

ORIGINAL RESEARCH

Aortic isthmus doppler assessment in fetuses with intrauterine growth restriction

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ABSTRACT

Objective: To assess the color Doppler flow velocity pattern of Aortic isthmus in fetuses with intra uterine growth restriction. To found the association of Aortic isthmus Doppler flow parameters and intra uterine growth restriction. **Introduction:** Fetal medicine has very crucial role in management of Intra-uterine growth restriction (IUGR), which is an important perinatal problem of morbidity and mortality of fetus. Fetal medicine helps to establish early diagnosis and timely intervention in undergoing to develop IUGR and already developed IUGR. Doppler imaging is very important tool to obtain this information and very effective than any other conventional tests. The Doppler has ability to guide management decisions regarding the appropriate timing of delivery. Doppler imaging of Aortic isthmus (AoI) has proposed potential monitoring tool for IUGR fetus. The AoI is an arterial connection between the two fetal vascular outputs positioned in parallel and acts as a link between the right and left ventricles. So, any condition affecting fetal hemodynamic involving ventricular outflow or peripheral vascular impedance will affect the flow pattern through AoI. **Material and methods:** This descriptive comparative study was performed on fetuses with suspected IUGR over a period of 24 months. 50 pregnant females of 24-40 weeks gestation who presented to OPD met the inclusion criteria. The fetuses, those are small for gestational age and had associated maternal pathologies/risk factors, abnormal umbilical artery Doppler waveforms and oligohydramnios were considered as cases. The parameters of cases compared with 50 controls, selected randomly from the referred healthy pregnant females. The role of Aortic isthmus Doppler indices (PI, RI, PSV, EDV) and of a semi-quantitative indicator (Isthmic Flow Index, IFI) was assessed in predicting IUGR by using sensitivity, specificity and predictive values. P-value of <0.05 was considered to be significant. **Results:** 29 out of 50 fetuses had IFI value < 1 suggesting reversed isthmus diastolic blood flow and 21 out of 50 had forward flow with IFI > 1. Mean RI and PI value in cases were 1.1354(+/- 0.23) and 7.5392(+/- 8.80), respectively which was significantly higher as compared to mean RI of 0.8086(+/- 0.099) (P-value <0.0001) and mean PI value of 2.6154(+/- 1.064) (P-value = 0.0002) in control cohort. Aortic isthmus PI value above 95th centile was found in 33/50 (66%) of cases. 7/50 (14%) cases had retrograde AoI flow while the umbilical artery Doppler indices were normal. **Conclusion:** PI and RI values of aortic isthmus in the IUGR fetuses were found to be significantly higher as compared to those in controls. The study parameters and analyzed outcome suggests association of reversed diastolic flow through AoI with IUGR.

Keywords: Aortic isthmus (AoI), intrauterine growth restriction (IUGR), Doppler indices

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INTRODUCTION

In the developing world, intra-uterine growth restriction (IUGR) is potential causes to increased morbidity and mortality of fetuses in perinatal period. Fetal medicine and Doppler ultrasound provides information to take management decisions for appropriate timing of delivery. Knowledge of the fetal circulation and the compensatory changes during fetal hypoxia has helped us to recognize the early signs of IUGR and improving the prognosis of high risk pregnancies [1].

Doppler Ultrasound is goldstandard [1] in the

management of the growth-restricted fetus. Pulsed-wave Doppler can be utilized to evaluate the direction and pulsatile nature of blood flow within vessels.

Aortic isthmus (AoI) Doppler evaluation has been proposed as a potential monitoring tool for IUGR. It is located between the origin of the left subclavian artery and the aortic end of the ductus arteriosus, and acts as a link between the right and left ventricles, So, any condition affecting fetal hemodynamics involving ventricular outflow or peripheral vascular impedance will affect the flow pattern through aortic isthmus [3,4,8-10].

The AoI Doppler of normal fetus showed forward flow throughout the cardiac cycle and diastolic deceleration phase was gradual and smooth. After 20 weeks, an incisura appeared at end-systole that progressively increased. A brief reversal of diastolic flow was recorded after 30 weeks of gestation. In conclusion, the morphology of the Doppler flow velocity waveform of the fetal aortic isthmus changes with gestation^[94].

The aortic isthmus flow profiles can provide information about fetal cardiovascular status and predict outcome in intrauterine growth restriction^[6]. Also, an increase in resistance to placental blood flow causes changes in aortic isthmus diastolic flow profile before any significant modification is observed in umbilical artery Doppler waveforms^[4]. Aortic isthmus Doppler thus may help in early diagnosis and improving the management of sick fetuses.

MATERIAL AND METHODS

The department of Radio diagnosis, GMCH, over a period of 18 months and included 50 pregnant females of 24-40 weeks gestation having clinical signs of IUGR with inclusion criteria and were followed up for their birth weight. The findings were compared with 50 fetuses which were matched with respect to gestational age and had no known maternal risk factors, normal biometry and normal umbilical artery waveforms. P-value of <0.05 was considered to be significant with type I error of 5%.

This is descriptive comparative study designed at tertiary health care institute with inclusion criteria/selection of cases based on combination of clinical and sonographic parameters (preeclampsia/previous IUGR/BOH, oligohydramnios,

fetal weight <10th percentile for the gestational age and increased umbilical artery PI>95th centile for the gestational age).

The control group was including 50 healthy cases without any risk factors. The exclusion parameters for study are twin / multiple gestations and IUFD.

The ultrasound and Doppler parameter were obtained after detailed clinical evaluation using 3-5 Mhz array transducer in both groups.

The fetal biometry included Biparietal diameter (BPD), Femur length (FL) and Abdominal circumference (AC) were calculated and compared with reference values for estimation of gestational age and fetal weight.

Fetal aortic isthmus was assessed in longitudinal aortic arch view and the ultrasound gate was placed just beyond the origin of left subclavian artery. The following parameter were assessed in each cases and control

- Peak systolic velocity (PSV)
- End diastolic velocity (EDV)
- Systolic-to-diastolic (S/D) ratio = PSV/EDV
- Resistive index (RI) = (PSV – EDV) / EDV
- Pulsatility index (PI) = (PSV – EDV)/ Mean velocity
- Isthmic flow index = (PSV + EDV)/ PSV

Statistical analysis was performed using SPSS 19.0. Doppler parameters including velocities and impedance indices were assessed against normal reference ranges using both 95th and 5th centile as cut-off for abnormal values. The predictive value of the Aortic isthmus Doppler parameters in assessing IUGR was estimated by using sensitivity, specificity and predictive values.

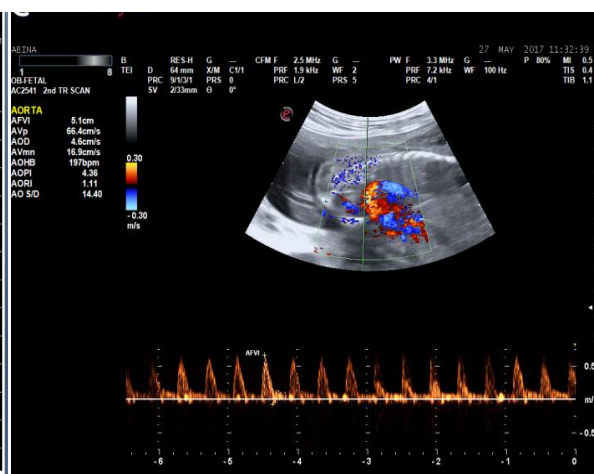
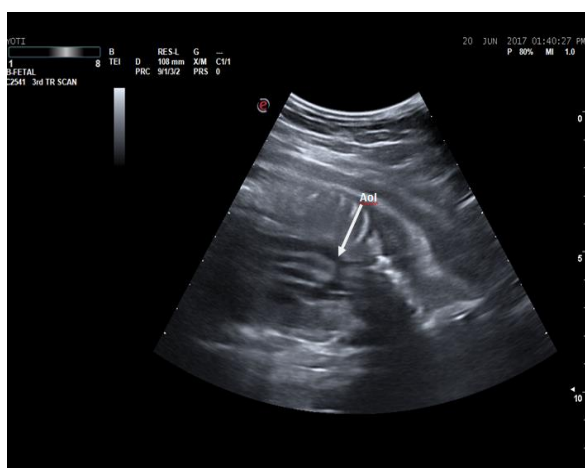


Fig.1: Ultrasound image showing the longitudinal view of aortic arch with the asterisk indicating the position of Aortic isthmus just distal to the origin of left subclavian artery.

Fig.2: Ultrasound image showing the normal pulsed Doppler waveforms of Aortic Isthmus with antegrade diastolic flow.

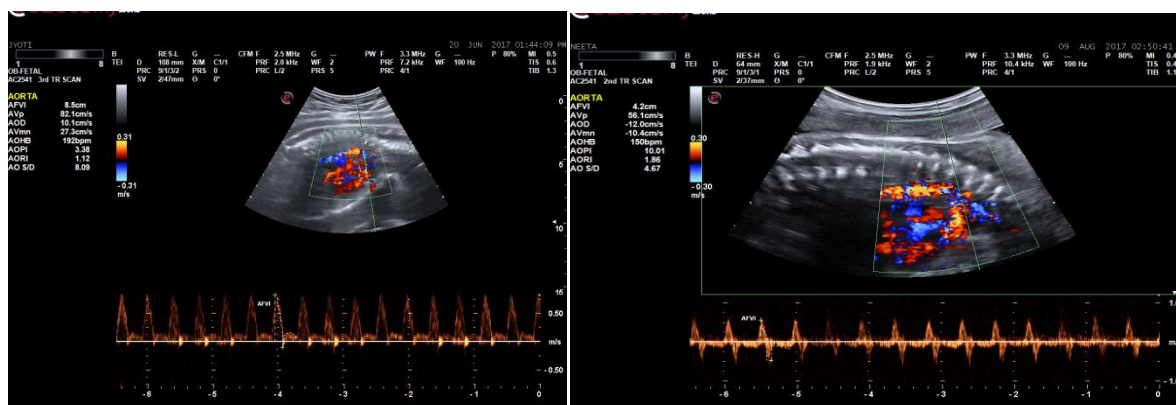


Fig.3: Normal pulse Doppler waveforms of AoI with a small end-systolic reversal however diastolic flow was forward.

Fig.4: Ultrasound image of Aortic isthmus in Longitudinal arch view showing retrograde pulsed Doppler flow

RESULT

The current study does not found any statistical difference in maternal age and gestational age between cases and controls at the time of diagnosis. Highest incidence of risk factor was found in 26-30 years of age group (52%). Most common risk factor was Preeclampsia found in 27 cases, out of which 14 cases were of 26-30 years age group. 17 out of 29 fetuses with IFI<1 were found in the maternal age group of 26-30 years.

Table No. 01: Distribution of clinical and Ultrasound findings in cases as per Maternal Age

IFI<1	Oligohydramnios	BOH	Preeclampsia n (%)	Previous IUGR n (%)	Maternal Age(years)
5 (10%)	9 (18%)	0	4 (8%)	0	20-25
17 (34%)	21 (42%)	3 (6%)	14 (28%)	5 (10%)	26-30
7 (14%)	10 (20%)	1 (2%)	8 (16%)	4 (8%)	31-35
0	1(2%)	0	1(2%)	0	>=36
29	41	4	27	9	Total

Table No.02: Demographic and obstetric data in cases with respect to antegrade and retrograde flow in AoI:

Retrograde(IFI<1) (n=29)	Antegrade(IFI>1) (n=21)	Risk factors
28 (20-33)	28 (22- 36)	Maternal Age(years, Median(range))
17 (58.62 %)	10 (47.62 %)	Preeclampsia (n %)
29 (26-34)	30 (26-35)	GA at Diagnosis (weeks,median (range))
27 (93.1%)	14 (66.6%)	Oligohydramnios
21 (72.41%)	10 (47.62%)	Abnormal Umbilical artery PI>95 th centile for GA
13 (44.83%)	4 (19.05%)	AREDV in UA

The 29/50 (58%) fetuses had reversed isthmic diastolic blood flow (IFI <1) and 21/50(42%) had forward flow (IFI > 1) . The all fetuses with reversed isthmic diastolic flow had IFI type- III while rest of the cases and the control cohort had IFI type I. Oligohydramnios was found in 41/50(82%) of cases and 7/50(14%) of controls. It was found significantly more in cases with reverse isthmic diastolic flow (27/29, 93.1%) as compared to cases with forward isthmic diastolic flow (14/21, 66.6%).

Table No. 05: Distribution of AoI Doppler indices in cases and controls:

P- value	Control	Cases	Doppler Indices
P >0.05	78.91 +/- 16.65	79.252 +/- 22.97	PSV
P < 0.0001	0.8086+/- 0.099	1.1354 +/- 0.23	RI
P = 0.0002	2.6154 +/- 1.064	7.5392 +/- 8.80	PI
P < 0.0001	14.872 +/- 9.22	-2.396 +/- 10.36	EDV

Mean values of AoI Doppler indices including PSV, EDV, RI and PI of the cases compared with control. Mean value of PSV and EDV in cases was 79.252(+/-22.97,P>0.05) and -2.396(+/-10.36,P<0.0001) respectively, and in controls was 78.919(+/-16.65) mean PSV and 14.872(+/-9.22) mean EDV; EDV of the cases was found to be significantly lower (P<0.0001) than that of control cohort. Also, Mean RI value in case cohort was 1.1354(+/-

0.23) as compared to 0.8086(+/- 0.099) in control cohort (P-value <0.0001) and PI values was 7.5392(+/- 8.80) in cases and 2.6154(+/- 1.064) in controls (P-value = 0.0002) signifying that Mean RI and PI were significantly higher in case cohort as compared to control cohort .

Table No. 06: Distribution of AoI Doppler indices in cases with antegrade and retrograde flow:

P- value	Retrograde (n= 29)	Antegrade (n = 21)	Doppler Indices
P >0.05	81.98 +/- 22.55	75.4 +/- 23.559	PSV
P = 0.0004	1.2286 +/- 0.24	1.0066 +/- 0.143	RI
P = 0.0055	10.43 +/- 10.69	3.547 +/- 1.07	PI
P < 0.0001	-9.806 +/- 5.86	7.838 +/- 5.02	EDV

The fetuses with retrograde flow in aortic isthmus had significant higher values of PI and RI as compared to fetuses with antegrade flow (p value <0.05).13/29 (42.83%) cases with reversed isthmic diastolic flow had associated AREDV in the umbilical artery. 7/50 (14%) cases had retrograde AoI flow while the umbilical artery Doppler indices were normal.

Table No. 07: Predictive value of Aortic isthmus Doppler indices in IUGR fetuses:

S.No	Predictive value		Specificity d/d+b	Sensitivity a/a+c	No. of findings				Doppler characteristics
	Negative	Positive			FN (c)	TN (d)	FP (b)	TP (a)	
1	61.9%	79.31%	68.42%	74.19%	8	13	6	23	Retrograde AoI flow (IFI<1)
2	70.58%	78.78%	63.15%	83.87%	5	12	7	26	AoI PI>95 th centile for GA
TP=True positive, TN=True negative, FP=False positive, FN=False negative									

The all fetuses were followed up till birth, and 31 /50 (62%) cases suspected to have IUGR were found to have birth weight less than 2SD below the mean reference values. P-value of <0.05 was considered to be significant.

Retrograde flow through aortic isthmus was found to be 74.19% sensitive and 68.42% specific with PPV of 79.31% and NPV of 61.9%.

Abnormal PI values (PI > 95th centile for gestational age) in aortic isthmus was found to be 83.87% sensitive and 63.15% specific in predicting IUGR with PPV of 78.78% and NPV of 70.58%.

Chi square test show significant association (P-value = 0.003042) of retrograde flow through Aortic isthmus with intrauterine growth restriction.

DISCUSSION

The Various previous studies [1-17,20-22] have described a strong association of retrograde flow through aortic isthmus with the IUGR, our study too confirms this observation. There were some cases that had reverse isthmic diastolic blood flow although the umbilical artery diastolic flow was forward; implying that Doppler study of flow velocity patterns of aortic isthmus can detect changes prior to those occurring in UA in IUGR.

Among the case cohort, 29 fetuses were classified as having AoI IFI Type III, which according to the definition described earlier, corresponds to retrograde flow through aortic isthmus. On the other hand, all fetuses in the control cohort had antegrade isthmic flow corresponding to IFI type 1. Also, PI and RI values of aortic isthmus and umbilical artery in case cohort were found to be significantly higher as compared to control cohort.

On comparing the Doppler indices of aortic isthmus and umbilical artery, it was found that the Umbilical

artery PI values were higher in fetuses with retrograde aortic isthmic blood flow than in those with antegrade flow. Also, 13/18(42.83%) fetuses with absent/reversed EDV in UA had retrograde AoI flow, suggesting that during severe placental insufficiency, compensatory mechanisms starts and there occurs redistribution of blood flow to more vital organs like brain and heart leading to reversal of blood flow through aortic isthmus.

AoI PI values were also found to be significantly higher in cases with IUGR regardless of the severity, suggesting that during placental insufficiency early adaptive changes can be reflected by it before hemodynamic decompensation begins.

Many studies have explored the role of AoI Doppler in IUGR fetuses and have found significant correlation, our study also agrees to their observations. But, some studies found no significant difference in the incidence of adverse perinatal outcome and flow velocity profile of aortic isthmus, yet they studied a small IUGR cohort so the findings need to be assessed further.

Experimental^[7] studies in chronic hypoxic models have shown that in cases with placental insufficiency, retrograde flow in AoI can occur prior to appearance of abnormality in UA Doppler indices, while some studies^[22] have reported consistent association of retrograde blood flow in aortic isthmus with the absent/reversed EDV in the UA. Our study had some cases with retrograde isthmic diastolic blood flow who were having normal umbilical artery Doppler indices.

The observation in our study can be explained by acknowledging the role of AoI in fetal circulation. During fetal life, brain and upper half of body are supplied by left ventricular output whereas the lower half and placenta are perfused by blood from right

ventricle reaching via ductus arteriosus. The AoI acts like a junction between the two vascular systems and so the characteristics of flow in it indicates the balance between their net impedances. Accordingly, in conditions of progressive placental insufficiency, the blood flow redistribution can be demonstrated earlier in AoI. Sonesson SE et al.^[18] studied 100 fetuses with abnormal UA- PI and found that absent/reversed EDV was more frequently seen in AoI than in UA. Rizzo et al.^[18] and Del Rio M et al.^[3] studied characteristics of AoI and Ductus venosus Doppler in IUGR fetuses and showed that abnormal velocity waveforms appear earlier in AoI than in DV. Del Rio et al.^[3] found no significant correlation of MCA Doppler indices and perinatal outcome.

As described by previous studies^[5-9] during placental insufficiency adaptive vascular changes occurs which cause increase in placental vascular resistance together with vasodilatation in cerebral vasculature, leading to increase flow of oxygenated blood to brain and heart and decrease in antegrade diastolic flow in AoI. As the placental insufficiency worsens, the isthmus diastolic flow further decreases and may disappear or in very severe conditions may become retrograde. Moreover, as the blood flow through AoI is decreasing during diastole, it is likely to reflect the increase in value of Doppler impedance indices in AoI. In our study it was observed that AoI PI value was significantly high in the cases with IUGR regardless of severity. Whether AoI PI can also help in the early detection of fetuses with placental insufficiency needs to be further investigated.

CONCLUSION

This study was design to assess the role of aortic isthmus Doppler in IUGR on the basis of IFI and PI indices.

- Preeclampsia concluded as most common risk factor of IUGR (53.2%).
- The isthmus flow index value <1 is suggested for retrograde blood flow through aortic isthmus (58% cases). The retrograde isthmus flow has significant associated with IUGR (p =0.003) and is a good predictor with sensitivity of 73.19% and specificity of 68.42%.
- AoI PI value > 95th centile was found in 66% cases as compared to 24% controls and reflecting potential role of abnormal AoI PI values in predicting IUGR.
- Approximately 14% cases with retrograde flow through AoI had normal flow velocity profile in umbilical artery that indicate Doppler indices of AoI can detect hemodynamic changes of IUGR earlier to umbilical artery Doppler waveforms changes .

The study data concluded a potential role of AoI Doppler parameters in diagnosing and management of intrauterine growth restriction early in its course and use as voluble tool to prevent perinatal injury. However, the large data needs for analysis using

longitudinal studies and randomized management trials to verify delivery timing based on the Doppler findings can affect outcome of IUGR fetuses.

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