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Determination of gestational age specific aortic isthmus indices for use as reference in third trimester doppler study

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Abstract
Background: Doppler study of umbilical artery, middle cerebral artery, uterine arteries and ductus venosus which is done routinely has its own limitations. The emergence of aortic isthmus index as an ideal parameter that provide an early detection of hemodynamic disturbance inside the fetus in the late pregnancy due to its position as a shunt between right and left ventricle, has inspired the study.
Aims and Objectives: To determine the gestational age specific changes in fetal aortic isthmus flow indices in third trimester gestation and to compare the changes with varying time period of third trimester of gestation.
Materials and Methods: A total of 124 normal pregnancies with gestational age of 27 to 40 weeks by LMP were included in the study. Study was done during July, 2018 to March, 2019 in BLK super speciality hospital, Pusa Road, New Delhi. Aortic isthmus doppler flow indices namely PSV, EDV, RI, PI, S/D, MD and TAMAX were automatically calculated in GE volusonE8 machine and GE P6 machine with 2-5 MHz sectoral array and compared by their LMP derived gestational ages. The correlations of doppler indices with gestational age was determined by linear regression equation.
Results: It was observed that PSV and TAMAX increases with gestational age with correlation coefficient r=0.436 and 0.414 respectively and p value <.005. MD and ED also show a positive increasing trend with gestational age.
Conclusions: This study provides normative values of PSV, EDV, PI and TAMAX with gestational age in third trimester of gestation. Studies are needed for prognostic value of these indices.

Keywords: aortic isthmus, hemodynamics, ductus arteriosus, fetus

1. Introduction
Doppler investigation of the fetus and placenta has evolved in the past years due to technological advances and better understanding of the pathophysiology involved in several fetal conditions. The assessment of fetal arteries gives information on perfusion of vital organs and regional blood flow. Uterine Doppler evaluation predicts most instances of early onset pre eclampsia and intrauterine growth restriction, but no evidence in favour of prophylactic strategies. Umbilical arteries only gives information on placental blood flow not reflecting the adaptation to hypoxia and consequences of the adaptation. The value of cerebral Doppler to predict adverse outcome in the small for gestatonal age (SGA) fetuses is limited with low sensitivities [1].
Abnormal ductus venosus flow develop 1 week prior to delivery in 40 – 80% of cases. This represents fetal cardiovascular decompensation and acidemia which may lead to adverse perinatal outcome [2].
Aortic isthmus doppler is also a sensitive parameter for evaluation of fetus with growth and cardiac abnormalities. Studies have shown an increment in specificity and positive predictive value of aortic isthmus doppler parameter when evaluating for an adverse perinatal outcome [3]. The aortic isthmus has been defined as a fetal watershed between the origin of left subclavian artery from the aortic arch and aortic end of ductus arteriosus, with a waveform representing the complex hemodynamic physiology associated with it. The systolic fraction consists of left and right ventricular output, and the diastolic consists of near downstream vascular impedance between the brachiocephalic and sub diaphragmatic fetal flows [4].

It's waveform changes slightly throughout gestation. In order to quantify the various waveform components several indices such as as the Isthmic flow index, resistance index, pulsatility index as well as the Isthmic systolic index have been targeted.

The AoI blood flow has been found to be abnormal approximately 1 week prior to abnormal ductus venosus flow, further studies regarding aortic isthmus indices are required to incorporating this index into clinical practice so as to avoid unnecessary preterm deliveries [5].

The normal ranges of the Doppler indices are essential for assessing their effectiveness. Various studies have reported different sonographic parameters thus undermining the accuracy of these indices when applied to different populations [6].

2. Aims and objectives

1. To evaluate the changes in the fetal Aortic Isthmus flow indices (AoI) in third trimester gestation.
2. To compare the age specific changes in the fetal Aortic Isthmus flow indices during the various time period of third trimester gestation.
3. To determine the association of the various Aortic Isthmus flow indices to the fetal hemodynamics during the third trimester gestation.

3. Materials and methods

The study subject consisted of 124 pregnant women reporting to the Department of Radio -diagnosis with normal single fetus from 27-40 weeks of gestation undergoing the routine third trimester scan during the study period of July, 2018 to March, 2019. Written permission from the study subjects considered for the study was taken with informed consent. The study was approved by the institutional ethical committee of BLK super speciality hospital, New Delhi. Absence of any structural malformation was confirmed by postnatal clinical examination and outcome. The research protocol was approved by the local ethics committee of BLK super speciality hospital.

Sampling technique: The sample for the study consisted of 124 pregnant women with normal single fetus from 27-40 weeks of gestation. The study subject comprised of those study subjects who visited the Department of Radio diagnosis of the BLK super speciality hospital and the scans were performed using Image-directed pulsed and Doppler equipment (GE Voluson E8 and GE P6 machine) having a multi frequency sector array 3-5 MHz trans abdominal transducer. The setting of the Doppler velocity was adjusted to high velocities in order to obtain a homogeneous colour of the blood flows of the great vessels, showing no aliasing. Before defining the reference ranges for aortic isthmus index interobserver reliability was measured by two independent observers, not aware of the observation of the other.

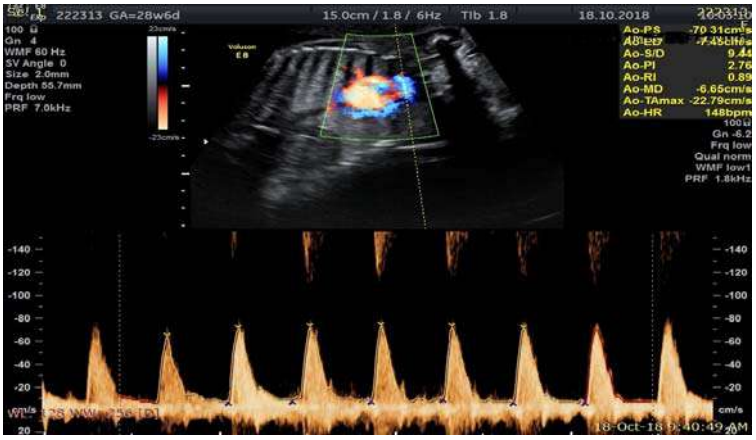

Fig 1: Figure representing the Doppler flow velocity waveforms of the aortic isthmus during 28th week of gestation.

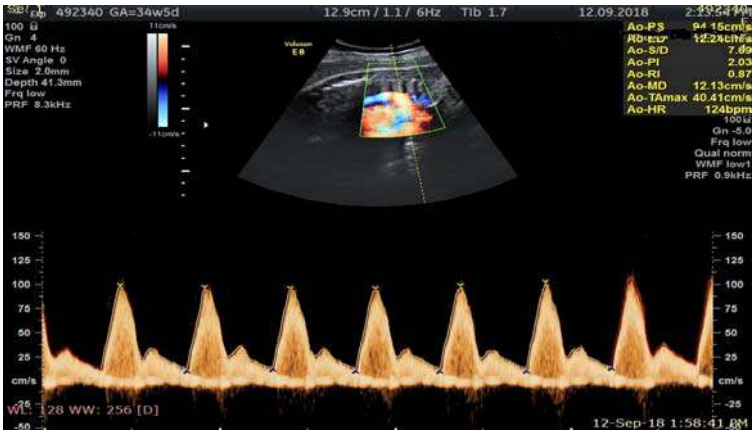

Fig 2: Figure representing the longitudinal view of the aortic isthmus along with the corresponding waveform of the fetus during 34th week of gestation.

4. Results

Out of total 124 subjects, the number of study subjects were variable with respect to their gestational age (table 1)

It was observed that there is an increasing trend in the Doppler indices Peak systolic velocity(PSV), End diastolic velocity(ED), Mean diastolic velocity(MD) and Time averaged maximum velocity(TAMAX) with the increase in the gestational age of the fetus and showed a significant linear correlation with increase in gestational age, whereas as the other doppler indices- Resistivity index(RI), Systole /Diastole ratio(S/D), Pulsatility Index (PI) do not show any trend with the gestational age. (Table 2).

The linear regression analysis of the Tamax, ED, PS, MD with gestational age deduced and the linear equation of the doppler indices with relation to gestational age can therefore be written as:

Tamax= -3.68+1.065(GA), ED= 0.515+0.289(GA), PSV= -4.916+2.60(GA), MD= 1.442+0.226(GA) (figure 3)

Table 1: Distribution of fetuses with respect to their gestational age (N=124)

Gestational age in weeks N=124	No. of patients (%)
27-29weeks	10(8)
29-31 weeks	22(17.6)
31-33 weeks	22(17.6)
33-35 weeks	19(15.2)
35-37 weeks	31(24.9)
37-39 weeks	18(14.4)
39-41weeks	2(1.6)

Table 2: Gestational age wise mean value of the various Doppler indices

	27	28	29	30	31	32	33	34	35	36	37	38	39	40
PI	2.1	2.1	2.2	2.2	2.2	2.3	2.4	2.3	2.2	2.4	2.4	2.1	2.3	2.3
RI	0.87	0.87	0.86	0.88	0.87	0.86	0.87	0.87	0.86	0.88	0.88	0.86	0.83	0.88
PSV	62.5	62.9	70	70.1	70.6	72.8	84.4	82.9	85	85.6	94.5	95.9	72.7	96.1
ED	8.1	8.4	9.2	8.1	8.9	9.5	10	10.8	11.4	9.7	10.6	12.8	8.9	11.4
S/D	7.8	7.2	8.3	8.4	8.9	7.7	8.5	7.8	8	8.9	8.7	8	8.1	8.3
MD	7.6	7.8	7.9	7.5	8.6	8.4	9.1	9.4	9.2	8	9.2	11.8	8.9	10.3
Tamax	25.4	25.6	27.3	27.7	27.6	2.9	30.4	30.9	33.4	31.4	34.7	41.8	26.9	36.4

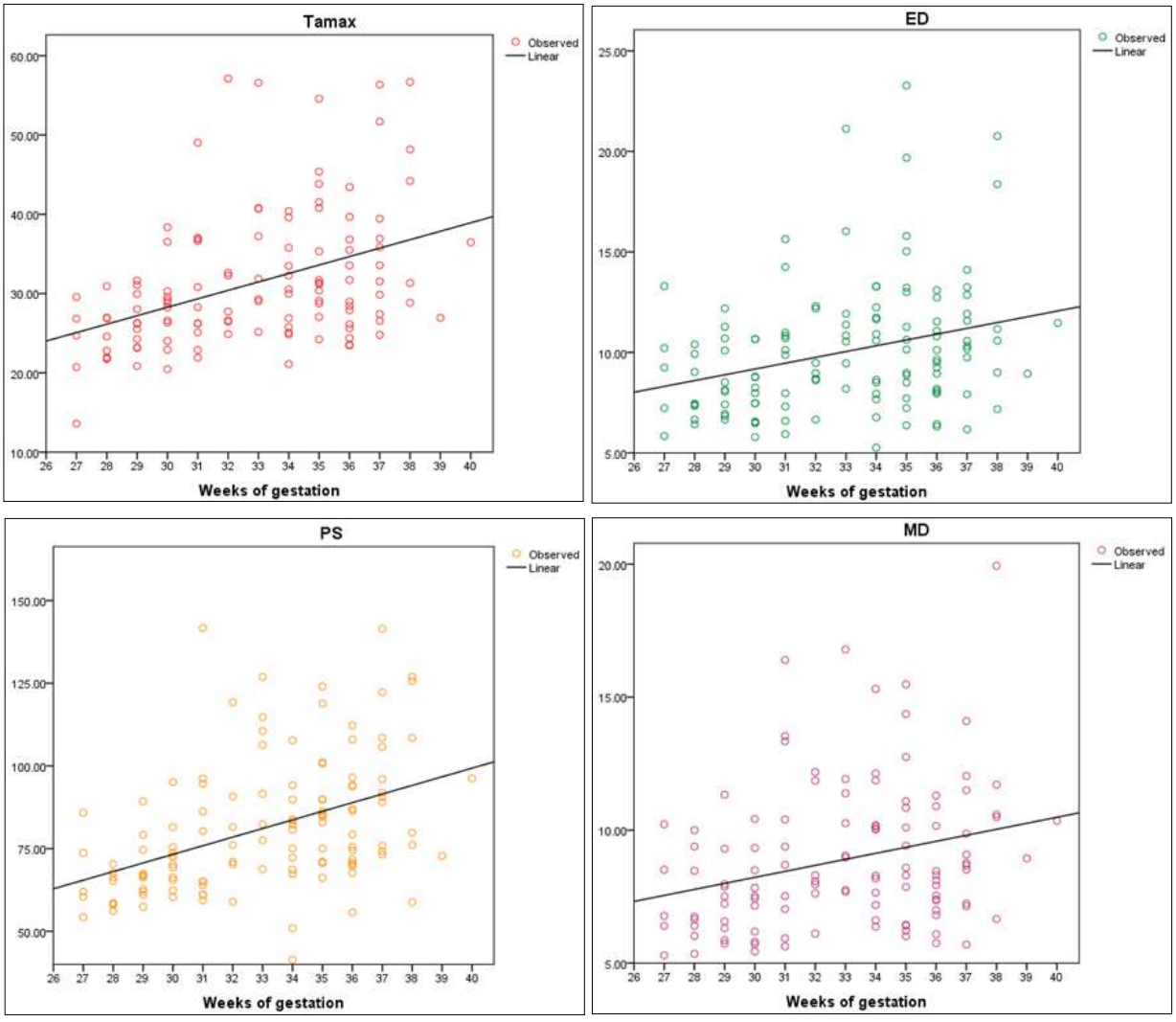

Fig 3: Scatter plot representing the linear regression analysis of the TAMAX, ED, PS, MD with gestational age.

5. Discussion

The study of the Doppler indices of the fetal AoI among study subjects with gestational age from 27 weeks to 40 weeks has revealed that there is an increasing trend and a significant linear correlation of the mean Doppler indices PSV, ED, MD and TAMAX with an increase in the gestational age of the fetus. However, there is no significant relationship of the PI, RI, and S/D Doppler indices with the increasing gestational age. This study is comparable to Vimpeli *et al.* [8], where it was observed that there was an increase in the AoI PSV with an increase in the gestational age of the fetuses. In a study by Rio *et al.* [7], it was reported that with the increase in the gestational age, a significant increase in PSV was observed in the fetuses. In another study by Thanasuan *et al.* [5], it was observed that there was a significant correlation of peak systolic velocity with gestational age of the fetus.

However in case of the RI values, it was observed that the mean value of the RI increased up to 21 weeks after which it was found to be constant up to 35 weeks. The RI further increased from the 36th week of gestation, The study reported by Rio *et al.* [7] also found that the RI value of the aortic isthmus Doppler increased with the increase in gestational age [7]. This study is contradictory to the study reported by Thanasuan *et al.* [5]. Where RI was constant during second half of pregnancy. The aortic isthmus PI was also found to increase with the increase in the gestational age with standard error of estimate 0.29. This observation is correlated with the study reported by Thanasuan *et al.* [5] where it was observed that the aortic isthmus PI was found to increase with the increase in the gestational age.

However, it was observed in this study that there was no significant association of the aortic isthmus PI, RI and S/D with the gestational age of the fetus.

This study therefore suggests that an increasing trend of PSV was similar to the study conducted by Del Rio *et al.* [7], Thanasuan [5] and Vimpeli [8]. An increasing trend of TAMAX was similar to the study reported by Del Rio *et al.* [7]. An increasing trend of EDV was contradictory to the study Del Rio *et al.* [7] and Thanasuan [5]. However, it was to be noted that there was no significant association of the aortic isthmus PI, RI and S/D with the gestational age of the fetus in this study.

6. Conclusion

This present study suggests the reference values of the gestational age specific fetal aortic isthmus doppler indices in third trimester.

Significant positive correlation of PSV, TAMAX, ED and MD with the increase in gestational age prognostically validates the use of these values as reference to detect early hemodynamic changes in third trimester.

7. Acknowledgement

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