was performed. C) Laboratory investigation: Standard laboratory tests routinely conducted for pregnant women were performed.

A Voluson 730 ultrasound instrument (GE Healthcare Austria GmbH, Seoul, South Korea) equipped with a 3 to 5 MHz convex array sector transducer for pulmonary Doppler was used to assess the fetus. The examination was conducted between 22 and 26 weeks (the end of the second trimester) and then again at 36 weeks (beginning of the 9th month).

A single member of the author's team conducted all ultrasound exams according to a specified methodology. After a normal ultrasound exam covering fetal biometry, estimated fetal weight, and amniotic fluid index, the examiner methodically examined the fetal heart, concentrating on the four-chamber view, the outflow tracts, and the three-vessel view. In the axial view of the thorax, the major pulmonary artery (MPA) was evident between the pulmonary valve and the bifurcation of the right and left branches.

In the MPA, a 3 mm Pulsed Doppler sample gate with a 15° insonation angle was installed. Doppler gain and scale were modified to present the velocity waveform with the peak systolic velocity (PSV) and early diastolic notch (EDN) clearly. The MPA waveform was characterized by a strong systolic peak and a tiny notch of reversed flow at the end of systole, sometimes known as a "spike and dome" pattern. This unique waveform was essential for distinguishing it from the wave of the ductus arteriosus.

After acquiring the optimal fetal MPA waveform, the major Doppler velocity variables, including the systolic/diastolic (S/D) ratio, pulsatility index (PI), resistance index (RI), PSV, and At/Et ratio, were manually traced three times and the average was recorded. By dividing the time interval from the beginning of ventricular systole to peak velocity (At) by the time interval from the beginning to the end of ventricular systole, the At/Et ratio was calculated (Et).

Following the Doppler examination, the fetuses were followed up for 24 hours postnatally.

Statistical analysis:

The collected data were updated, coded, and tabulated using IBM SPSS Statistics for Windows, Version 25. Calculating descriptive statistics, such as the mean and standard deviation (±SD) for numerical data and frequency and percentage for nonnumerical data. Examining the normality of the data distribution using the Shapiro-Wilk test. Analytical statistics requires the use of one-way ANOVA and Kruskal-Wallis tests, respectively, to determine the statistical significance of differences between study groups for parametric and nonparametric variables. The unpaired Student's t-test and the Mann-Whitney test were used to evaluate demographic data including age, height, weight, BMI, and parity. For non-parametric data, the Friedman test was utilized, while the chi-square test was used to analyze the relationship between qualitative variables. To determine the degree of relationship between quantitative data, a Spearman correlation analysis was conducted, and logistic regression analysis was utilized to forecast risk factors. We assessed fetal pulmonary Doppler measurements as predictors of gestational age and fetal weight using univariate regression. The significance level was set at P-value < 0.05 with a 95% confidence interval, validating the correctness of odds ratios (OR) based on the size of the confidence interval.

3. Results

This prospective study was conducted on 60 pregnant women selected from the outpatient clinic of Obstetrics and Gynecology department of Benha University Hospitals, fetuses age (22-40 weeks) to evaluate FMPAP and its correlation with GA.

Demographic characteristics, Gravidity and parity, Gestational age (weeks), Fetal biometry during the first visit of the studied sample were shown in **Table 1**.

Table (1) Demographic characteristics, Gravidity and parity, Gestational age (weeks), Fetal biometry during the first visit of the studied sample

All patients (n= 60)	Mean & SD	Median	Range	IQR
Age (years)	27.90 ± 5.291	29.00	18.00, 37.00	23.00, 32.75
Height (cm)	161.85 ± 4.422	161.50	154.00, 170.00	158.00, 165.00
Weight (kg)	75.79 ± 4.378	76.25	67.50, 85.00	72.30, 79.00
BMI (kg/m^2)	28.91 ± 0.727	28.71	27.99, 32.88	28.49, 29.16
Gravidity	2.25 ± 0.914	2.00	1.00, 4.00	1.25, 3.00
Parity	1.10 ± 0.796	1.00	0.00, 2.00	0.00, 2.00
Gestational age (weeks)	24.12 ± 0.993	24.00	23.00, 26.00	23.00, 25.00
BPD (cm)	5.32 ± 0.403	5.36	4.61, 6.00	4.97, 5.70
FL (cm)	4.60 ± 0.317	4.67	4.01, 5.08	4.30, 4.90
AC (cm)	17.97 ± 1.439	18.07	15.38, 20.30	16.76, 19.30
AFI	14.70 ± 0.728	14.73	13.17, 16.80	14.06, 15.20
Estimated fetal weight (gm)	712 ± 110.09	720	510, 940	610, 790

The mean S/D was (6.93 ± 0.290) ranged from 6.34 to 7.71, their mean PI was (2.29 ± 0.225) ranged from 1.81 to 2.73, their mean RI was (0.86 ± 0.087) ranged from 0.63 to 1.02, their mean PSV was (64.67 ± 5.218) ranged from 48.63 to 77.38, their mean At/Et ratio was (0.22 ± 0.072) ranged from 0.06 to 0.38, and their mean PAP was (65.52 ± 6.782) ranged from 51.92 to 79.32. The mean S/D was (6.84 ± 0.289) ranged from 6.25 to 7.59, their mean PI was (2.20 ± 0.223) ranged from 1.75 to 2.62, their mean RI was (0.77 ± 0.085) ranged from 0.58 to 0.96, their mean PSV was (66.74 ± 5.188) ranged from 50.98 to 78.57, their mean At/Et ratio was (0.32 ± 0.064) ranged from 0.18 to 0.48, and their mean PAP was (48.48 ± 5.303) ranged from 36.00 to 63.00. The mean BPD was (8.52 ± 0.403 cm) ranged from 8.11 to 9.5 cm, their mean FL was (6.90 ± 0.317 cm) ranged from 6.31 to 7.38 cm, their mean AC was (29.97 ± 1.439 cm) ranged from 27.38 to 32.30 cm, their mean AFI was (12.20 ± 0.728) ranged from 10.97 to 14.50, and their mean estimated fetal weight was (2512 ± 110.09 gm) ranged from 2310 to 2740 gm.

Table (2) Fetal pulmonary doppler assessment during the first visit, Fetal biometry assessment during the second visit of the studied sample

22-26 weeks	Mean & SD	Median	Range	IQR
S/D	6.93 ± 0.290	6.89	6.34, 7.71	6.74, 7.14
PI	2.29 ± 0.225	2.29	1.81, 2.73	2.13, 2.46
RI	0.86 ± 0.087	0.87	0.63, 1.02	0.80, 0.93
PSV	64.67 ± 5.218	64.41	48.63, 77.38	61.64, 68.67
At/Et ratio	0.22 ± 0.072	0.23	0.06, 0.38	0.17, 0.27
PAP	65.52 ± 6.782	65.80	51.92, 79.32	60.49, 70.72
Second visit				
S/D	6.84 ± 0.289	6.82	6.25, 7.59	6.69, 7.05
PI	2.20 ± 0.223	2.19	1.75, 2.62	2.03, 2.37
RI	0.77 ± 0.085	0.78	0.58, 0.96	0.70, 0.84
PSV	66.74 ± 5.188	67.01	50.98, 78.57	63.81, 70.77
At/Et ratio	0.32 ± 0.064	0.32	0.18, 0.48	0.27, 0.36
PAP	48.48 ± 5.303	48.50	36.00, 63.00	44.25, 51.00
Fetal biometry assessment during the second visit				
BPD (cm)	8.82 ± 0.403	8.86	8.11, 9.50	8.47, 9.20
FL (cm)	6.90 ± 0.317	6.97	6.31, 7.38	6.60, 7.20
AC (cm)	29.97 ± 1.439	30.07	27.38, 32.30	28.76, 31.30
AFI	12.20 ± 0.728	12.53	10.97, 14.50	11.56, 12.70
Estimated fetal weight (gm)	2513 ± 110.09	2520	2310, 2740	2110, 2590

The mean S/D, PI, RI, and PAP were statistically significantly higher during the first visit than during the second visit. While the mean PSV and At/Et ratio were statistically significantly lower during the first visit than during the second visit.

Table (3) Comparison of fetal pulmonary doppler assessment during the first and second visits of the studied sample

	22-26 weeks	36 weeks	95% CI	P
S/D	6.93 ± 0.290	6.84 ± 0.289	0.08, 0.09	< 0.001
PI	2.29 ± 0.225	2.20 ± 0.223	0.08, 0.09	< 0.001
RI	0.86 ± 0.087	0.77 ± 0.085	0.08, 0.09	< 0.001
PSV	64.67 ± 5.218	66.74 ± 5.188	-2.22, -1.92	< 0.001
At/Et ratio	0.22 ± 0.072	0.32 ± 0.064	-0.11, -0.09	< 0.001
PAP	65.52 ± 6.782	48.48 ± 5.303	15.53, 18.53	< 0.001

The mean S/D, PI, RI, PSV and At/Et ratio and PAP at the first visit were statistically significantly negatively correlated with gestational age.

Table (4) Correlation between fetal pulmonary doppler assessment at the first visit and fetal gestational age

Gestational age	**Correlation coefficient**	**P**
S/D	-0.661	< 0.001
PI	-0.728	< 0.001
RI	-0.697	< 0.001
PSV	-0.616	< 0.001
At/Et ratio	-0.689	< 0.001
PAP	-0.728	< 0.001

P is significant when < 0.05.

The mean S/D, PI, RI, PSV and At/Et ratio and PAP at the first visit were statistically significantly negatively correlated with fetal weight. S/D, PI, RI, PSV and At/Et ratio and PAP at the first visit were statistically significantly positively correlated with NICU admission.

Table (5) Correlation between fetal pulmonary doppler assessment at the first visit and fetal weight and NICU admission

Fetal weight	Correlation coefficient	P
S/D	-0.548	< 0.001
PI	-0.574	< 0.001
RI	-0.565	< 0.001
PSV	-0.563	< 0.001
At/Et ratio	-0.558	< 0.001
PAP	-0.580	< 0.001
NICU admission	**Correlation coefficient**	**P**
S/D	0.537	< 0.001
PI	0.548	< 0.001
RI	0.538	< 0.001
PSV	0.518	< 0.001
At/Et ratio	0.331	< 0.001
PAP	0.393	< 0.001
P is significant when < 0.05.		

S/D, PI, RI, PSV and At/Et ratio and PAP were statistically significantly predictors of fetal gestational age. S/D, PI, RI, PSV and At/Et ratio and PAP were statistically significantly predictors of fetal weight.

Table (6) Univariate regression analysis for the fetal pulmonary doppler parameters as predictors of fetal gestational age and fetal weight

Gestational age	R2	B	Constant	P
S/D	43.7%	-2.26	39.78	< 0.001
PI	53.0%	-3.21	31.46	< 0.001
RI	48.6%	-7.97	30.98	< 0.001
PSV	38.0%	-0.12	31.7	< 0.001
At/Et ratio	47.5%	-9.49	26.21	< 0.001
PAP	53.0%	-0.11	31.1	< 0.001
Fetal weight	**R2**	**B**	**Constant**	**P**
S/D	30.6%	-209	2162	< 0.001
PI	33.3%	-281	1357	< 0.001
RI	31.9%	-714	1328	< 0.001
PSV	30.7%	-11.65	1467	< 0.001
At/Et ratio	31.4%	-853	902	< 0.001
PAP	34.1%	-9.45	1332	< 0.001
P is significant when < 0.05.				

5. Discussion

In this study, the mean gestational age varied from 23 to 26 weeks (24.12 ± 0.993). In late preterm and early term pregnancies, evaluating the fetal MPA Doppler value improves the prediction of infant RDS. Late preterm newborns are born between 34 and 36+6 weeks of gestation, while term infants are born between 37 and 38 weeks. **[4].**

Prior to 34 weeks, the chances of fetal lung immaturity are quite high, and a FLM test is useless. Fetuses born after 39 weeks are at minimal risk for RDS **[5]**. Before attempting to deliver a baby between 34 and 38+6 weeks of gestation, an obstetrician must screen for FLM due to the likelihood of RDS developing **[6]**.

In the current study, the mean S/D, PI, PSV, RI, and At/Et ratio and PAP at both of the first and second visit were statistically significantly negatively correlated with gestational age, and S/D, PI, RI, PSV and At/Et ratio and PAP were found to be predictors of fetal gestational age. Similar to our results, **Sosa-Olavarria et al. (2019)** study suggest that the estimated FMPAP decreases with advancing GA. In 337 pregnant women, the pressure of the fetal pulmonary artery was measured using Doppler ultrasonography. Their data revealed that the Doppler acceleration time of the fetal main pulmonary artery rises as FMPAP declines. In addition, a strong negative connection was found between FMPAP and gestational age. In conclusion, they found that fetal pulmonary artery pressure falls as gestational age increases [7].

The At/Et ratio of the fetal pulmonary artery rises with gestational age, from 0.14 at 18 weeks to 0.2 at 38 weeks, as found by Azpurua et al. This is attributable in part to a lengthening of the At interval from 24 to 36 ms during the same time period, as well as a gradual reduction in pulmonary vascular resistance and increase in pulmonary blood flow with increasing GA [8].

In their research, Mohamed et al. examined third-trimester fetuses using MPA Doppler indicators to predict FLM. This research demonstrates that the pulmonary vasculature's resistance decreases as the fetus nears term. MPA At/Et was shown to be favorably connected with GA, while S/D ratio, PI, and RI were found to be negatively correlated. Increasing pulmonary artery lumen, vascular flexibility, and ongoing lung angiogenesis may explain for the negative relationship between GA and RI as GA increases [4].

In 288 healthy babies between 22 and 42 weeks of gestation, Guan et al. (2015) found a significant relationship between GA and At, At/Et, PSV, end-diastolic velocity, and mean velocity [9].

Using a non-invasive MFPAP computation may assist in predicting if postnatal detection of infant pulmonary hypertension will occur. The prognosis and prediction of pulmonary hypertension in individuals with congenital diaphragmatic hernia may serve as an example of the utility of the procedure [10].

Sosa-Olavarra and Diaz-Guerrero (has previously observed a gradual lengthening of the acceleration time and, therefore, an increase in the AT/ET ratio as GA progresses [11].

In addition, Schenone et al. had previously shown a favorable link between the AT/ET ratio (PATET) and amniocentesis lung maturity tests [12].

Subhedar and Shaw found that the pulmonary artery pressure is elevated in infants with respiratory distress syndrome and decreases when the condition improves. When the illness progresses into chronic lung disease, the opposite occurs [13].

Granstam et al. showed that acceleration times less than 100 milliseconds suggest a significant likelihood of pulmonary hypertension [14].

In this study, the mean S/D, PI, RI, PSV and At/Et ratio and PAP at the first visit were statistically significantly negatively correlated with fetal weight. Also, our results showed that S/D, RI, PI, PSV and At/Et ratio and PAP were predictors of fetal weight.

Hosseinzadeh et al. observed a significant correlation between pulmonary artery PI and fetal growth limitation in fetuses with feto-placental vascular insufficiency. Due to respiratory distress and the demand for oxygen and CPAP, these newborns were more likely to be admitted to the NICU early. As evaluated by pulmonary artery Doppler velocity, the probability of early hospitalization for newborn respiratory distress in FGR babies with placental insufficiency was considerably greater than in non-FGR infants [15].

Numerous investigations on fatal Doppler evaluation in instances of FGR have been undertaken, including examinations of the umbilical artery, middle cerebral artery, and venous duct (venosus ductus). Hidaka et al. connected ductus venosus Doppler to postnatal outcomes in FGR fetuses with placental insufficiency in newborns with a mean gestational age of 28 weeks and 2 days in a comparable research. Two of the surviving babies were identified with developmental problems. According to their findings, there was a positive correlation between the pH of the umbilical artery and the PI of the venosus ductus. It has been inconsistently reported how long it takes between the first detection of absent end-diastolic velocity in the umbilical artery (UA-AEDV) and birth. Three occurrences were separated by more than twenty days, with the longest stretching thirty-five days [16].

Ghosh and Gudmundsson studied the Doppler ultrasonography of the uterine and umbilical arteries in fetuses with FGR as predictors of perinatal outcome. They detected aberrant uterine artery velocimetry in 33.4% of single pregnancies and abnormal umbilical artery velocimetry in 4.2% of single pregnancies. There was a statistically significant correlation between uterine and umbilical artery Doppler findings and unfavorable pregnancy outcomes [17].

Another research compared the middle cerebral artery color Doppler to the umbilical artery in predicting newborn outcomes in 150 third-trimester FGR pregnancies. The fetal weight was ascertained via ultrasonography. Doppler evaluation was performed on the umbilical and middle cerebral arteries of fetuses diagnosed with FGR prior to birth. 126 moms gave birth to SGA (small-for-gestational-age) babies, while 24 women gave birth to non-SGA babies. The PI of the middle cerebral artery did not vary significantly between the two groups **[18]**.

Our results showed that S/D, PI, RI, PSV and At/Et ratio and PAP at the first visit were statistically significantly positively correlated with NICU admission.

Moety et al. found that fetuses with neonatal RDS had substantially lower At/Et and PSV as well as greater PI and RI than fetuses without RDS. This indicates that babies with RDS have increased pulmonary vascular resistance and pressure, as well as lower pulmonary blood flow, in comparison to infants without RDS. In their investigation, after accounting for GA, the difference between the two groups for At/Et, PI, and RI remained significant. These three parameters may thus be utilized as independent RDS development predictions [19].

In two prior investigations, MPA At/Et was also shown to be considerably reduced in preterm fetuses with RDS, consistent with our findings **[9, 20]**.

Schenone et al. (2014) discovered that MPA At/Et and the TDx- FLM-II (measured in the amniotic fluid) were positively correlated, suggesting that a higher At/Et is linked with a better developed lung and a reduced risk of RDS [12].

Compared to fetuses who did not develop neonatal RDS, fetuses that had RDS had substantially lower At/Et and higher PI, RI and S/D ratios in the research by Mohamed et al. [4].

In contrast, Azpurua et al. discovered an inverse association between At/Et and the amniocentesis-obtained lecithin/sphingomyelin ratio. Their study was unable to explore the relationship between At/Et and the development of clinical RDS since their sample size (29 fetuses) was insufficient and just one infant was diagnosed with RDS [8].

6. Conclusion

Doppler velocimetry has been shown to be beneficial for measuring not just fetal pulmonary maturity, but also the FMPAP, and we hope that future study will reveal that estimates of the MFPAP may be able to predict whether or not the newborn will develop pulmonary hypertension. Therefore, we may use Doppler velocimetry as a reliable noninvasive method for forecasting fetal pulmonary artery pressure.

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