

Doppler Parameters of the Fetal Aortic Isthmus Among Women Attending Women's Health Hospital of Assiut University

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Abstract:

Background: Fetal circulation forms two parallel circuits with two ventricular pumps perfusing one systemic circulation. In this context, the left ventricle supplies the coronary and brachiocephalic circulations, and the right ventricle supplies the subdiaphragmatic circulation and placenta. The aortic isthmus (AoI) is the fetal watershed whose waveform reflects its complex hemodynamic physiology. Many indices exist to quantify the different components of that waveform, including the pulsatility index, resistance index, isthmic flow index, and, recently, the isthmic systolic index.

Aim of Work: To establish Doppler parameters of the fetal aortic isthmus.

Patients and Methods: A cross-sectional study was conducted on 357 females with singleton pregnancy at the Women's Health Hospital, Assiut University, from 2021 to 2023. Patients signed informed consent. A fetal color Doppler was performed, measuring the pulsatility and resistance indexes. Assiut Faculty of Medicine approved the study. **Results:** Our study aims to establish reference ranges for the waveforms of blood flow velocity (FVW) in the fetal aortic isthmus. Our study showed that AoI-PI ranged from 0.87 to 11.14 with a mean of 2.34 ± 1.13 , while the AoI-RI ranged from 0.40 to 8.60 with a mean of 0.93 ± 0.49 . At the gestational age of 28 weeks, the mean gestational age in our study was a reference AoI-PI of 2.76 and a reference AoI-RI of 1.35. A regression analysis for PI and RI correlated to advancing gestation showed a significant increase in PI ($r=0.12$, $p=0.022$) and a significant weak increase in RI ($r=0.11$, $p=0.037$).

Conclusion: Our study showed figures that were mainly consistent with other studies worldwide.

Keywords: Aortic isthmus; Pulsatility index; Resistive index.

Introduction:

Fetal circulation forms two parallel circuits with two ventricular pumps, perfusing only one systemic circulation [1]. In this context, the left ventricle (LV) supplies the coronary and brachiocephalic circulations, and the right ventricle (RV) supplies the subdiaphragmatic circulation and placenta [19, 3, 23]. This parallel arrangement makes it important to have tools to assess LV and RV separately [2, 37]. During normal fetal development, the RV is predominant, and the mean cardiac output is around 13-25% greater than the LV [23]. In a

hemodynamically compromised fetus, as in intrauterine growth restriction (IUGR), it is hypothesized that the RV is affected earlier and to a greater degree than the LV [30, 2]. This RV strain pattern can be established by the earlier dilation, hypertrophy, and dysfunction compared to LV changes [30].

This also means that anatomically, LV and RV share in the AoI flow in opposite directions [19, 3]. LV is responsible for the systolic antegrade flow, whereas the RV is responsible for systolic retrograde flow through the AoI [8]. The direction of systolic AoI blood flow is thus calculated by

comparing LV and RV stroke volumes to downstream vascular impedances [19].

The aortic isthmus (AoI) is the fetal watershed whose waveform reflects its complex hemodynamic physiology. The systolic domain represents left and right ventricular systolic ejection, and the diastolic domain represents the comparative downstream vascular impedance between the brachiocephalic and subdiaphragmatic fetal circulations [11].

Many indices exist to quantify the different components of that waveform, including the pulsatility index, resistance index, isthmus flow index, and, recently, the isthmus systolic index. Promising preliminary studies apply these indices to both cardiac, congenital, and extracardiac pathologies, including intrauterine growth restriction and twin-twin transfusion syndrome [11].

AoI waveforms were examined in many pathologies, including: IUGR, twin-twin transfusion syndrome, fetuses of diabetic mothers, congenital diaphragmatic hernia, ventricular septal defect, coarctation of the aorta, and other congenital heart diseases.

There are no studies on aortic isthmus parameters for the Egyptian population. This study aims to establish Doppler parameters of the fetal aortic isthmus (AoI) in the Egyptian population, represented by women attending the Women's Health Hospital of Assiut University. This will be the first study in the region regarding this subject.

Aim of the Work

This work aims to establish Doppler parameters of the fetal aortic isthmus (AoI) among women attending the Women's Health Hospital of Assiut University.

Patient and Methods

Study Population:

It is a cross-sectional study conducted on 357 females with singleton pregnancies at the Women's Health Hospital at Assiut University from 2021 to 2023. Patients signed informed consent.

IRB No.: 17101140, Assiut Faculty of Medicine approved the study.

All patients will be subjected to the following:

- Fetal color Doppler. The following parameters were measured as mean values of at least three clear consecutive waveforms: pulsatility index and resistance index. One operator took readings. Image-directed pulsed and color Doppler equipment SONACE X8 MEDISSON with a multifrequency sector array transabdominal transducer was used.
- The color Doppler maximum velocity settings were adjusted to high velocities so that the blood flows of the great vessels were homogeneous in color, showing no aliasing. The high-pass filter was set at 50 Hz, and energy output levels were lower than 50 mW/cm². The sample volume size was adapted to the vessel diameter to cover it entirely.
- All recordings used for measurements were performed without fetal movements, and the scanning plane was adjusted to obtain an insonation angle as close to 0° as possible and < 30°. All AoI Doppler measurements were sampled from either the longitudinal aortic arch or the three vessels and trachea (3VT) sonographic planes since both views of this vascular segment have been shown to provide reproducible Doppler parameters.
- Full medical and obstetric history.
- General examination, blood pressure.

Inclusion Criteria:

- 1- Normal singleton fetus.
- 2- Gestational age (18 -36 weeks).
- 3- Gestational age confirmed by sonography in the first trimester, or known date for conception.
- 4- Normal fetal growth (>10th and < 90th centile growth curves) and normal umbilical artery Doppler pattern at the assessment time.

Exclusion Criteria:

- 1- Multiple pregnancy.
- 2- Unsure fetal age.
- 3- Abnormal fetal growth.
- 4- Abnormal umbilical artery Doppler at the time of recruitment.

Statistical Analysis

The data were tabulated and statistically analyzed using SPSS version 26.0, Microsoft Excel 2016, and the MedCalc program software version 19.1.

Results

Table (1): Demographic characteristics of the patients

Parameters		Studied women (No. = 357)	
		No.	%
Age groups	Less than 20 years	11	3.1%
	20 -30 years	257	72.0%
	More than 30 years	89	24.9%
Age (years)	Mean± SD	27.58± 4.83	
	Median	27.0	
	Range	17.0- 42.0	

Table (2): Distribution of obstetric history among the pregnant women.

Parameters		Studied women (No. = 357)	
		No.	%
Parity	primigravida	99	27.7%
	Para 1	83	23.2%
	Para 2	92	25.8%
	≥Para 3	83	23.2%
	Mean± SD	1.55± 1.34	
	Median	1.0	
	Range	0.0- 7.0	
Abortion	No	226	63.3%
	Once	97	27.2%
	Twice	26	7.3%
	≥ 3 times	8	2.2%
	Mean± SD	0.49± 0.75	
	Median	0.0	
	Range	0.0- 4.0	

Table (3): Aortic Isthmus Doppler among pregnant women.

Aortic Isthmus Doppler		Studied women (No. = 357)
AoI-PI	Mean± SD	2.63± 0.39
	Median	2.63
	Range	1.59- 4.24
AoI-RI	Mean± SD	0.86± 0.05
	Median	0.86
	Range	0.75- 0.99
S/D	Mean± SD	8.51± 6.29
	Median	7.1
	Range	3.07- 63.5

Table (4): The gestational-age-related reference ranges for Doppler parameters (PI & RI) in the AoI

		PI			RI			S/D		
		P 5	Mean	P95	P 5	Mean	P95	P 5	Mean	P95
GA	16	2.78	2.78	2.78	0.82	0.82	0.82	5.69	5.69	5.69
	17	3.17	3.17	3.17	0.90	0.90	0.90	10.33	10.33	10.33
	18	2.06	2.66	3.45	0.84	0.87	0.91	6.10	7.92	11.50
	19	1.78	2.89	3.61	0.76	0.84	0.91	4.22	6.67	11.00
	20	2.30	2.68	3.28	0.80	0.86	0.96	4.97	9.03	23.06
	21	2.05	2.77	3.81	0.80	0.87	0.99	4.96	7.23	9.77
	22	2.19	2.79	3.70	0.80	0.87	0.98	5.00	10.97	63.50
	23	2.10	2.55	3.05	0.78	0.86	0.98	4.60	9.31	50.00
	24	2.04	2.59	3.28	0.81	0.87	0.92	5.34	8.21	13.29
	25	2.05	2.64	4.24	0.79	0.87	0.95	3.07	7.87	20.00
	26	2.01	2.56	3.39	0.75	0.86	0.95	3.95	8.22	20.00
	27	1.82	2.54	3.60	0.76	0.85	0.97	4.19	8.21	33.00
	28	2.15	2.57	3.36	0.79	0.87	0.92	4.92	8.59	12.50
	29	2.20	2.71	3.18	0.79	0.87	0.94	4.75	8.84	14.96
	30	2.01	2.66	3.36	0.81	0.88	0.97	5.14	11.62	31.00
	31	2.05	2.61	3.23	0.80	0.85	0.93	5.10	7.49	13.84
	32	1.80	2.45	2.90	0.78	0.86	0.97	4.70	8.89	33.00
	33	2.00	2.51	2.91	0.79	0.85	0.91	4.60	7.00	11.11
	34	2.16	2.62	2.94	0.80	0.86	0.98	4.79	11.50	49.00
	35	2.02	2.59	2.99	0.77	0.84	0.89	4.44	6.48	9.42
	36	2.11	2.57	2.92	0.77	0.83	0.88	4.40	6.07	8.61

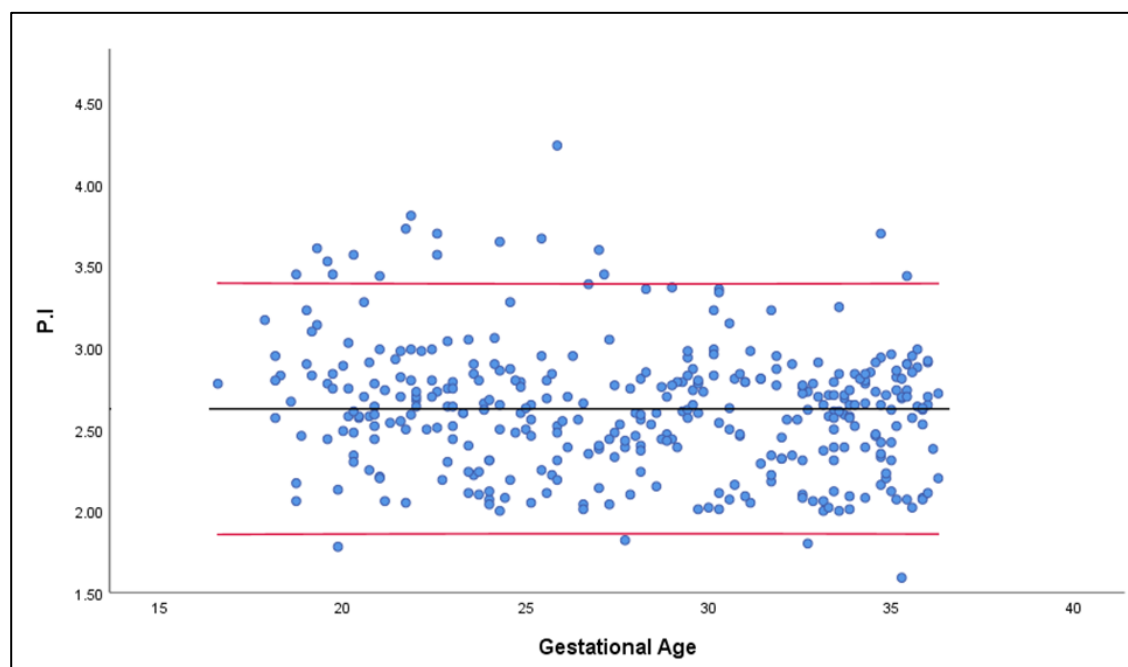


Figure (1): Regression analysis for PI

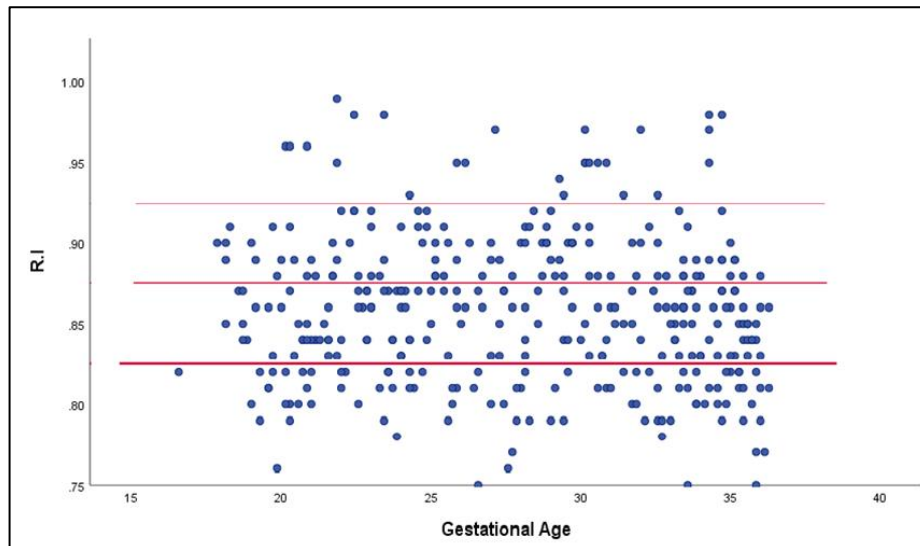


Figure (2): Regression analysis for RI

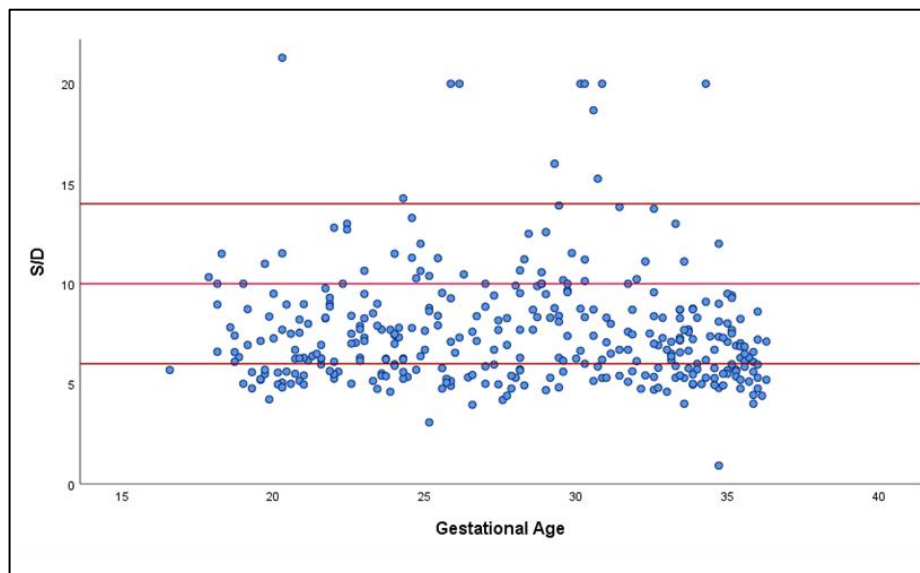


Figure (3): Regression analysis for S/D ratio

Discussion

This study was conducted on 357 females with singleton pregnancies at the Women's Health Hospital at Assiut University from 2021 to 2023.

The age group distribution of the subjects was as follows: A majority of 72.0% were between 20 and 30 years, 24.9% were above 30 years, and the remaining 3.1% were less than 20 years of age. It showed that the age of subjects ranged from 17.0 to 42.0 years, which makes the mean age of the subjects 27.44 ± 4.83 years with a median of 27 years.

Gestational age was assessed by ultrasound and by the date of the last period. Gestational age by ultrasound showed a

mean of 27.97 ± 5.44 weeks, which was very close to that assessed by date, with a mean of 27.99 ± 5.42 weeks.

Regarding fetal biometry, the biparietal diameter had a mean of 6.93 mm. Head circumference had a mean of 25.11 mm. Abdominal circumference had a mean of 23.50 mm. Femur length had a mean of 5.17 mm. The estimated fetal weight had a mean of 1349.17 gm.

Many studies that compared menstrual dating to ultrasound dating in the first two trimesters found ultrasound dating superior. So, a combined approach is advised for accurate results [7].

This was our approach in seeking accuracy in determining gestational age, as

this is a matter of importance given the task at hand: establishing normal parameters of AoI indices in Egyptian fetuses.

Coming to the main aim of the study, aortic isthmus Doppler findings, three indices were assessed, namely the aortic isthmus pulsatility index (AoI-PI), the aortic isthmus resistance index (AoI-RI), and the S/D ratio as a secondary outcome.

AoI-PI ranged from 1.59 to 4.24 with a mean of 2.63 ± 0.39 , the AoI-RI ranged from 0.75 to 0.99 with a mean of 0.86 ± 0.05 , while the S/D ratio ranged from 3.07 to 63.5 with a mean of 8.51 ± 6.29 .

When referring to the reference gestational-age-related Doppler parameters (PI & RI) in the AoI at gestational age 28 weeks, which was the mean gestational age in our study, the reference AoI-PI was 2.76, while the reference AoI-RI was 1.35 [4].

This was consistent with the study by Sachal and colleagues in New Delhi in 2020, which was conducted on 124 normal pregnancies with gestational ages of 27 to 40 weeks and showed a mean PI of 2.1 and a mean RI of 0.87.

A regression analysis for PI and RI with advancing gestation showed a significant increase in PI ($r=0.12$, $p=0.022$) and a significant weak increase in RI ($r=0.11$, $p=0.037$).

Our findings regarding the increasing trend in PI were consistent with the findings by Del Rio and colleagues in 2006, where 458 normal singleton fetuses from 19 to 37 completed weeks' gestation showed a slightly significant increasing trend with gestational age.

This, however, wasn't the case with RI, where the study showed that the RI remained constant during the second half of pregnancy.

In this study, the PI was 2.2562, and the RI was 0.8984, which were close to the figures recorded in our study.

On the other hand, this was inconsistent with the previously mentioned study by Sachal and colleagues in 2020, where a linear regression equation was used, similar to in our study, to find the correlation between Doppler indices and advancing

gestational age, and found no significant change in the PI and RI with the increasing gestational age.

In another cross-sectional study by Thanasuan and colleagues in 2014, 240 Asian singleton pregnant women at 24–38 weeks of gestation were assessed for setting normal values for fetal aortic Doppler indices. PI significantly correlated with gestational age ($P=0.03$), whereas no significant change of RI with advancing gestation was observed. This, again, is partly in agreement with our study regarding the PI but in disagreement regarding the RI.

In this study, PI was 1.74, and RI was 0.87. Although this is within the normal ranges of the 5th and 95th percentiles, it is of lower values than in our study.

Our study's regression analysis for the S/D ratio with advancing gestation also showed a non-significant weak decrease in the S/D ratio ($r=-0.084$, $p=0.111$).

To conclude, our study showed figures that were mainly consistent with other studies worldwide.

Conclusion

The aortic isthmus (AoI) is a fetal watershed whose waveform reflects its hemodynamic physiology complexity [11].

Our study showed that AoI-PI ranged from 0.87 to 11.14 with a mean of 2.34 ± 1.13 , while the AoI-RI ranged from 0.40 to 8.60 with a mean of 0.93 ± 0.49 .

At the gestational age of 28 weeks, the mean gestational age in our study, the reference AoI-PI, was 2.76, while the reference AoI-RI was 1.35 [4].

A regression analysis for PI and RI with advancing gestation showed a significant increase in PI ($r=0.12$, $p=0.022$) and a significant weak increase in RI ($r=0.11$, $p=0.037$).

This was partly in agreement with several studies and reflective of our population.

References:

1. Abdelrazzaq K, Yeniel AÖ, Ergenoglu AM, Yildirim N, Akercan F, Karadadaş N. Fetal aortic isthmus Doppler measurements for prediction of perinatal morbidity and mortality associated with fetal growth restriction. *Acta Obstet Gynecol Scand*. 2013;92(6):656-661.
2. Acharya G, Pavlovic M, Ewing L, Nollmann D, Leshko J, Huhta JC. Comparison between pulsed-wave Doppler- and tissue Doppler-derived Tei indices in fetuses with and without congenital heart disease. *Ultrasound Obstet Gynecol*. 2008;31(4):406-411.
3. Acharya G. Technical aspects of aortic isthmus Doppler velocimetry in human fetuses. *Ultrasound Obstet Gynecol*. 2009;33(6):628-633.
4. Ayoola OO, Bulus P, Loto OM, Idowu BM. Normogram of umbilical artery Doppler indices in singleton pregnancies in south-western Nigerian women. *J Obstet Gynaecol Res*. 2016;42(12):1694-1698.
5. Baschat AA, Gembruch U, Harman CR. The sequence of changes in Doppler and biophysical parameters as severe fetal growth restriction worsens. *Ultrasound Obstet Gynecol*. 2001;18(6):571-577.
6. Bonnin P, Fouron JC, Teyssier G, Sonesson SE, Skoll A. Quantitative assessment of circulatory changes in the fetal aortic isthmus during progressive increase of resistance to umbilical blood flow. *Circulation*. 1993;88(1):216-222.
7. Butt K, Lim KI. Guideline no. 388-determination of gestational age by ultrasound. *J Obstet Gynaecol Can*. 2019;41(10):1497-1507.
8. Chabaneix J, Fouron JC, Sosa-Olavarria A, Gendron R, Dahdah N, Berger A, et al. Profiling left and right ventricular proportional output during fetal life with a novel systolic index in the aortic isthmus. *Ultrasound Obstet Gynecol*. 2014;44(2):176-181.
9. Del Rio M, Martinez JM, Figueras F, Bannasar M, Olivella A, Palacio M, et al. Doppler assessment of the aortic isthmus and perinatal outcome in preterm fetuses with severe intrauterine growth restriction. *Ultrasound Obstet Gynecol*. 2008;31(1):41-47.
10. Del Rio M, Martinez JM, Figueras F, Lopez M, Palacio M, Gómez O, et al. Reference ranges for Doppler parameters of the fetal aortic isthmus during the second half of pregnancy. *Ultrasound Obstet Gynecol*. 2006;28(1):71-76.
11. Tynan D, Alphonse J, Henry A, Welsh AW. The aortic isthmus: a significant yet underexplored watershed of the fetal circulation. *Fetal Diagn Ther*. 2016;40(2):81-93.
12. Ferraz MM, Araújo FD, Carvalho PR, Sá RA. Aortic isthmus Doppler velocimetry in fetuses with intrauterine growth restriction: a literature review. *Rev Bras Ginecol Obstet*. 2020;42(5):289-296.
13. Figueras F, Benavides A, Del Rio M, Crispi F, Eixarch E, Martinez JM, et al. Monitoring of fetuses with intrauterine growth restriction: longitudinal changes in ductus venosus and aortic isthmus flow. *Ultrasound Obstet Gynecol*. 2009;33(1):39-43.
14. Figueras F, Gratacós E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. *Fetal Diagn Ther*. 2014;36(2):86-98.
15. Fouron JC, Gosselin J, Amiel-Tison C, Infante-Rivard C, Fouron C, Skoll A, et al. Correlation between prenatal velocity waveforms in the aortic isthmus and neurodevelopmental outcome between the ages of 2 and 4 years. *Am J Obstet Gynecol*. 2001;184(4):630-636.
16. Fouron JC, Gosselin J, Raboisson MJ, Lamoureux J, Tison CA, Fouron C, et al. The relationship between an aortic isthmus blood flow velocity index and the postnatal neurodevelopmental status of fetuses with placental circulatory insufficiency. *Am J Obstet Gynecol*. 2005;192(2):497-503.
17. Fouron JC, Siles A, Montanari L, Morin L, Ville Y, Mivelaz Y, et al. Feasibility and reliability of Doppler flow recordings in the fetal aortic isthmus: a multicenter evaluation. *Ultrasound Obstet Gynecol*. 2009;33(6):690-693.
18. Fouron JC, Zarelli M, Drblik SP, Lessard M. Flow velocity profile of the fetal aortic isthmus through normal gestation. *Am J Cardiol*. 1994;74(5):483-486.

19. Fouron JC. The unrecognized physiological and clinical significance of the fetal aortic isthmus. *Ultrasound Obstet Gynecol.* 2003;22(5):441-447.
20. Gámez F, Rodríguez MJ, Tenías JM, García J, Pintado P, Martín R, et al. Reference ranges for the pulsatility index of the fetal aortic isthmus in singleton and twin pregnancies. *J Ultrasound Med.* 2015;34(4):577-584.
21. Hecher K, Snijders R, Campbell S, Nicolaides K. Fetal venous, arterial, and intracardiac blood flows in red blood cell isoimmunization. *Obstet Gynecol.* 1995;85(1):122-128.
22. Kennelly MM, Farah N, Hogan J, Reilly A, Turner MJ, Stuart B. Longitudinal study of aortic isthmus Doppler in appropriately grown and small-for-gestational-age fetuses with normal and abnormal umbilical artery Doppler. *Ultrasound Obstet Gynecol.* 2012;39(4):414-420.
23. Kiserud T. Physiology of the fetal circulation. *Semin Fetal Neonatal Med.* 2005;10(6):493-503.
24. Mäkilallio K, Vuolteenaho O, Jouppila P, Räsänen J. Ultrasonographic and biochemical markers of human fetal cardiac dysfunction in placental insufficiency. *Circulation.* 2002;105(17):2058-2063.
25. National Center for Health Statistics (US). *Health, United States, 2020-2021.* Hyattsville, MD: National Center for Health Statistics; 2021.
26. Rizzo G, Capponi A, Vendola M, Pietrolucci ME, Arduini D. Relationship between aortic isthmus and ductus venosus velocity waveforms in severe growth restricted fetuses. *Prenat Diagn.* 2008;28(11):1042-1047.
27. Rizzo G, Capponi A, Vendola M, Pietrolucci ME, Arduini D. Use of the 3-vessel view to record Doppler velocity waveforms from the aortic isthmus in normally grown and growth-restricted fetuses: comparison with the long aortic arch view. *J Ultrasound Med.* 2008;27(11):1617-1622.
28. Rosen RD, Bordoni B. Embryology, aortic arch. In: *StatPearls.* Treasure Island, FL: StatPearls Publishing; 2020.
29. Ruskamp J, Fouron JC, Gosselin J, Raboisson MJ, Infante-Rivard C, Proulx F. Reference values for an index of fetal aortic isthmus blood flow during the second half of pregnancy. *Ultrasound Obstet Gynecol.* 2003;21(5):441-444.
30. Rychik J. Fetal cardiovascular physiology. *Pediatr Cardiol.* 2004;25(3):201-209.
31. Sharma S, Tiwari A, Ganeshan PK, Malhotra P. Determination of gestational age specific aortic isthmus indices for use as reference in third trimester Doppler study. *Int J Radiol Diagn Imaging.* 2020;3(3):05-08.
32. Short E. Normal development of the aortic isthmus. *J Anat.* 1968;102(Pt 3):553-557.
33. Tantuwai B, Das V, Mala YM. Correlation of Doppler assessment of fetal aortic isthmus with perinatal outcome in intrauterine growth restriction. *Int J Reprod Contracept Obstet Gynecol.* 2018;7(9):3780-3785.
34. Thanasuan S, Phithakwatchara N, Nawapan K. Reference values for fetal aortic isthmus blood flow parameters at 24 to 38 weeks' gestation. *Prenat Diagn.* 2014;34(3):241-245.
35. Tynan D, Alphonse J, Henry A, Welsh AW. The aortic isthmus: a significant yet underexplored watershed of the fetal circulation. *Fetal Diagn Ther.* 2016;40(2):81-93.
36. Unterscheider J, Daly S, Geary MP, Kennelly MM, McAuliffe FM, O'Donoghue K, et al. Predictable progressive Doppler deterioration in IUGR: does it really exist? *Am J Obstet Gynecol.* 2013;209(6):539.e1-539.e7.
37. Welsh AW, Meriki N, Henry A. The 'Delta-MPI': a new measure for unilateral fetal myocardial strain and its normal gestational range (abstract OP27.04). *Ultrasound Obstet Gynecol.* 2012;40(Suppl 1):136