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Uterine artery Doppler study in first and second trimester of pregnancy

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Abstract
In the non pregnant state and in early pregnancy, Doppler interrogation of the UtA typically demonstrates steep systolic slope early diastolic notch low end diastolic velocities. The waveforms remain essentially high resistance. UtA impedance can be affected by various factors such as maternal heart rate, antihypertensive use hormonal changes in the menstrual cycle, and chronic hyperandrogenism in the polycystic ovarian syndrome. Informed consent from each patient was obtained. Gestational age was calculated from the last menstrual period and confirmed by crown—rump length measurement. Abiding by the inclusion exclusion criteria patients were selected into the study. Clinical history including clinical risk factors to develop hypertension in pregnancy were noted, physical examination was done. The P1 doppler index showed a statistical significance for adverse outcomes like preeclampsia (p 0.002), low birth weight (LBW) (p = 0.04), and with 47 adverse outcomes (p = 0.02) from 11- 14 weeks. We had 17 cases of LBW, out of which only 4 (23.5%) were there not attributed to any complications, all the rest occurred as a part of prematurity caused by preeclampsia, fetal growth restriction (FGR) and oligoamnios.

Keywords: Uterine artery Doppler, oligoamnios, FGR

Introduction
Implantation and trophoblastic invasion of the placenta play a crucial role in its development as an organ for the transport of nutrients and oxygen to the fetus. Placental remodeling occurs in two stages. In normal pregnancy after implantation of the blastocyst there is rapid proliferation of the trophoblast and they extent into the endometrium and stroma from the anchoring villi (the stem villi that anchor the chorionic sac and placenta to the decidua basailis).As a result of which the myoelastic (15-20 micrometer) lining of the spiral artery is now lined with trophoblastic and hyalinematerial (300-500micromete). By the end of 1St trimester the trophoblastic invasion is up to myometriodecidual part, by the 14-16 week of gestation reaches up to the intramyometrial part and is complete by 18 weeks to 24 weeks [1]. The loss of smooth muscle and elastica from the spiral arteries converts the uteroplacental circulation into a low resistance, high capacitance system. Defective implantation may also play a causative role in preterm labour, placental abruption, and second-trimester miscarriages. Uterine artery flow increases very gradually from 77mL/mt at 5 weeks to 159 mL/mt at 10 weeks there after more rapidly at 665 mL/mt at 16 weeks, thereby producing a continuous flow during diastole. Vascular impedance reduces exponentially or linearly with increase in the peak systolic velocity. In women who develop preeclampsia there is failure of trophoblast invasion of the uterine vasculature with the result that the spiral arteries retain the muscle elastic coating and impedance to blood flow persists. A similar mechanism of failed trophoblast invasion and high resistance has been described in women who subsequently deliver infants with growth restriction [2].
In the non pregnant state and in early pregnancy, Doppler interrogation of the UtA typically demonstrates steep systolic slope early diastolic notch low end diastolic velocities. The waveforms remain essentially high resistance. UtA impedance can be affected by various factors such as maternal heart rate, antihypertensive use hormonal changes in the menstrual cycle, and chronic hyperandrogenism in the polycystic ovarian syndrome. Uterine artery impedance varies according to the phase of the ovarian cycle. Kujrak *et al*. 1993 observed 150 women that average RI during the proliferative phase was 0.88+1-0.04 (2SD). The RI starts to drop one day prior to ovulation reached a nadir of 0.84 +/-0.04(2SD) on day 18 and remained at this level for the rest of the cycle [3]. Resistance to blood flow within the uteroplacental circulation is transmitted upstream to the uterine arteries and can be measured as an increased PI or RI.

Uterine artery PI values are affected by ethnicity and are lower in women with a high body mass index (BMI). UtA PI and RI values decrease with increasing gestational age, a change that is thought to be secondary to a fall in impedance in uterine vessels following trophoblastic invasion. Pregnancy changes was described by Campbell *et al*. 1993 as pregnancy evolves, the diastolic phase augments, the gradient of the deceleration phase reduces, the notch disappears in the first trimester in 27 % of pregnancies, although its disappearance is sometimes not simultaneous in both uterine arteries. Flow changes in the uterine arteries are expressed as modification in Doppler indices [4]. At the onset of pregnancy, these indices show a few differences compared with their values in the absence of pregnancy. From the 12 weeks - 26th weeks of pregnancy there is progressive lowering in these indices. In addition, the indices are lower in the artery homolateral to the implantation. The difference between the arteries is more evident from the 8th week and they appear after the 24th week. The finding are clearly related to the histological changes in the spiral arteries caused by the trophoblastic invasion of these vessels. There is a gradual disappearance of notch. 20% of these patients retain notch by 20 weeks and >9% by 24 weeks. Hence, by 24-26 weeks, notch disappears and so does the difference between S/D ratio of the placental and non placental sites [5, 6].

Methodology

Study design: Prospective observational study

Study setup: Outpatient and inpatient departments of Obstetrics and Gynecology

The sample size: 247 patients

Inclusion criteria

- Gestational age between 10 weeks 6 days to 14 weeks.
- Any gravida with singleton pregnancy.
- Delivery at our institute.

Exclusion criteria

- Patients who are not compliant or available for follow up.
- Fetal congenital malformations.
- Multiple gestations.

Informed consent from each patient was obtained. Gestational age was calculated from the last menstrual period and confirmed by crown—rump length measurement. Abiding by the inclusion exclusion criteria patients were selected into the study. Clinical history including clinical risk factors to develop hypertension in pregnancy were noted, physical examination was done. IAA Doppler wave form analysis was done anywhere in between 10 weeks 6 days to 14 weeks of gestation along with nuchal translucency (NT) scan, again UtA Doppler was done at any time between 19 to 24 weeks as a part of fetal anomaly scan. Sample size was 247 pregnancies out of which we obtained 217 cases. From the 217 cases, 20 cases were lost to follow up and 4 resulted in first trimester abortions. So finally after tending to the inclusion criteria we had a total of 193 pregnant followed up throughout their pregnancy into the Women.

We used Philips HD 11 XE machine with the cy of 3.5-5 MHz. The Doppler filter was set 50-100 Hz. Analysis of for prediction of abnormal pregnancy outcomes was improved by the h Pulsed doppler and assessment of notching. With Color Doppler, identification of right and left uterine arteries at the level of the cervicocorporeal junction was done transabdominally.

Results

Table 1: Distribution of R1 values in 11-14 weeks (RI-1)

RI-1	Frequency	Percent
<5th percentile (0-0.04)	4	2.1%
≥5to < 95th percentile (0.5-0.7)	166	86.0%
≥ 95th percentile (>0.8)	23	11.9%
Total	193	100.0

Table 2: Distribution of P1 values in 11-14 weeks (PI-1)

PI-1	Frequency	Percent
<5th percentile (0-0.09)	36	18.7%
≥5to < 95th percentile (1.10-2.47)	148	76.7%
≥ 95th percentile (≥2.48)	9	4.7%
Total	193	100.0

Table 3: Distribution of notch in 11-14 weeks (Notch-1)

Notch-1	Frequency	%
Early diastolic notch	19	9.8%
No early diastolic notch	174	90.2%
Total	193	100.0

Table 4: Distribution of R1 in 19-24 weeks (RI-2)

RI-2	Frequency	%
≥5 percentile to < 95th percentile	143	74.1%
≥ 95th percentile	50	25.9%
Total	193	100.0

Table 5: Distribution of patients in 19-24 weeks (PI-2)

PI-2	Frequency	%
<5 percentile	I	.5%
≥5 percentile to < 95th percentile	164	85.0%
≥ 95th percentile	28	14.5%
Total	193	100.0

Table 6: Distribution of notch in 19-24 weeks (Notch-2)

Notch-2	Frequency	%
Early diastolic notch	13	6.7%
No early diastolic notch	180	93.3%
Total	193	100.0

Discussion

Hypertensive disorders and its complications in pregnancy are a major burden in the health sector in developing countries. We have utilized the non invasive techniques of doppler ultrasonography to study the root cause of hypertensive disorders being the abnormal 2nd wave of trophoblastic invasion of spiral arteries. We have also researched into the extent of trophoblastic invasion that happens in the late first trimester. More importantly the increased resistance in uterine artery doppler indices occur long before clinical appearance of the disease. After statistical analysis of the results obtained in our study we have observed significant difference between < 5th percentile, > 5th to <95th percentile and > 95th percentile in the mean uterine artery UtA Doppler indices like RI, PI and presence of an early diastolic notch, in those pregnancies where we have obtained an adverse outcome.

The P1 Doppler index showed a statistical significance for adverse outcomes like preeclampsia (p 0.002), low birth weight (LBW) (p = 0.04), and with 47 adverse outcomes (p = 0.02) from 11- 14 weeks. We had 17 cases of LBW, out of which only 4 (23.5%) were there not attributed to any complications, all the rest occurred as a part of prematurity caused by preeclampsia,

fetal growth restriction (FGR) and oligoamnios. When P1 values from 11-14 weeks was greater than or equal to 95th centile we could identify 66% of patients who had adverse outcomes. Similar to our study Gomez *et al*. could identify 54.7% of complicated pregnancies. They also showed that these Pregnancies had a significantly higher mean PI (2.04 vs. 1.75; p < 0.05, t-test) [7].

Early diastolic notch from 11-14 weeks has been observed to be clinically significant for gestational hypertension (GH) with a p value of 0.001 and for its complications like for preeclampsia p value was 0.002, for FGR p value was 0.009, for preterm delivery p value was 0.028 and for oligoaminos p value was 0.02 and with the 47 adverse outcomes p value was 0.006. In our study we had prevalence of 58.8% for bilateral early diastolic notch with adverse outcomes. Edward Haynes *et al*. has shown a bilateral ea similar prevalence of bilateral early diastolic notch (58%; < 0.05, Chi-square p test).

After the analysis of the doppler indices from 11-14 weeks we have come to a consensus that in 11-14 weeks, PI combined with early diastolic notch, is the most predictive Doppler index. Cnossen J *et al*. study also showed similar conclusions [8].

Coming to the analysis of doppler indices from 19-24 weeks the PI values were significant for GH with p value value of 0.001 and for Oligoaminos with p value of 0,0001. For adverse outcomes the p value was 0.005 and high risk pregnancies p value was 0.005. The P1 values from 19-24 weeks had sensitivity of 48.9%, specificity of 83.6.%, positive predictive value (PPV) of 14% and negative predictive value (Npv) of 80%. Our study was comparable with Mojgan Barati *et al*. who found that for predicting preeclampsia, the mean UtA PI had to have a specificity of 95.5%, found sensitivity of 79%, a NPV of 98.9%, and a P PV of 88.2% [9, 10].

RI from 19-24 weeks, was more sensitive than PI from 19-24 weeks. There was significance for GH with a value of 0.001, for preelampsia with a p value of 0.019, for FGR with a p value of 0.001, for oligoaminos with a p value of 0.0001, and for LBW with a P value of 0.012. Significance was obtained with the 47 adverse outcomes with a p value of 0.0001 and with high risk pregnancy showed a p value of 0.035.

Conclusion

- Early diastolic notch from 11-14 weeks has been observed to be clinically significant for gestational hypertension (GH)
- RI from 19-24 weeks, was more sensitive than PI from 19-24 weeks

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